Section A1 Applicant

Annex Point IIA1

1.1 Applicant

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1.2 Manufacturer of Active Substance (if different)

Name: Mitsui Chemicals Agro, Inc.
Address: Shiodome City Center
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Japan

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Telephone: +81-3-3573-9677
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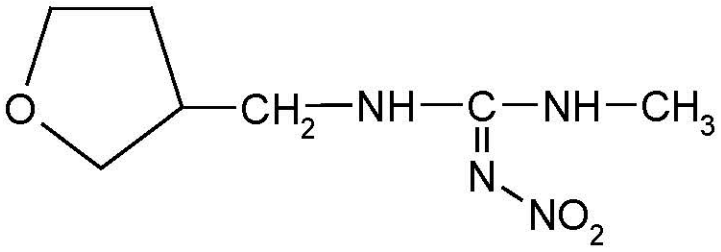
Location of manufacturing plant:
Mitsui Chemicals, Inc.
Omuta Works
30 Asamuta-Machi, Ohmuta Shi
Fukuoka 836-8610, Japan

1.3 Manufacturer of Product(s) (if different)

1) Product – Dinotefuran 2% bait

As above

Section A2 Identity of Active Substance

Subsection (Annex Point)			Official use only
2.1	**Common name (IIA2.1)**	Dinotefuran	
2.2	**Chemical name IUPAC (IIA2.2)**	(*RS*)-1-methyl-2-nitro-3-(tetrahydro-3-furylmethyl)guanidine	
2.3	**Manufacturer´s development code number(s) (IIA2.3)**	MTI-446	
2.4	**CAS No and EC numbers (IIA2.4)**	Non-entry field	
2.4.1	**CAS-No**	165252-70-0	
	Isomer 1	Not applicable (see A2.8.1)	
	Isomer 2	Not applicable (see A2.8.1)	
2.4.2	**EC-No**	Justification for non-submission → see Section A2.4.2_Justification	
2.4.3	**Other**	CIPAC number: 749	
2.5	**Molecular and structural formula, molecular mass (IIA2.5)**		
2.5.1	**Molecular formula**	$C_7H_{14}N_4O_3$	
2.5.2	**Structural formula**		
2.5.3	**Molecular mass**	202.2 g/mole	
2.6	**Method of manufacture of the active substance (IIA2.1)**	Confidential information → see Section A2.6_Confidential	
2.7	**Specification of the purity of the active substance, as appropriate (IIA2.7)**	≥ 991 g/kg Confidential information → see Section A2.7_Justification__Confidential	

Section A2 Identity of Active Substance

2.8	**Identity of impurities and additives, as appropriate (IIA2.8)**	Confidential information → see: Section A2.8-1_Confidential Section A2.8-2_Confidential Section A2.8-3_Confidential Section A2.8-4_Confidential
2.8.1	**Isomeric composition**	Confidential information → see: Section A2.8.1_Confidential
2.9	**The origin of the natural active substance or the precursor(s) of the active substance (IIA2.9)**	Justification for non-submission → see Section A2.9_Justification

Figure A2.8.1-1: NMR chart of dinotefuran at 0 °C

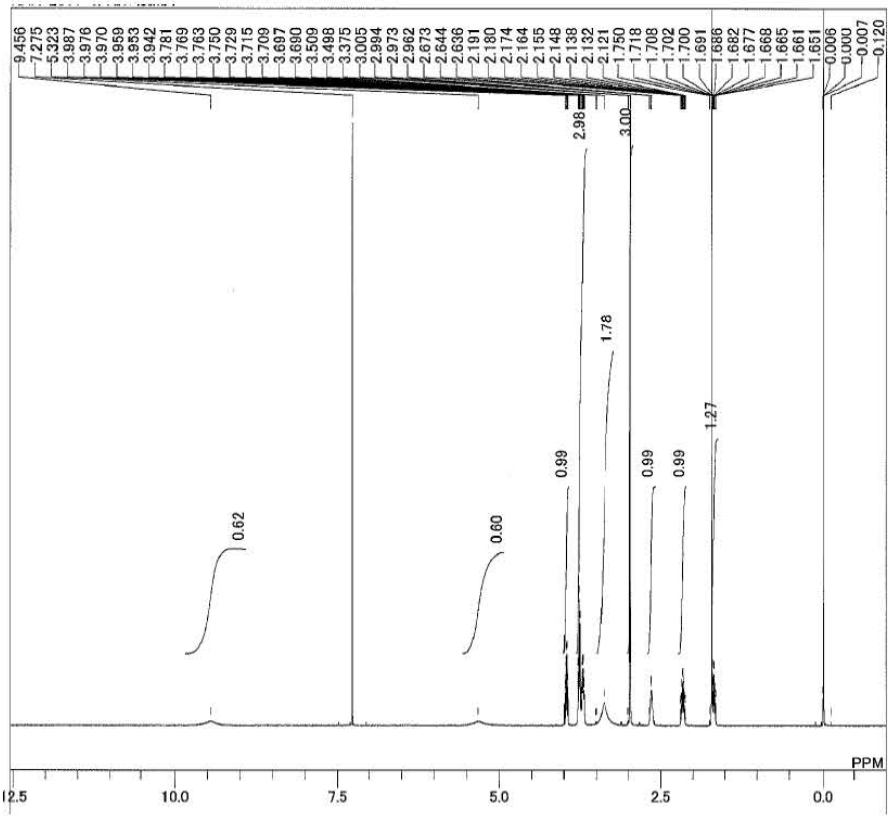
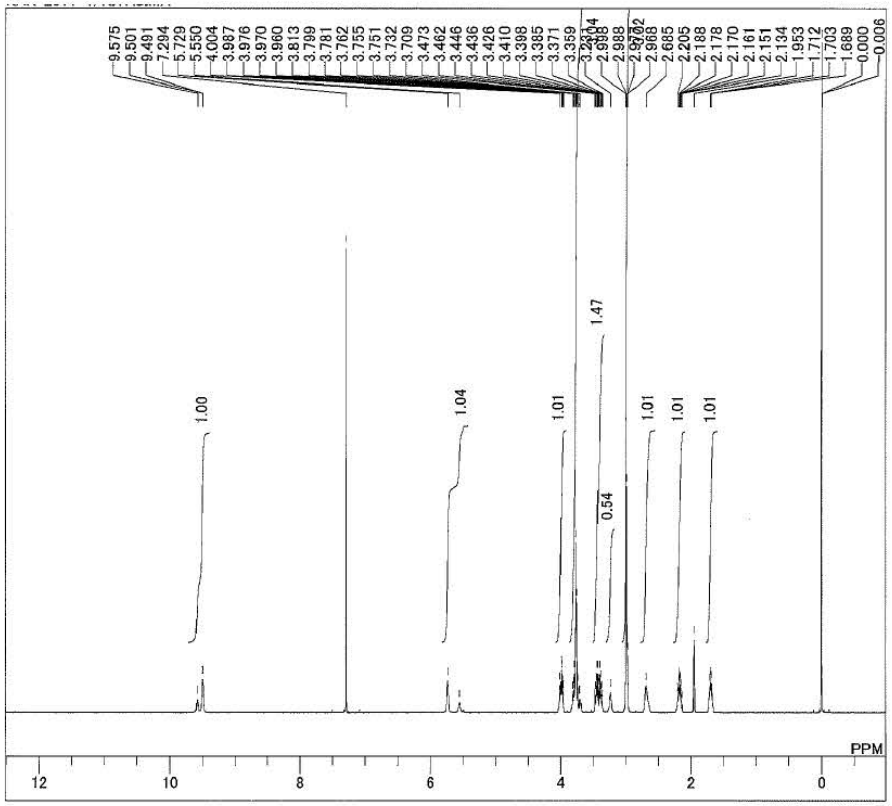


Figure A2.8.1-2: NMR chart of dinotefuran at -40 °C



Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	December 2012
Materials and methods	Sufficient acceptable information or waivers have been provided to support the information provided.
Conclusion	The information provided is acceptable.
Reliability	1
Acceptability	Acceptable
Remarks	
	COMMENTS FROM ...
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section A2.4.2 **Annex Point IIA, II. 2.4**	**EC Number**	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	**Official use only**
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [ ]** **Other justification [X]**	
Detailed justification:	Submission is for first entry to Annex I in the EU therefore dinotefuran has not been assigned an EC number.	
Undertaking of intended data submission [ ]	Not applicable	
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	December 2012	
Evaluation of applicant's justification	The applicant's justification is accepted. The information will become available once the active substance has been evaluated in the EU.	
Conclusion	The applicant's justification is accepted. No data for this annex point are required.	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date		
Evaluation of applicant's justification		
Conclusion		
Remarks		

Section A2.9 Annex Point IIA, II. 2.9	A2.9, The origin of the natural active substance or the precursor(s) of the active substance	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [ ]** **Other justification [X]**	
Detailed justification:	Dinotefuran is produced by chemical synthesis and the precursors of dinotefuran are not natural in origin.	
Undertaking of intended data submission [ ]	Not applicable	
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	December 2012	
Evaluation of applicant's justification	The justification is acceptable.	
Conclusion	The justification is acceptable.	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date		
Evaluation of applicant's justification		
Conclusion		
Remarks		

Section A3 Physical and Chemical Properties of Active Substance

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.1 Melting point, boiling point, relative density (IIA3.1)								X
3.1.1 Melting point	OECD 102 OPPTS 830.7200	99.9 %, Batch TKP-03-149	107.5 °C (SD = 0.12 °C)	none	Y	1	Malinski M.F., 2000a	
3.1.2 Boiling point	OECD 103 OPPTS 830.7220	99.9 %, Batch TKP-03-149	Does not boil	none	Y	1	Malinski M.F., 2000a	X
3.1.3 Decomposition temperature	OECD 103 OPPTS 830.7220	99.9 %, Batch TKP-03-149	Decomposition at 208°C	none	Y	1	Malinski M.F., 2000a	
3.1.4 Relative density	OECD 109 OPPTS 830.7300	99.9 %, Batch TKP-03-149	Density = 1.40 g/cm^3 at 20 °C	none	Y	1	Malinski M.F., 2000a	
3.2 Vapour pressure (IIA3.2)								
Vapour pressure 1	OECD 104 OPPTS 830.7950	99.9 %, Batch TKP-03-149	Vapour pressure: < 1.7 x 10^{-6} Pa at 30°C	none	Y	1	Malinski M.F., 2000a	X
Vapour pressure 2	OECD 104 EEC A.4	99.5% Batch OT-9536	Vapour pressure: 5.0 x 10^{-5} Pa at 25°C	none	Y	1	Sydney, P., 1996	
3.2.1 Henry´s Law Constant (Pt. I-A3.2)			Justification of non-submission				See Section → IIIA3.2.1 Justification	
3.3 Appearance (IIA3.3)								
3.3.1 Physical state	none	99.6% Batch EBI-5-101	Solid (crystalline)	none	N	1	Shimono S., 1999a	

Section A3 Physical and Chemical Properties of Active Substance

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.3.2 Colour	none	99.6% Batch EBI-5-101	White	none	N	1	Shimono S., 1999b	
3.3.3 Odour	none	99.6% Batch EBI-5-101	Odourless	none	N	1	Shimono S., 1999c	
3.4 Absorption spectra (IIA3.4)								
UV/VIS **IR** **NMR** **MS**	OECD 101 OPPTS 830.7050 For UV	99.9%, Batch TKP-03-149	Spectra determined and found to be consistent - UV-vis (at pH 2, 7 and 11) - FTIR - H^+-NMR - ^{13}C-NMR - MS (GC-MS and HPLC-MS $(M-H)^-$) UV: λ_{max} = 268 nm (water) and extinction coefficient (ε) = 12400 (/mol/cm)	none	Y	1	Malinski M.F., 2000a	X
3.5 Solubility in water (IIA3.5)								
Water solubility 1	OECD 105 OPPTS 830.7840	99.9%, Batch TKP-03-149	Solubility in unbuffered water: 39.83 g/L (pH 6.98) at 20°C	none	Y	1	Malinski, M.F., 2000a	X
Water solubility 2	OECD 105 EEC A.6	99.5% Batch OT-9536	Solubility in water: 54.3 ± 1.3 g/L at 20°C	none	Y	1	Sydney, P., 1996	
3.6 Dissociation constant								
Dissociation 1	OECD 112 OPPTS 830.7370	99.9%, Batch TKP-03-149	pK_a = 12.6 (pH range 11.6 – 12.8)	none	Y	1	Malinski, M.F., 2000a	

Section A3 Physical and Chemical Properties of Active Substance

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
Dissociation 2	OECD 112	99.5% Batch OT-9536	No dissociation (pH range 1.4 – 12.3)	none	Y	1	Sydney, P., 1996	X
3.7 Solubility in organic solvents, including the effect of temperature on solubility (IIIA3.1)	OECD 105 OPPTS 830.7840	99.9%, Batch TKP-03-149	At 20 ± 0.5 °C Hexane: 9.0 µg/L Heptane: 10.5 µg/L Xylene: 71.85 mg/L Toluene: 148.6 mg/L Dichloromethane: 60.86 g/L Acetone: 57.84 g/L Methanol: 57.18 g/L Ethanol: 19.37 g/L Ethyl acetate: 5.17 g/L	none	Y	1	Malinski, M.F., 2000a	
3.8 Stability in organic solvents used in b.p. and identity of relevant breakdown products (IIIA3.2)			Justification of non-submission				See Section → IIIA3.8_ Justification	

Section A3 Physical and Chemical Properties of Active Substance

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.9 Partition coefficient n-octanol/water (IIA3.6)								
- log P_{ow} 1	OECD 107 OPPTS 830.7550	99.9%, Batch TKP-03-149	log P_{ow} = - 0.549 at 25°C (i.e. P_{ow} = 0.283)	none	Y	1	Malinski M.F., 2000a	X
- log P_{ow} 2	OECD 107 EEC A.8 EPA/FIFRA 63-11	99.5% Batch OT-9536	At pH 5: log P_{ow} = - 0.915 (i.e. P_{ow} = 0.122) At pH 7: log P_{ow} = - 0.644 (i.e. P_{ow} = 0.227) At pH 9: log P_{ow} = - 0.760 (i.e. P_{ow} = 0.174)	none	Y	1	Sydney, P., 1996	
3.10 Thermal stability, identity of relevant breakdown products (IIA3.7)	OECD 113 OPPTS 830.6313 (DSC and TGA)	99.9%, Batch TKP-03-149	Dinotefuran is considered to be stable at room temperature because no decomposition or chemical transformation was found below 150°C and no weight loss (>5%) was observed below 150°C.	none	Y	1	Malinski M.F., 2000a	
3.11 Flammability, including auto-flammability and identity of combustion products (IIA3.8)								
Flammability	ECC A.10	99.2% Batch 2100910	Dinotefuran is not highly flammable.	none	Y	1	Tognucci, A., 2001a	X
Auto-flammability	EEC A.16	99.2% Batch 2100910	Dinotefuran is not auto-flammable.	none	Y	1	Tognucci, A., 2000	

Section A3 Physical and Chemical Properties of Active Substance

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.12 Flash-point (IIA3.9)			Justification of non-submission				See Section → IIIA3.12_ Justification	
3.13 Surface tension (IIA3.10)	OECD 115 EEC A.5	99.2% Batch 2100910	Dinotefuran is not surface active: Surface tension of dinotefuran in water (at a concentration of about 0.1%): 72 mN/m at 20.2°C ± 0.2°C.	none	Y	1	Tognucci, A., 2001c	X
3.14 Viscosity			Justification of non-submission				See Section → IIIA3.14_ Justification	
3.15 Explosive properties (IIA3.11)	EEC A.14	99.2% Batch 2100910	Dinotefuran is not explosive	none	Y	1	Angly, H., 2001	X
3.16 Oxidizing properties (IIA3.12)	EEC A.17	99.2% Batch 2100910	Dinotefuran has oxidizing properties: The burning rate of the fastest dinotefuran is significantly faster than the fastest barium nitrate/cellulose mixture.	none	Y	1	Tognucci A., 2001b	X
	Equivalent to O.1, Part III, 34.4.1 UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria	Described as "technical"	Not oxidising. The burning rate of dinotefuran/cellulose 1:1 and 4: 1 is slower than the potassium bromate/cellulose mixture.	none	N		Seki I., 2004	X
3.17 Reactivity towards	OPPTS 830.6317	98.9%	Stable for at least 12 months at	none	Y	1	Tognucci, A.,	

Section A3 Physical and Chemical Properties of Active Substance

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
container material (IIA3.13)	OPPTS 830.6320	Batch 5400810	25° C and 60% relative humidity. The containers (black plastic bags) showed no significant alteration.				2003	

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	December 2012
Materials and methods	**The following specific test methods were used:** 3.1.1 Melting point: OECD 102 (DSC) 3.1.2 Boiling point : OECD 103 (DSC) 3.1.4 Relative Density : OECD 109 (pycnometer) 3.5 Solubility in water: OECD 105 (flask) 3.8 Solubility in solvents: OECD 105 (flask) 3.9 Partition coefficient n-octanol/water OECD 107 (shake flask) 3.13 Surface tension EEC A5 (ring tensiometer) **3.1.2 Boiling point** No boiling point was determined as decomposition of the test material occurred before boiling. **3.2 Vapour pressure** For study 1 the value was estimated by calculation on the basis of an estimated LOQ and was not determined at the correct temperature. For study 2 the test was conducted at 25°C. **3.4 Absorption spectra (IIA3.4)** UV/Vis tested at pH 2, 7 and 11. λ_{max} = 268 nm. No absorption maxima at or > 290 nm Extinction coefficient (ε) at λ_{max} : pH 2 = 12,450 $M^{-1}cm^{-1}$ pH 7= 12,400 $M^{-1}cm^{-1}$ pH 11 = 11,200 $M^{-1}cm^{-1}$ **3.5 Solubility in water** For study 1 the effects of pH and temperature were not considered. For study 2 the effects of both pH and temperature were considered with the following results: Purified water, 10°C 39.0 ±2.1 g/l Purified water, 20°C 54.3 ±1.3 g/l Purified water, 30°C 89.7 ±2.5 g/l pH 5.0 buffer solution, 20°C 52.3 ±1.0 g/l pH 7.0 buffer solution, 20°C 54.5 ±0.8 g/l pH 9.0 buffer solution, 20°C 51.2 ±1.8 g/l It can be concluded that dinotefuran is readily soluble in water. pH does not have a significant effect on the water solubility. The solubility increases with increasing temperature. **3.6 Dissociation constant** Study 2 concluded that dinotefuran did not dissociate over the relevant environmental pH range (1.4-12.3). For study 1 the pKa was estimated to be > 12.

3.7 Solubility in organic solvents

The effect of temperature was not studied.

3.9 Partition coefficient n-octanol/water

For study 2 the test was conducted at 25°C.

3.11 Flammability, including auto-flammability and identity of combustion products

For flammability the test item could not be ignited during the preliminary tests therefore dinotefuran is not classified as "highly flammable".

3.13 Surface tension

The test was conducted at the maximum concentration of 0.1% i.e. 1 g/l. This is acceptable based on the water solubility of dinotefuran.

3.15 Explosive properties

Dinotefuran did not demonstrate explosive properties under the effect of flame or when subjected to shock or friction in line with the test method.

3.16 Oxidizing properties

Further details of the Tognucci A., 2011b test results are given below:

Burning rate of barium nitrate/cellulose control mixtures:

Ratio of barium nitrate/ cellulose (% w/w)	Burning rate (sec/mm)
70/30	0.73
60/40	0.61
50/50	0.71

Burning rate of dinotefuran/cellulose mixtures:

Ratio of dinotefuran/ cellulose (% w/w)	Burning rate (sec/mm)	Reaction
10/90	1.06	Burning with constant flame
20/80	0.88	Burning with constant flame
30/70	0.95	Burning with constant flame
40/60	0.80	Burning with constant flame
50/50	0.50	Burning with constant flame
60/40	0.49	Burning with constant flame
70/30	0.43	Burning with constant flame
80/20	0.92	Burning with constant flame

	90/10 | - | No burning, test item melted. Further details of the Seki, I., 2004 test results are given below: Burning rate of potassium bromate/cellulose control mixtures: **Ratio of potassium bromate/ cellulose (% w/w)** | **Average Burning rate** 2:3 | 1 min 7 sec 3:7 | 3 min 13 sec Burning rate of dinotefuran/cellulose mixtures: **Ratio of dinotefuran/ cellulose** | **Average Burning rate** 1:1 | 10 min 30 sec 4:1 | 9 min 52 sec
Conclusion	Dinotefuran is a white odourless crystalline solid, with a melting point of *ca* 108°C; a boiling point could not be determined since the substance decomposed at 208°C. With a vapour pressure of 5 x 10^{-5} Pa at 25°C, it can be considered as not volatile. Dinotefuran is not surface active but is readily soluble in water; the solubility was not significantly affected by pH. The log octanol/water partition co-efficient was -0.64 at pH7 therefore the active substance does not have the potential to bio accumulate. Dinotefuran is not classified with regard to flammability and explosive properties; however it demonstrates oxidising properties on the basis of test method EC A17. A non-GLP test conducted according to the UN GHS test indicates that dinotefuran does not demonstrate oxidising properties
Reliability	1
Acceptability	The studies are considered acceptable
Remarks	The effects of temperature on the solubility in organic solvents and partition coefficient were not studied.
	COMMENTS FROM...
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section A3.12 **Annex Point IIA, III. 3.9.**	**Flash-point**	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	**Technically not feasible [X]** **Scientifically unjustified [ ]**	
Limited exposure [ ]	**Other justification [ ]**	
Detailed justification:	Not required as dinotefuran is a solid.	
Undertaking of intended data submission [ ]	Not applicable	
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	December 2012	
Evaluation of applicant's justification	The applicant's justification is accepted.	
Conclusion	The applicant's justification is accepted. No further data are required	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date		
Evaluation of applicant's justification		
Conclusion		
Remarks		

Section A3.14 Annex Point IIA, III. 3.9.	Viscosity	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] Limited exposure [ ]	Technically not feasible [X] Scientifically unjustified [ ] Other justification [ ]	
Detailed justification:	Not required as dinotefuran is a solid.	
Undertaking of intended data submission [ ]	Not applicable	
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	December 2012	
Evaluation of applicant's justification	The applicant's justification is acceptable.	
Conclusion	The applicant's justification is acceptable. No further data are required	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date		
Evaluation of applicant's justification		
Conclusion		
Remarks		

Section A3.2.1 Annex Point IIA, III. 3.2.1	Henry's Law Constant	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [X]** **Scientifically unjustified [ ]** **Other justification [ ]**	
Detailed justification:	The Henry's Law Constant for dinotefuran at 20°C was not calculated because of the lack of actual vapour pressure results. - The solubility of dinotefuran in water at 20°C was determined to be 39.83 g/L. - The experiment for the vapour pressure determination of the dinotefuran was performed at three different temperatures: 30°C, 40°C and 50°C. At the end of the experiment, no dinotefuran was detected, so, no experimental vapour pressure could be determined at 30°C, 40°C and 50°C. Estimated "less than" vapour pressure were calculated for the three experimental temperatures (30, 40 and 50°C) and the values are reported: **Temperature** (°C) / **Vapour Pressure** (Pa) 30 / $< 1.7 \times 10^{-6}$ 40 / $< 1.8 \times 10^{-6}$ 50 / $< 2.1 \times 10^{-6}$ Furthermore, the vapour pressure of dinotefuran at 20°C, extrapolated by linear regression of experimental results was not possible to be performed.	
Undertaking of intended data submission [ ]	Not applicable	
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	December 2012	
Evaluation of applicant's justification	The applicant's justification is accepted. Data were also available for the vapour pressure at 25°C; however extrapolation by linear regression was not possible due to the lack of experimentally determined data points at other temperatures.	
Conclusion	The applicant's justification is accepted. No further data are required.	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date		
Evaluation of applicant's justification		
Conclusion		
Remarks		

Section A3.8 **Annex Point IIA, III. 3.8.**	**Stability in the organic solvents used in biocidal products and the identity of relevant breakdown products**	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	**Official use only**
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [X]** **Other justification [ ]**	
Detailed justification:	Not required as the active substance as manufactured does not include an organic solvent.	
Undertaking of intended data submission [ ]	Not applicable	
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	December 2012	
Evaluation of applicant's justification	The applicant's justification is accepted.	
Conclusion	The applicant's justification is accepted. No further data are required	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date		
Evaluation of applicant's justification		
Conclusion		
Remarks		

Section A4_1-1
Annex Point IIA4.1 & IIIA-IV.1

Analytical Methods for Detection and Identification

Determination of pure active substance and, where appropriate, for relevant degradation products, isomers and impurities of active substances and their additives (e.g. stabilisers)

Official use only

1 REFERENCE

1.1	**Reference**	Kumanomido M., 2005, Analysis of active ingredient and impurities in dinotefuran technical, Japan Analytical Chemistry Consultants Co., Ltd., unpublished report no. GT0504, November 16, 2005.
1.2	**Data protection**	Yes
1.2.1	Data owner	Mitsui Chemicals Agro, Inc.
1.2.2	Criteria for data protection	Data on new a.s. for first entry to Annex I

2 GUIDELINE AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes JMAFF 12 Nousan No. 8147 JMAFF 13 Seisan No. 3987 EPA Guideline OPPTS 830.1700
2.2	**GLP**	Yes
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Preliminary treatment**	
3.1.1	Enrichment	Preparation of the sample: Technical grade dinotefuran was dissolved in acetonitrile:10 mmol/L potassium dihydrogenphosphate aqueous solution (7:93 v/v) with the internal standard (sulphanilamide). Five production batches of dinotefuran technical were assayed.
3.1.2	Cleanup	Not required
3.2	**Detection**	
3.2.1	Separation method	HPLC: Hewlett-Packard HP1100 series Column: L-column ODS, pore size 5 µm, 4.6 mm x 250 mm Temperature: 40 °C Mobile phase: Acetonitril : 10 mmol/L potassium dihydrogenphosphate aqueous solution (7 : 93 v/v) Flow rate: 1.0 mL/min Detection: 270 nm Injection volume: 5 µL Retention time: Dinotefuran: ca. 11.6 min Sulfanilamide (internal standard): ca. 5.4 min
3.2.2	Detector	Photodiode array detector G1315A
3.2.3	Standard(s)	Internal standard: 2500 mg/L of sulphanilamide.
3.2.4	Interfering substance(s)	None

Section A4_1-1 **Analytical Methods for Detection and Identification**

Annex Point IIA4.1 & IIIA-IV.1 **Determination of pure active substance and, where appropriate, for relevant degradation products, isomers and impurities of active substances and their additives (e.g. stabilisers)**

3.3	**Linearity**		
3.3.1	Calibration range	Calibration curve of dinotefuran was prepared in the range of concentrations from 24 to 480 mg/L. The linearity of response was confirmed by the correlation coefficient.	X
3.3.2	Number of measurements	Analysis of dinotefuran was performed in triplicate. Each analysis was performed by two injections. Mean values of peak area to ratio were used to determine the content of the active ingredient (%).	
3.3.3	Linearity	Correlation coefficient of dinotefuran was over 0.999.	X
3.4	**Specifity: interfering substances**	No interference was found.	
3.5	**Recovery rates at different levels**	440 mg/L dinotefuran solution was prepared and analysed. Analysis was performed in triplicate. Recoveries are shown in the following table:	X

Dinotefuran

	Sample number	% Recovery		% RSD
		Found	Mean	
Dinotefuran	1	100	100	0
	2	100		
	3	100		

3.5.1	Relative standard deviation	See 3.5	
3.6	**Limit of quantification**	The limit of quantification (LOQ) for dinotefuran is determined to be 6%.	
3.7	**Precision**		
3.7.1	Repeatability	See 3.5 Recovery rates at different levels	X
3.7.2	Independent laboratory validation	Not performed	

Section A4_1-1	**Analytical Methods for Detection and Identification**
Annex Point IIA4.1 & IIIA-IV.1	**Determination of pure active substance and, where appropriate, for relevant degradation products, isomers and impurities of active substances and their additives (e.g. stabilisers)**

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1	**Materials and methods**	Guidelines: JMAFF 12 Nousan No. 8147, JMAFF 13 Seisan No. 3987, EPA Guideline OPPTS 830.1700 No relevant deviations from test guidelines. Methods: The active ingredient content in dinotefuran technical grade was analysed and quantified employing HPLC. The analysis was performed in triplicate and the mean values of peak area ratio of dinotefuran to the internal standard (sulphanilamide) were used to determine the content of the active ingredient.
4.2	**Conclusion**	The method validation results confirm that this method was valid for determining the content of dinotefuran in dinotefuran technical grade.
4.2.1	Reliability	1
4.2.2	Deficiencies	No

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	December 2012
Materials and methods	Linearity and specificity have been sufficiently addressed. For linearity 5 different concentrations were analysed. Accuracy data are not required. Precision (repeatability) in terms of SANCO 3030/99 has not been fully addressed as only 3 determinations were made instead of the expected 5, however the method is considered acceptable.
Conclusion	The method is considered acceptable for determining dinotefuran content in the technical material.
Reliability	1
Acceptability	Acceptable
Remarks	
	COMMENTS FROM...
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section A4_1-2
Annex Point IIA4.1 & IIIA-IV.1

Analytical Methods for Detection and Identification

Analytical method for the determination of pure active substance and, where appropriate, for relevant degradation products, isomers and impurities of active substances and their additives (e.g. stabilisers)

Official use only

1 REFERENCE

1.1	**Reference**	Kumanomido, M., 2005, Analysis of active ingredient and impurities in dinotefuran technical, Japan Analytical Chemistry Consultants Co., Ltd., unpublished report no. GT0504, November 16, 2005.
1.2	**Data protection**	Yes
1.2.1	Data owner	Mitsui Chemicals Agro, Inc.
1.2.2	Criteria for data protection	Data on new a.s. for first entry to Annex I

2 GUIDELINE AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes JMAFF 12 Nousan No. 8147 JMAFF 13 Seisan No. 3987 EPA Guideline OPPTS 830.1700
2.2	**GLP**	Yes
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Preliminary treatment**	
3.1.1	Enrichment	Preparation of the sample: Technical grade dinotefuran was dissolved in acetonitrile : purified water (40:60 v/v)
3.1.2	Cleanup	Not required.
3.2	**Detection**	
3.2.1	Separation method	HPLC: Hewlett-Packard HP1100 series Column: Thermo Hypersil GOLD, pore size 5 µm, 4.6 mm x 250 mm Temperature: 45 °C Mobile phase: (A) Purified water (B) Acetonitrile/purified water (20:80 v/v)

Gradient conditions:

0 min (B:15%) → 35 min (B:95%) → 50 min (B:95%)

	Time (min)	A (%)	B (%)
1	0	85	15
2	35	5	95
3	50	5	95

Section A4_1-2 **Annex Point IIA4.1** **& IIIA-IV.1**	**Analytical Methods for Detection and Identification** **Analytical method for the determination of pure active substance and, where appropriate, for relevant degradation products, isomers and impurities of active substances and their additives (e.g. stabilisers)**

		Flow rate: 0.9 mL/min Detection: 254 nm Injection volume: 2 µL Retention time: Impurity profile is confidential; please see the Confidential Annex.	
3.2.2	Detector	Photodiode array detector G1315A	
3.2.3	Standard(s)	Analytical standard (100 mg/L) of each impurity (impurity profile is confidential; please see the Confidential Annex).	
3.2.4	Interfering substance(s)	None	
3.3	**Linearity**		
3.3.1	Calibration range	Calibration curves of each impurity were prepared in the range of concentrations from 2 to 20 mg/L. The linearity of response was confirmed by the correlation coefficient.	X
3.3.2	Number of measurements	Analysis of impurities was performed in duplicate. Each analysis was performed by two injections. Mean values of peak area were used to determine the content of each impurity (%).	
3.3.3	Linearity	Correlation coefficients of each impurity were over 0.999.	
3.4	**Specificity: interfering substances**	No interference was found.	
3.5	**Recovery rates at different levels**	16 mg/L mixed standard solution of the impurities were prepared and analysed to calculate the recovery rate. Analysis was performed in triplicate. Recoveries are shown in the following tables: Impurities: Impurity profile is confidential; please see the Confidential Annex.	X
3.5.1	Relative standard deviation	See 3.5	
3.6	**Limit of quantification**	The limit of quantification (LOQ) for the impurities is determined to be 0.01%.	
3.7	**Precision**		
3.7.1	Repeatability	See 3.5 Recovery rates at different levels	
3.7.2	Independent laboratory validation	Not performed	

Section A4_1-2	**Analytical Methods for Detection and Identification**
Annex Point IIA4.1 & IIIA-IV.1	**Analytical method for the determination of pure active substance and, where appropriate, for relevant degradation products, isomers and impurities of active substances and their additives (e.g. stabilisers)**

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1	**Materials and methods**	Guidelines: JMAFF 12 Nousan No. 8147, JMAFF 13 Seisan No. 3987, EPA Guideline OPPTS 830.1700 No relevant deviations from test guidelines. Methods: The impurities in technical grade dinotefuran are analysed and quantified employing HPLC. The analysis was performed in duplicate and the mean values of peak area were used to determine the content of the each impurity.
4.2	**Conclusion**	The method validation results confirm that this method was valid for determining the contents of the impurities (impurity profile is confidential; please see the Confidential Annex) in dinotefuran technical.
4.2.1	Reliability	1
4.2.2	Deficiencies	No

Section A4_1-2	**Analytical Methods for Detection and Identification**
Annex Point IIA4.1 & IIIA-IV.1	**Analytical method for the determination of pure active substance and, where appropriate, for relevant degradation products, isomers and impurities of active substances and their additives (e.g. stabilisers)**

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	December 2012
Materials and methods	Linearity and specificity have been sufficiently addressed. For linearity 4 standard concentrations were analysed. For accuracy standard addition was not used. Precision (repeatability) in terms of SANCO 3030/99 has not been fully addressed as only 3 determinations were made instead of the expected 5, however the method is considered acceptable.
Conclusion	The method is considered acceptable for determining impurities in the technical material.
Reliability	1
Acceptability	Acceptable
Remarks	
	COMMENTS FROM...
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section A4 2(a)
Annex Point IIA4.2 & IIIA-IV.1

Analytical Methods for Detection and Identification
(a) Soil

Official use only

1 REFERENCE

1.1	**Reference**	Wais A., 2001, Validation of the residue analytical method for MTI-446 in soil, RCC Ltd., unpublished report no. 739923, May 2, 2001.
1.2	**Data protection**	Yes
1.2.1	Data owner	Mitsui Chemicals Agro, Inc.
1.2.2	Criteria for data protection	Data on new a.s. for first entry to Annex I

2 GUIDELINE AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes Residue Analytical Method, Guideline 96/46/EC, July 16, 1996 European Commission, Guidance Document on Residue Analytical Methods, SANCO/825/00 rev. 6, June 20, 2000 European Commission, Residues: Guidance for Generation and Reporting Methods of Analysis in Support of Pre-Registration Data Requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414, SANCO/3029/99 rev.4, July 11, 2000 – Working Document.
2.2	**GLP**	Yes
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Preliminary treatment**	
3.1.1	Enrichment	<u>Extraction</u> Dinotefuran was extracted according to the following procedure: - Wet soil was weighed into screw-top glass bottles. - Acetonitrile/water mixture (8:2, v/v) and hydrochloric acid (32%) were added, and the suspension was stored over night at room temperature. - The suspension was then shaken for approximately 30 minutes and then it was filtered on Celite and the filtercake was rinsed with acetonitrile. - The filtercake was transferred into the extractions bottle and re-extracted with acetonitrile. Next, the suspension was filtered and the filter was rinsed with acetonitrile. - The combined filtrates were transferred into a round bottom flask. The acetonitrile/water was evaporated to aqueous remainder at reduced pressure at about 40 °C.

Section A4 2(a)
Annex Point IIA4.2 & IIIA-IV.1

Analytical Methods for Detection and Identification (a) Soil

3.1.2 Cleanup

Hexan-water Partition

- Aqueous residue remaining from extraction was then transferred to a cylinder and made-up to volume using distilled water.
- Part of this solution was transferred to a separatory funnel. Sodium chloride and hexane were added and the sample was shaken using a laboratory shaker. After separation of the phases, the upper hexane phase was discarded.
- The hexan-water partition was repeated with additional hexane. After phase separation, the upper hexane phase was also discarded. Remaining hexane was removed by rotary evaporation at low pressure.
- The residue was transferred to a flask and sodium chloride was added and dissolved. Distilled water was then added and shaken. The sample was stored for three days at room temperature.

1st Liquid-liquid Partition (Extrelut 20)

- The solution of sample material was transferred into an Extrelut 20 column.
- Elution was performed using dichloromethane.
- The solution was evaporated to dryness under low pressure by rotary evaporation.
- The residue was re-dissolved in methanol using an ultra sonic bath.

Clean up (Bond Elut PSA)

- The sample solution was transferred onto the cartridge and was allowed to pass through.
- The collected solution was evaporated to dryness under reduced pressure using rotary evaporation.
- The residue was re-dissolved in methanol using an ultra sonic bath.
- Distilled water was added to the methanol solution.

Clean up (ENVI Carb SPE)

- The sample solution was transferred onto the cartridge and was allowed to pass through.
- The cartridge was rinsed with distilled water followed by methanol/water mixture (1:9, v/v).
- Elution was performed with acetonitrile/water mixture (2:8, v/v).
- The collected solution was evaporated to dryness under reduced pressure using rotary evaporation.

2st Liquid-liquid Partition (Extrelut 20)

- The aqueous reminder of sample material was transferred into an Extrelut 20 column.
- Elution was performed using dichloromethane.
- The solution was evaporated to dryness by rotary evaporation at

Section A4 2(a) **Analytical Methods for Detection and Identification**

Annex Point IIA4.2 & IIIA-IV.1 **(a) Soil**

low pressure.

- The residue was re-dissolved in water using an ultra sonic bath and then was filtered.

3.2 Detection

3.2.1 Separation method

HPLC/UV:

Auto sampler:	Varian 9095
Pump:	Varian 9012
Column:	Waters RP8 Symmetry shield, 5 µm; 250 mm x 4.6 mm
Column oven:	Jones
Temperature:	40 °C
Solvent systems:	A: water/methanol (90:10 v/v) B: water/methanol (10:90 v/v)

Time (min)	A	B
0	100	0
18.0	100	0
19.1	0	100
29.0	0	100
30.0	100	0
40.0	100	0

Injection volume:	100 µL
Flow:	1.0 mL/min
Retention time:	11.3 – 11.5 min

HPLC/DAD:

Auto sampler:	Merck-Hitachi L-7200
Pump:	Merck-Hitachi L-7100
Column:	Hypersil BDS C18, 3 µm; 100 mm x 4.6 mm
Temperature:	Ambient temperature
Solvent systems:	H_3PO_4 (0.05%) / acetonitrile (97:3)
Flow	1.0 mL/min
Injection volume:	100 µL
Retention time	8.6 – 9.4 min

3.2.2 Detector

UV Detector (Varian 9050 UVD): wavelenght at 270 nm.

DAD Detector (Merck-Hitachi L-7450): DAD at 200 – 400 nm, single UV at 254 nm

3.2.3 Standard(s)

Analytical standard of dinotefuran: external standard.

3.2.4 Interfering substance(s)

None

3.3 Linearity

3.3.1 Calibration range

Calibration was performed using standards in the range of 0.02 - 2.0 µg/mL.

3.3.2 Number of measurements

7 measurements

3.3.3 Linearity

Correlation coefficient ranged from 0.997 to 1.000

Section A4 2(a)
Annex Point IIA4.2 & IIIA-IV.1

Analytical Methods for Detection and Identification (a) Soil

3.4 Specifity: interfering substances

There was no interference with other substances observed at the retention times of dinotefuran above 30% of the limit of quantification as well as above the limit of detection.

3.5 Recovery rates at different levels

The results for recovery of dinotefuran in soil are presented in the following table:

Fortification Level (mg/kg)	Number of analysis	Recovery (%) Mean	Range	RSD (%)
0.01	5	99.2	85.1 – 109.3	10.0
0.10	5	91.1	88.7 – 96.0	3.2
0.50	5	77.0	71.8 – 85.3	6.6

3.5.1 Relative standard deviation

See 3.5 above.

3.6 Limit of quantification

The limit of quantification was found to be 0.01 mg/kg deriving from the lowest fortification level.

3.7 Precision

3.7.1 Repeatability

See 3.5 Recovery rates at different levels.

3.7.2 Independent laboratory validation

The independent laboratory validation (MacGregor J.A., Van Hoven R.L., and Nixon, W.B., 2002; Report no. 236C-106) was performed and the results are reported in the table below:

Fortification Level (mg/kg)	Number of analysis	Recovery (%) Mean	Range	RSD (%)
0.01	3	103	101 – 107	3.11
0.10	3	94.3	93.2 – 94.9	1.01
0.50	3	96.4	94.5 – 99.6	2.87

Section A4 2(a)
Annex Point IIA4.2 & IIIA-IV.1

Analytical Methods for Detection and Identification
(a) Soil

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1	**Materials and methods**	Guidelines: Residue Analytical Method, Guideline 96/46/EC, July 16, 1996 European Commission, Guidance Document on Residue Analytical Methods, SANCO/825/00 rev. 6, June 20, 2000 European Commission, Residues: Guidance for Generation and Reporting Methods of Analysis in Support of Pre-Registration Data Requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414, SANCO/3029/99 rev.4, July 11, 2000 – Working Document. No relevant deviations from test guidelines. Methods: Soil samples were treated with acetonitrile/water mixture (8:2, v/v) and hydrochloric acid (32%), this suspension was shaked and then filtered on Celite. The filtercake was extracted with acetonitrile, and the solvent evaporated by reduced pressure. To the aqueous residue was applied a hexan-water partition. The sample solution was then eluted with dichloromethane on an Extrelut 20 column (1st liquid-liquid partition). The dichloromethane was evaporated under reduced pressure and the dry residue dissolved in methanol. This methanol solution was further cleaned by passing first through a Bond Elut PSA cartridge and then through an ENVI Carb cartridge. The aqueous reminder was eluted with dichloromethane on an Extrelut 20 column (2st liquid-liquid partition). The concentrations of dinotefuran were determined by HPLC-UV.
4.2	**Conclusion**	The analytical method was valid for the determination of dinotefuran in soil.
4.2.1	Reliability	1
4.2.2	Deficiencies	No
4.2.3		

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	January 2013
Materials and methods	Linearity was determined at 7 concentrations over the range.02-2.0 µg/ml (0.005 – 0.5 mg/kg soil). The type of soil used for both the primary validation study and the ILV was sandy loam. The LOQ of 0.01 mg/kg is considered sufficient. The method is acceptably validated according to EU guidance in terms of linearity, accuracy, repeatability and reproducibility and is considered acceptable as a monitoring method; however a confirmatory technique is not available. A method of analysis for the determination of dinotefuran in water has also been provided. This method uses HPLC-MS/MS and so could be used as a confirmatory technique if needed.
Conclusion	The method is considered acceptable as a monitoring method.

Section A4 2(a)
Annex Point IIA4.2 & IIIA-IV.1

Analytical Methods for Detection and Identification
(a) Soil

Reliability	1
Acceptability	The studies are acceptable.
Remarks	HPLC-UV/DAD is not considered highly specific therefore a confirmatory method must be fully validated. This can be provided before product authorisation.

	COMMENTS FROM ...
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section A4 2(b) Annex Point IIA4.2 & IIIA-IV.1	Analytical Methods for Detection and Identification (b) Air

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	**Technically not feasible [ ]** **Scientifically unjustified [X]**	
Limited exposure [ ]	**Other justification [ ]**	
Detailed justification:	This needs to be submitted e.g. if the substance is volatile (i.e. if the vapour pressure ≥0.01 Pa) or sprayed, or occurrence in air is otherwise probable. The vapour pressure of dinotefuran is < 1.7 x 10^{-6} Pa at 30°C and its intended use in the reference product is as gel bait.	
Undertaking of intended data submission [ ]	Not applicable	

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	January 2013
Evaluation of applicant's justification	The vapour pressure was estimated to be < 1.7 x 10^{-6} Pa at 30°C and determined to be 5.0 x 10^{-5} Pa at 25°C (See section A3 point 3.2). Methods of analysis for air are not required if the substance is not volatile. On the basis of the vapour pressure data provided a method of analysis for air is not required. Methods are also not required if no relevant exposure according to application technique is likely to occur. In the case of dinotefuran application by spraying is not envisaged therefore a method of analysis for air is not required.
Conclusion	The applicant's justification is acceptable.
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	
Evaluation of applicant's justification	
Conclusion	
Remarks	

Section A4 2(c)
Annex Point IIA4.2 & IIIA-IV.1

Analytical Methods for Detection and Identification (c) Water

Official use only

1 REFERENCE

1.1	**Reference**	Schreitmüller J., 2002a, Development and Validation of a Residue Analytical Method for MTI-446 in Drinking, Ground and Surface Water, RCC Ltd., unpublished report no. 841987, April 30, 2002. Schreitmüller J., 2002b, First amendment to report: Development and Validation of a Residue Analytical Method for MTI-446 in Drinking, Ground and Surface Water, RCC Ltd., unpublished report no. 841987, May 21, 2002.
1.2	**Data protection**	Yes
1.2.1	Data owner	Mitsui Chemicals Agro, Inc.
1.2.2	Criteria for data protection	Data on new a.s. for first entry to Annex I

2 GUIDELINE AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes Residue Analytical Method, Guideline 96/46/EC, July 16, 1996 European Commission, Guidance Document on Residue Analytical Methods, SANCO/825/00 rev. 6, June 20, 2000 European Commission, Residues: Guidance for Generation and Reporting Methods of Analysis in Support of Pre-Registration Data Requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414, SANCO/3029/99 rev.4, July 11, 2000 – Working Document.
2.2	**GLP**	Yes
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Preliminary treatment**	
3.1.1	Enrichment	<u>Solid Phase Extraction</u> Dinotefuran was extracted according to the following procedure: - The Empore Extraction Disk was moistened with acetone and dried under vacuum. - The extraction disk was rinsed and conditioned with isopropanol and methanol followed by distilled water. - The sample solution was transferred onto the disk and allowed to pass through. - The extraction disk was then dried under vacuum.
3.1.2	Cleanup	Dinotefuran was clean-up according the following procedure: - Elution was performed with methanol. - The solvent evaporated under low pressure by rotary evaporator. - The residue was re-dissolved in water using an ultra sonic bath.

Section A4 2(c)
Annex Point IIA4.2 & IIIA-IV.1

Analytical Methods for Detection and Identification
(c) Water

3.2 Detection

3.2.1 Separation method

HPLC-MS/MS:

Auto sampler:	Merck-AS 4000
Pump:	Merck-Hitachi L-7100
Column:	Luna C18 (2) Phenomenex, 5 µm; 150 mm x 3 mm
Pre-Column:	Security Guard C18 Phenomenex 5 µm; 4 mm x 3 mm
Solvent systems:	A: 0.1% IPCC-MS 3 in water/methanol (95:5, v/v) B: 0.1% IPCC-MS 3 in methanol

Time (min)	A	B
0	100	0
5	100	0
10	20	80
15	20	80
15.1	100	0
20	100	0
21	100	0
23	100	0

Injection volume:	50 µL
Flow:	0.5 mL/min
Washing solution:	water/methanol (95:5, v/v)
Retention time:	About 11 min

MS/MS:

Ionization mode:	APCI; Positive; Centroid
Vaporizer Temperature:	450°C
Capillary temperature:	200°C
Sheat:	70 psi N_2
Capillary voltage:	5.8 V
Discharge current:	4.0 µA
Spray voltage	about 4.2 kV
Scan mode:	SRM (Single Reaction Monitoring)

	MTI-446
Parent mass	203
Center mass	129
Width	±6
Scan time (sec)	0.5
Collision energy (V)	-17

3.2.2 Detector: MS Detector TSQ (700), Xcalibur 1.0 SR1 for Windows NT, Finnigan MAT.

3.2.3 Standard(s): Analytical standard of dinotefuran: external standard.

3.2.4 Interfering substance(s): None

3.3 Linearity

3.3.1 Calibration range: Calibration was performed using standards in the range of 0.963 – 77.076 µg/L.

Section A4 2(c)
Annex Point IIA4.2 & IIIA-IV.1

Analytical Methods for Detection and Identification (c) Water

3.3.2	Number of measurements	9 measurements
3.3.3	Linearity	Correlation coefficient was 0.999.
3.4	**Specifity: interfering substances**	There was no interference with other substances observed at the retention times of dinotefuran above 30% of the limit of quantification as well as above the limit of detection.
3.5	**Recovery rates at different levels**	The results for recovery of dinotefuran in water are presented in the following table:

Fortification Level (mg/kg)	Number of analysis	Recovery (%) Mean	Range	RSD (%)
Drinking water				
0.1	5	96.9	70.5 – 127.7	27.2
1	5	93.0	78.3 – 111.1	13.2
Ground water				
0.1	5	91.5	79.0 – 111.1	13.8
1	5	87.1	83.7 – 96.1	5.9
Surface water				
0.1	5	104.2	99.1 – 108.3	3.6
1	5	101.1	96.6 – 106.4	4.2

3.5.1	Relative standard deviation	See 3.5.
3.6	**Limit of quantification**	The limit of quantification was found to be 0.10 µg/L derived from the lowest fortification level.
3.7	**Precision**	
3.7.1	Repeatability	See 3.5 Recovery rates at different levels.
3.7.2	Independent laboratory validation	Not performed.

Section A4 2(c)
Annex Point IIA4.2 & IIIA-IV.1

Analytical Methods for Detection and Identification (c) Water

		4 APPLICANT'S SUMMARY AND CONCLUSION
4.1	**Materials and methods**	Guidelines: Residue Analytical Method, Guideline 96/46/EC, July 16, 1996 European Commission, Guidance Document on Residue Analytical Methods, SANCO/825/00 rev. 6, June 20, 2000 European Commission, Residues: Guidance for Generation and Reporting Methods of Analysis in Support of Pre-Registration Data Requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414, SANCO/3029/99 rev.4, July 11, 2000 – Working Document. No relevant deviations from test guidelines. Methods: Water samples were passed through an Empore extraction disk and then eluted with methanol. The concentrations of dinotefuran were determined by HPLC-MS/MS.
4.2	**Conclusion**	The analytical method was valid for the determination of dinotefuran in drinking, ground and surface water.
4.2.1	Reliability	1
4.2.2	Deficiencies	No

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	January 2013
Materials and methods	Validation data were provided for one ion transition only. For drinking water the precision data were outside the acceptable limits given in EU guidance (RSD = 26%) for the LOQ fortification level. However recovery data at the LOQ for both surface and ground water were within acceptable limits and recovery data at the higher fortification level were acceptable in all matrices
Conclusion	The method is considered acceptable for one ion transition only. Validation data for a second ion transition would be required in order to fully meet the requirements. The method is considered suitable as a monitoring method subject to the submission of validation data for a second ion transition. The LOQ of 0.1 µg/L is considered sufficient as the $PNEC_{water}$ for dinotefuran is 0.228 µg/L.
Reliability	1
Acceptability	The study is acceptable.
Remarks	Further validation data fro the second ion transition is required. This can be provided before product authorisation.
	COMMENTS FROM ...
Date	
Results and discussion	

Section A4 2(c)	Analytical Methods for Detection and Identification
Annex Point IIA4.2 & IIIA-IV.1	(c) Water

Conclusion
Reliability
Acceptability
Remarks

Section A4 2(d) Annex Point IIA4.2 & IIIA-IV.1	Analytical Methods for Detection and Identification (d) Animal and human body fluids and tissues	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	**Technically not feasible [ ]** **Scientifically unjustified [X]**	
Limited exposure [ ]	**Other justification [ ]**	
Detailed justification:	Not required as the active substance dinotefuran is not classified as toxic or highly toxic	
Undertaking of intended data submission [ ]	Not applicable	

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	January 2012
Evaluation of applicant's justification	The applicant's justification is acceptable as dinotefuran is not classified as' toxic' or 'very toxic'.
Conclusion	The applicant's justification is acceptable.
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	
Evaluation of applicant's justification	
Conclusion	
Remarks	

Section 4.3 Annex Point IIIA IV.1	**Analytical methods including recovery rates and the limits of determination for the active substance, and for residues thereof, in/on food or feedstuffs and other products where relevant**	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	**Technically not feasible [ ]** **Scientifically unjustified [ ]**	
Limited exposure [ ]	**Other justification [X]**	
Detailed justification:	Not required: Dinotefuran is intended for indoor use, therefore it is not intended to be used in a manner which may cause contact with food or feedstuffs (e.g. when used for disinfection in food production or transportation, in the food processing industry or catering services), or intended to be placed on, in or near soils in agricultural or horticultural use.	
Undertaking of intended data submission [ ]	Not applicable	

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	January 2013
Evaluation of applicant's justification	The applicant's justification is acceptable
Conclusion	The applicant's justification is acceptable
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	
Evaluation of applicant's justification	
Conclusion	
Remarks	

Section A5 Effectiveness against target organisms and intended uses

Subsection (Annex Point)			Official use only
5.1	**Function (IIA5.1)**	PT 18 Insecticide	
5.2	**Organism(s) to be controlled and products, organisms or objects to be protected (IIA5.2)**	In relation to use in insecticide biocidal product dinotefuran 2% bait.	
5.2.1	Organism(s) to be controlled (IIA5.2)	Efficacy of the active ingredient tested against the German cockroach (*Blattella germanica).* See Table A5.3-1 below.	
5.2.2	Products, organisms or objects to be protected (IIA5.2)	Not applicable	
5.3	**Effects on target organisms, and likely concentration at which the active substance will be used (IIA5.3)**		
5.3.1	Effects on target organisms (IIA5.3)	Dinotefuran is the active ingredient providing insecticidal activity. Refer to summary table, Table A5.3-1 below. See section B5 and B5.10 for results of efficacy tests with the biocidal product.	
5.3.2	Likely concentrations at which the A.S. will be used (IIA5.3)		
	PT18	2% dinotefuran bait	
5.4	**Mode of action (including time delay) (IIA5.4)**		
5.4.1	Mode of action	Contact and ingestion: Dinotefuran is a neonicotinoid in the nitroguanidine class. It appears that dinotefuran acts as an agonist of insect nicotinic acetylcholine receptors, but it is postulated that dinotefuran affects the nicotinic acetylcholine binding in a mode that differs from other neonicotinoid insecticides.	
5.4.2	Time delay	Rapid knockdown and death within several hours after contact or ingestion of dinotefuran.	x
5.5	**Field of use envisaged**		

Section A5 Effectiveness against target organisms and intended uses

	(IIA5.5)		
	MG03: Pest control	Product type PT18: Insecticides	
5.6	**User (IIA5.6)**		
	Industrial	Not applicable – the active ingredient dinotefuran is not produced in Europe.	
	Professional	The biocidal formulation, dinotefuran 2% bait, is supplied ready to use in a syringe style applicator tube. It is intended for indoor use only as a spot treatment to control cockroaches. It is not intended for outdoor use or for use where there is risk of contamination to food or feedingstuffs.	
	General public	Not applicable – intended for professional use only.	
5.7	**Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies (IIA5.7)**		
5.7.1	Development of resistance	No significant resistance development against dinotefuran has been reported.	
5.7.2	Management strategies	Management strategies for the development of resistance are not required as no significant resistance has been reported.	x
5.8	**Likely tonnage to be placed on the market per year (IIA5.8)**	An estimated 2 tonnes of the active ingredient dinotefuran is likely to be placed on the European market per year.	

Section A5 Effectiveness against target organisms and intended uses

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	29/07/2013
Materials and methods	N/A
Conclusion	**5.4.2** The UK CA considers that as the time to achieve an acceptable level of mortality was in days, rather than minutes, the statement in this section should be 'Knockdown and mortality is achieved within several hours after application of a 2 % dinotefuran bait formulation. Rapid knockdown and death is observed within minutes after contact with the active substance. **5.7.2** The Applicant has provided the following statement in Doc IIA '*Strategies to reduce the risk of resistance developing such as recommendations to treat to levels that ensure complete kill of target pest infestations and to use dinotefuran alternately with substances with a different mode of action can be implemented at end-use product approval. Similarly, monitoring programs to confirm that target pests remain susceptible to dinotefuran will need to be implemented in relation to product approvals as target pests will vary with product and geography*'.
Reliability	N/A
Acceptability	Applicant's version is considered acceptable in support of the approval of the active substance.
Remarks	N/A
	COMMENTS FROM ...
Date	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Table A5.3-1: Summary table of experimental data on the effectiveness of the active substance against target organisms at different fields of use envisaged, where applicable

<table>
<tr><th>Function</th><th>Field of use envisaged</th><th>Test substance</th><th>Test organism(s)</th><th>Test method</th><th>Test conditions</th><th>Test results: effects, mode of action, resistance</th><th>Reference*</th></tr>
<tr>
<td>MG03: Pest control</td>
<td>PT18: Insecticide</td>
<td>0.1 % dinotefuran (when diluted with water)</td>
<td>German cockroach (Blattella germanica), males and females, adult, laboratory culture from test facility.</td>
<td colspan="2">Test substance applied directly to cockroaches from a distance of circa 20 cm using a hand held atomiser at an application rate of 1 mL per replicate. Negative control applied in same manner using water only. 4 replicates per treatment.
10 cockroaches confined in plastic containers. Assessment of knockdown and mortality conducted at circa 5, 10, 15, 20, 30 minutes, 1, 2, 4, 24, 48 hours after initial treatment exposure.
Temperature: ranged from 18.6°C to 25.7°C.
Relative humidity: ranged from 20% to 32.2%.
Statistics: the numbers of knockdown and dead cockroaches were combined to give total affected. Percentages were then calculated. No statistical analysis was performed as nearly all values were 100%.</td>
<td>Application of dinotefuran at 0.1% resulted in 95% affected (knockdown and dead) German cockroaches at 48 hours after treatment. Control mortality low. Concluded that dinotefuran technical highly effective when applied as a direct spray against German cockroaches in terms of knockdown and mortality.
The summary table below shows percentage affected (knockdown and dead) German cockroaches exposed to dinotefuran 0.1% and negative control, over a 48 hour experimental period (means ± standard errors, n=4)
<table>
<tr><th rowspan="2">Time post application</th><th colspan="2">German cockroaches</th></tr>
<tr><th>Dinotefuran 0.1%</th><th>Negative control (water)</th></tr>
<tr><td>5 min</td><td>17.5 (± 7.5)</td><td>2.5 (± 2.5)</td></tr>
<tr><td>10 min</td><td>92.5 (± 4.8)</td><td>5 (± 2.9)</td></tr>
<tr><td>15 min</td><td>97.5 (± 2.5)</td><td>5 (± 2.9)</td></tr>
<tr><td>20 min</td><td>97.5 (± 2.5)</td><td>5 (± 2.9)</td></tr>
<tr><td>30 min</td><td>97.5 (± 2.5)</td><td>5 (± 2.9)</td></tr>
<tr><td>1 hour</td><td>100 (± 0)</td><td>5 (± 2.9)</td></tr>
<tr><td>2 hours</td><td>100 (± 0)</td><td>5 (± 2.9)</td></tr>
<tr><td>4 hours</td><td>100 (± 0)</td><td>5 (± 2.9)</td></tr>
<tr><td>24 hours</td><td>100 (± 0)</td><td>2.5 (± 2.5)</td></tr>
<tr><td>48 hours</td><td>95 (± 4.8)</td><td>5 (± 2.9)</td></tr>
</table>
</td>
<td>Heaven, H., (2011)</td>
</tr>
</table>

*** Reference**

Heaven, H., 2011, Laboratory bioassay to determine the efficacy of dinotefuran technical against German cockroaches (*Blattella germanica*) and houseflies (*Musca domestica*), i2L Research Ltd., unpublished report no. 11/07, April 13, 2011.

Study Summary 1

			Official use only
		1 REFERENCE	
1.1	**Reference**	Heaven, H., 2011, Laboratory bioassay to determine the efficacy of dinotefuran technical against German cockroaches (*Blattella germanica*) and houseflies (*Musca domestica*); i2L Research Ltd., unpublished report no. 11/07, April 13, 2011.	X
1.2	**Data protection**	Yes	
1.2.1	Data owner	Mitsui Chemicals Agro, Inc.	
1.2.2	Criteria for data protection	Data on new a.s. for first entry to Annex I	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	GLP, non-Guideline study	
2.2	**Deviations**	Not applicable	
		3 MATERIALS AND METHODS	
3.1	**Test Material**	As given in section 2	X
3.1.1	Lot/Batch number	KO9A3559	
3.1.2	Specification		
3.1.2.1	Description	White crystalline solid	
3.1.2.2	Purity	99.4%	
3.1.2.3	Stability	Expiration date: October 2012	
3.2	**Test Animals**	Non-entry field	
3.2.1	Species	1. German cockroach (*Blattella germanica*) 2. Houseflies (*Musca domestica*)	X
3.2.2	Source	1. Obtained from a culture maintained at i2L 2. Obtained from a culture maintained at i2L	
3.2.3	Sex	1. Males/females 2. Males/females	
3.2.4	Age at study initiation	1. Mixed age adults 2. Aged 3 to 5 days old	
3.2.5	Number of animals per group	1. 10 German cockroaches per treatment 2. 10 Houseflies per treatment	
3.2.6	Control animals	Yes, negative control (water)	
3.3	**Administration**	Spray application directly onto insects.	X
3.4	**Test Solution**	Dinotefuran was diluted with water and applied at one concentration from a distance of approximately 20 cm using a hand held atomiser	X
3.4.1	Concentration	0.1%	X
3.4.2	Application rate	1 mL per replicate	X
3.5	**Testing Procedure**		
3.5.1	Test system	Ten German cockroaches were confined in plastic containers, each	

		measuring 9 cm in diameter and 4.5 cm high. Ten houseflies were placed in 1136 mL size plastic containers. The base of the containers was lined with filter paper to absorb any excess liquid. The insects were then sprayed and cockroaches were transferred into fresh clean plastic containers immediately after spraying. Houseflies were transferred after 15 minutes post treatment.	
3.5.2	Duration of the test	48 hours	
3.5.3	Number or replicates	4 replicates for each treatment for each species, giving a total of 16 tests.	X
3.6	**Test conditions**		
3.6.1	Temperature	Ranged from 18.6°C to 25.7°C	
3.6.2	Relative humidity	Ranged between 20% and 32.2% throughout duration of the study.	
3.7	**Examinations**	Assessments of knockdown and mortality were carried out at approximately 5, 10, 15, 20, 30 minutes, 1, 2, 4, 24, 48 hours post initial exposure to treatments. Cockroaches were provided with water (damp cotton wool) and a bran pellet following the 4 hour assessment. Houseflies were provided with sugar water following the 4 hour assessment.	
3.8	**Statistics**	The numbers of knocked and dead cockroaches / houseflies were combined to give a total affected. Percentages were then calculated. No statistical analysis was performed as nearly all values were 100%.	
		4 RESULTS	
4.1	**Efficacy**		
4.1.1	Test treatment	Application of dinotefuran at 0.1% resulted in 95% affected (knock down and dead; see Table A5.2.1-1) German cockroaches (see Figure A5.2.1-1) and houseflies (see Figure A5.2.1-2), at 48 hours post treatment.	X
4.1.2	Control	Control mortality was low in both species.	
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	Guidelines: No applicable guideline. Method: Test substance applied directly to cockroaches from a distance of circa 20 cm using a hand held atomiser at an application rate of 1 mL per replicate. Negative control applied in same manner using water only. 4 replicates per treatment. 10 cockroaches confined in plastic containers. Assessment of knockdown and mortality conducted at circa 5, 10, 15, 20, 30 minutes, 1, 2, 4, 24, 48 hours after initial treatment exposure.	
5.2	**Results and discussion**	Application of dinotefuran at 0.1% resulted in 95% affected (knock down and dead) German cockroaches and houseflies, at 48 hours post treatment. Control mortality was low in both species.	X
5.3	**Conclusion**	It can be concluded that dinotefuran technical was highly effective when applied as a direct spray against German cockroaches and houseflies, in terms of knockdown and mortality	X
5.3.1	Reliability	1	X

5.3.2 Deficiencies Not applicable

Table A5.2.1-1: Percentage affected (knock down and dead) *B. germanica* and *M. domestica* exposed to dinotefuran 0.1% and a negative control, over a 48 hour experimental period (means ± standard errors, n=4)

Time post application	German cockroaches		Houseflies	
	Dinotefuran 0.1%	Negative control (water)	Dinotefuran 0.1%	Negative control (water)
5 min	17.5 (± 7.5)	2.5 (± 2.5)	70 (± 7.1)	0 (± 0)
10 min	92.5 (± 4.8)	5 (± 2.9)	92.5 (± 2.5)	0 (± 0)
15 min	97.5 (± 2.5)	5 (± 2.9)	100 (± 0)	0 (± 0)
20 min	97.5 (± 2.5)	5 (± 2.9)	100 (± 0)	0 (± 0)
30 min	97.5 (± 2.5)	5 (± 2.9)	100 (± 0)	0 (± 0)
1 hour	100 (± 0)	5 (± 2.9)	100 (± 0)	0 (± 0)
2 hours	100 (± 0)	5 (± 2.9)	100 (± 0)	0 (± 0)
4 hours	100 (± 0)	5 (± 2.9)	100 (± 0)	0 (± 0)
24 hours	100 (± 0)	2.5 (± 2.5)	92.5 (± 7.5)	2.5 (± 2.5)
48 hours	95 (± 4.8)	5 (± 2.9)	95 (± 5)	17.5 (± 2.5)

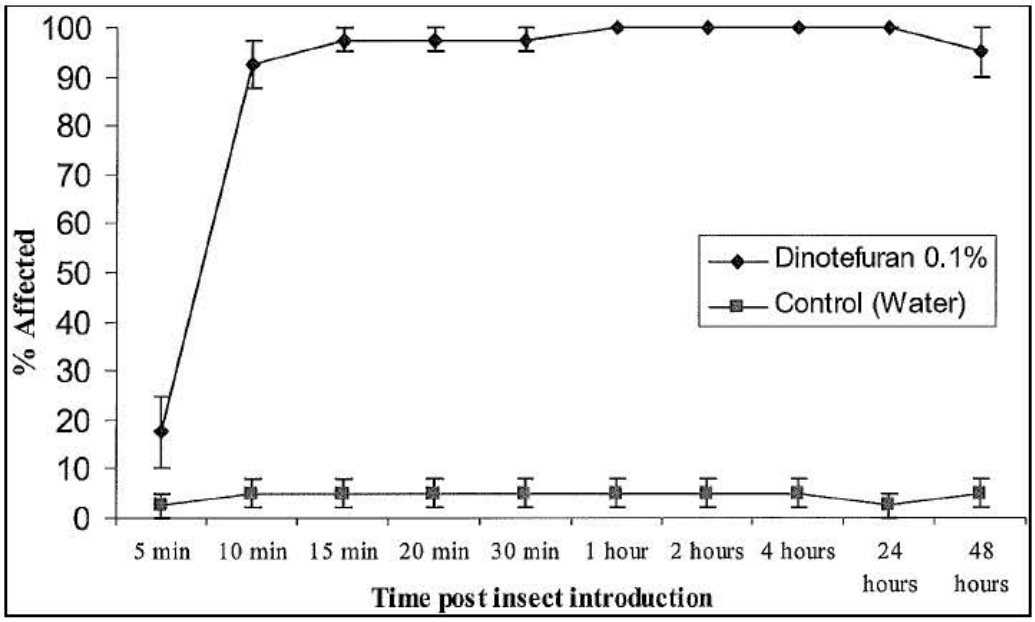


Figure A5.2.1-1: Percentage affected (knock down and dead) *B. germanica* exposed to dinotefuran 0.1% and a negative control, over a 48 hour experimental period (means ± standard errors, n=4)

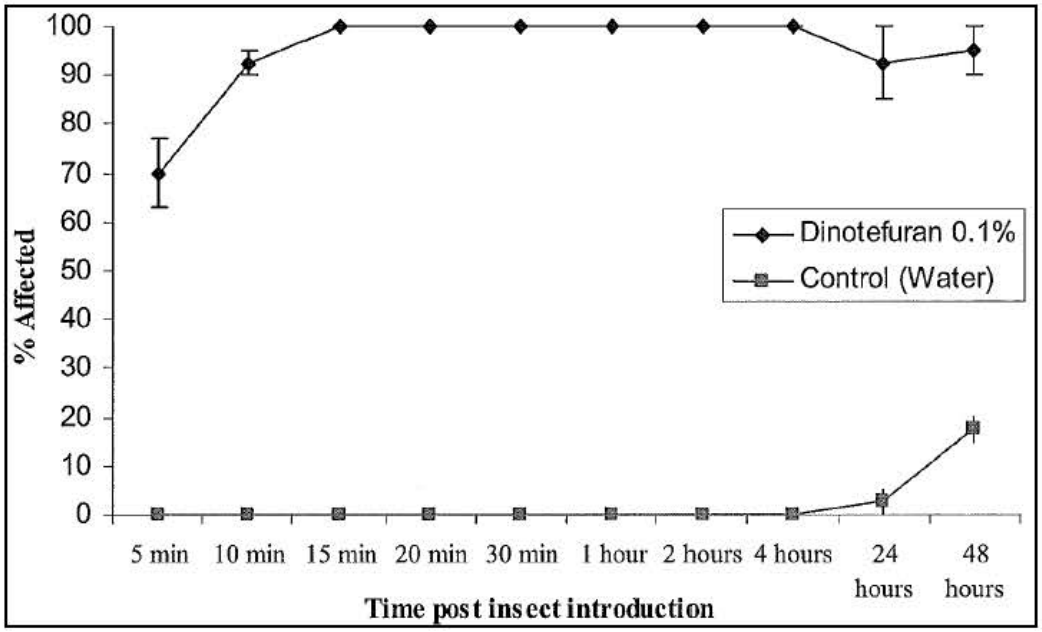


Figure 5.2.1-2: Percentage affected (knock down and dead) *M. domestica* exposed to dinotefuran 0.1% and a negative control, over a 48 hour experimental period (means ± standard errors, n=4)

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	29/07/2013
Materials and Methods	The UK CA accepts the Applicant's version, with the following comments. **1.1 & 3.2.1** The study also investigated the efficacy of dinotefuran against *Musca domestica*. However, the Applicant has stated in Document A5, Section 5.2.1 - 'Organisms to be controlled' - that the efficacy of the active ingredient has been tested against the German cockroach (*Blattella germanica*). Therefore, this evaluation only assesses the effectiveness of dinotefuran against *B. germanica*. **3.1** The test substance was technical grade dinotefuran (99.4 %). **3.3, 3.4, 3.4.1 & 3.4.2** The study was conducted to show that technical grade dinotefuran has an effect against a target organism. Although in the study, dinotefuran was sprayed directly onto the insects at a concentration of 0.1 % dinotefuran, the UK CA considers this to be acceptable as the applicant is only required to demonstrate the innate activity of the active substance. **3.5.3** For *B. germanica* and *M. domestica* dinotefuran was applied at 1 concentration with 4 replicates for the treatment and the control. **5.3.1** The efficacy template does not require the applicant to state a number for the reliability indicator. Although the study was not conducted to an internationally recognised test standard, the UK CA considers the methodology used to be acceptable. The UK CA therefore considers the reliability indicator to be 2 (see below).
Results and discussion	The UK CA accepts the Applicant's version, with the following comments. **4.1.1 & 5.2** The results showed that dinotefuran produced 97.5 % knockdown/mortality of *B. germanica* after 15 minutes. The results also showed that after 1 and 24 hours, dinotefuran produced 100.0 and 95.0 % knockdown/mortality of *B. germanica*, respectively. After 48 hours post treatment, the results showed that 95.0 % knockdown/mortality was achieved. The results for the controls showed 5.0 % knockdown/mortality after 15 minutes. The results also showed that after 1 and 24 hours, 5.0 and 2.5 % knockdown/mortality was observed, respectively. After 48 hours, the results showed 5.0 % knockdown/mortality. The UK CA considers the results as demonstrating the innate efficacy of technical grade dinotefuran, applied at a concentration of 0.1 %, against *B. germanica*. The UK CA therefore considers the results to be acceptable in support of the Annex I inclusion of dinotefuran.
Conclusion	**5.3** The UK CA agrees with the Applicant's conclusion.
Reliability	2
Acceptability	The UK CA considers the data to be acceptable in support of the approval of the active substance.
Remarks	The Applicant has not used the correct study summary template for efficacy. However, as all of the required information has been provided, the UK CA does not consider this to be an issue. All data and endpoints presented in the study summary have been checked against the original study and are correct.

COMMENTS FROM ...
Date
Materials and Methods
Results and discussion
Conclusion
Reliability
Acceptability
Remarks

Section A6.1.1-1 **Acute Toxicity**
Annex Point IIA6.1 **Oral**
Rat

			Official use only
		1 REFERENCE	
1.1	**Reference**	[redacted] 1997, Acute oral toxicity study of MTI-446 in rats, [redacted], unpublished report no. [redacted] 6648-118, December 9, 1997.	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Mitsui Chemicals Agro, Inc.	
1.2.2	Criteria for data protection	Data on new a.s. for first entry to Annex I	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Yes OECD 401 (1987), which is equivalent to 92/69/EEC (method B1) EPA-FIFRA, Subdivision F, § 81-1 (1982) JMAFF 59 NohSan No. 4200 (1985)	
2.2	**GLP**	Yes	
2.3	**Deviations**	No	
		3 MATERIALS AND METHODS	
3.1	**Test material**	As given in section 2	
3.1.1	Lot/Batch number	22-00110	
3.1.2	Specification		
3.1.2.1	Description	White powder	
3.1.2.2	Purity	96.5% + 2% water, purity of dried material 99.1%	
3.1.2.3	Stability	Expiration date: May 14, 2001	
3.2	**Test Animals**	Non-entry field	
3.2.1	Species	Rat	
3.2.2	Strain	Crl:CD[SD]BR (SPF)	
3.2.3	Source	[redacted]	
3.2.4	Sex	Male and female	
3.2.5	Age/weight at study initiation	8 - 15 weeks old, weighing 233 to 299g	
3.2.6	Number of animals per group	Dose range-finding study: 4 groups of one animal/sex. In phase I of the main study: 5/sex/500 mg/mL group; 5/females/100 and 3000 mg/mL group Phase II of the main study: 5/sex/ 50, 100, 150mg/mL group; 5/females/200 mg/mL group; 5/males/250 mg/mL group	X
3.2.7	Control animals	No	

Section A6.1.1-1		**Acute Toxicity**	
Annex Point IIA6.1		**Oral**	
		Rat	
3.3	**Administration/ Exposure**	Oral	
3.3.1	Postexposure period	14 days	
		Oral	
3.3.2	Type	Gavage	
3.3.3	Concentration	500, 1000, 2000, 3000, 4000 and 5000 mg/kg bw	
3.3.4	Vehicle	0.5% carboxymethylcellulose in distilled water	
3.3.5	Concentration in vehicle	Dose range-finding study: 25, 50, 150 and 250 mg/mL (males & females) Phase I of main study: 100 and 3000 mg/mL (females only), 500 mg/mL (males and females) Phase II of main study: 50, 100 and 150 mg/mL (males and females), 200 mg/mL (females only), 250 mg/mL (males only)	X
3.3.6	Total volume applied	Dose range-finding study: 20mL/kg bw Phase I of main study: 10mL/kg bw Phase II of main study: 20mL/kg bw	
3.3.7	Controls	No	
3.4	**Examinations**	Morbidity/mortality, clinical observations, body weights, necropsy and abbreviated *port mortem* examination.	
3.5	**Method of determination of LD_{50}**	Determined by a modified Behrens-Reed-Muench cumulant method.	
3.6	**Further remarks**	The LD_{50} and 95% confidence limits were calculated for the individual sexes and the sexes combined. A test mixture dose volume of 20 mL/kg bw was used for the range-finding study and phase II of main study, a volume of 10 mL/kg bw was used for phase I of main study.	
		4 RESULTS AND DISCUSSION	
4.1	**Mortality**	In the dose range-finding study, the females treated at 3000 or 5000mg/kg bw died on day 1. All other animals survived the observation period. In phase I of the main study, there were no deaths at any dose level administered at a treatment volume of 10mL/kg bw. The LD_{50} for dinotefuran administered at 10mL/kg bw was > 5000mg/kg bw. In phase II of the main study, deaths occurred in females treated at ≥2000mg/kg bw and in males treated at ≥3000mg/kg bw. All deaths in phase II occurred on the day of dosing or on the day following dosing. See Table A6.1.1.1-1	
4.2	**Clinical signs**	In phase I of the main study, two females at 5000mg/kg bw showed transient staggering gait on the day of treatment only and red staining of the face persisting for up to 3 days. One female treated at 3000mg/kg bw also showed transient staggering gait on the day of treatment. A male at 5000mg/kg bw showed transient excessive salivation and a female at 1000mg/kg bw showed red staining of the	

Section A6.1.1-1 Annex Point IIA6.1		Acute Toxicity Oral Rat	
		face. All other animals were of normal appearance and behavior. In phase II of the main study, treatment-related clinical signs were apparent at dose levels of ≥2000mg/kg bw and included hypoactivity, staggering gait, hunched posture, prostration, red-stained face, miosis, lacrimation, salivation, tachypnea, dyspnea, soft feces, yellow staining of the uro-genital area, tonic or clonic convulsions and tremors. Clinical signs were generally transient but occasionally persisted for up to 3 days after treatment.	X
4.3	**Pathology**	Necropsy and *post mortem* examination did not reveal any treatment-related gross lesions in either decedents or survivors killed at the end of the observation period.	
4.4	**Body weight**	All survivors except one female at 5000mg/kg bw in phase I showed body weight gain during the observation period.	
4.5	**LD_{50}**	The acute oral median lethal dose (LD_{50}) and 95% confidence limits were calculated to be 2804 mg/kg bw and 1947-4037 mg/kg bw for males, 2000 mg/kg bw and 1354-2954 mg/kg bw for females and 2450 mg/kg bw and 1942-3090 mg/kg bw for the sexes combined.	
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	Guidelines: OECD 401 (1987), which is equivalent to 92/69/EEC (method B1); EPA-FIFRA, Subdivision F, § 81-1 (1982); JMAFF 59 NohSan No. 4200 (1985) No relevant deviations from test guidelines. Method: Dose range finding study: 1 male and 1 female per group, administered dinotefuran at dose levels of 500, 1000, 3000 and 5000mg/kg bw. Phase I: 5 males and 5 females per group treated with 5000 mg dinotefuran/kg bw, 2 groups of females treated with 1000 and 3000 mg/kg bw. Phase II: 5 males per group treated with 1000, 2000, 3000 and 5000 mg dinotefuran/kg bw and 5 females per group treated with 1000, 2000, 3000 and 4000 mg/kg bw. Dinotefuran administered orally by gavage as suspension in CMC, 14-day observation period.	
5.2	**Results and discussion**	Rat, dinotefuran,: oral LD_{50} 2804 mg/kg bw for males, 2000 mg/kg bw for females and 2450 mg/kg bw for the sexes combined.	
5.3	**Conclusion**	Non-entry field	
5.3.1	Reliability	1	
5.3.2	Deficiencies	No	

Table A6.1.1.1-1 Mortality and time of death

Dose level (mg/kg bw)	Number dying / number tested					
	Dose range-finding study (treatment volume 20mL/kg bw)		Main study - phase I (treatment volume 10mL/kg bw)		Main study - phase II (treatment volume 20mL/kg bw)	
	Male	Female	Male	Female	Male	Female
500	0 / 1	0 / 1	-	-	-	-
1000	0 / 1	0 / 1	-	0 / 5	0 / 5	0 / 5
2000	-	-	-	-	0 / 5	3[b] / 5
3000	0 / 1	1[a] / 1	-	0 / 5	3[b] / 5	4[b] / 5
4000	-	-	-	-	-	5[c] / 5
5000	0 / 1	1[a] / 1	0 / 5	0 / 5	-	-

[a] died on day 1;
[b] died on day of treatment;
[c] 4 died on day of treatment and one on day 1;
- not tested

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*7/9/12*
Materials and Methods	*As described by Applicant but with the following amendments:* *Sections 3.2.6 & 3.3.5– In Phase I of the study 5 females were dosed with 100, 300 and 500 mg/ml or 1000, 3000 and 5000 mg/kg.*
Results and discussion	*As described by Applicant but with the following addition:* *In Phase II of the study, 3/5 females in the 1000 mg/kg group exhibited red stained faces on the day of treatment and 1male in the same dose group exhibited a scab on the face on days 2-14.*
Conclusion	*As described by Applicant.*
Reliability	*As described by Applicant.*
Acceptability	*Acceptable.*
Remarks	
	COMMENTS FROM ...
Date	
Materials and Methods	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section A6.1.1-2 **Acute Toxicity**
Annex Point IIA6.1 **Oral**
Mouse

Official use only

		1 REFERENCE
1.1	**Reference**	[redacted] 1997, Acute oral toxicity study of MTI-446 in mice, [redacted], [redacted] 6648-119, unpublished report no. December 9, 1997 [redacted] 2000, First amendment to report - Acute oral toxicity study of MTI-446 in mice, [redacted], unpublished report no. [redacted] 6648-119, April 5, 2000
1.2	**Data protection**	Yes
1.2.1	Data owner	Mitsui Chemicals Agro, Inc.
1.2.2	Criteria for data protection	Data on new a.s. for first entry to Annex I
		2 GUIDELINES AND QUALITY ASSURANCE
2.1	**Guideline study**	Yes OECD 401 (1981), which is equivalent to 92/69/EEC (method B1) EPA-FIFRA, Subdivision F, § 81-1 (1982) JMAFF 59 NohSan No. 4200 (1985)
2.2	**GLP**	Yes
2.3	**Deviations**	No
		3 MATERIALS AND METHODS
3.1	**Test material**	As given in section 2
3.1.1	Lot/Batch number	22-00110
3.1.2	Specification	
3.1.2.1	Description	White powder
3.1.2.2	Purity	96.5% + 2% water, purity of dried material 99.1%
3.1.2.3	Stability	Expiration date: May 14, 2001
3.2	**Test Animals**	
3.2.1	Species	Mouse
3.2.2	Strain	Crl:CD1[ICR]BR (SPF)
3.2.3	Source	[redacted]
3.2.4	Sex	Male and female
3.2.5	Age/weight at study initiation	4 - 10 weeks old, weighing 23.0 to 29.6g
3.2.6	Number of animals per group	Dose range-finding study: 4 groups of one animal/sex Main study: 3 groups of 5 animals/sex
3.2.7	Control animals	No

Section A6.1.1-2		Acute Toxicity
Annex Point IIA6.1		Oral
		Mouse
3.3	**Administration/ Exposure**	Oral
3.3.1	Post-exposure period	14 days
		Oral
3.3.2	Type	Gavage
3.3.3	Concentration	500, 1000, 2000, 3000 and 5000 mg/kg bw
3.3.4	Vehicle	0.5% carboxymethylcellulose in distilled water
3.3.5	Concentration in vehicle	Dose range-finding study: 25, 50, 150 and 250 mg/ml Main study: 50, 1000 and 150 mg/ml
3.3.6	Total volume applied	20 mL/kg bw
3.3.7	Controls	No
3.4	**Examinations**	Morbidity/mortality, clinical observations, body weights, necropsy and abbreviated *post mortem* examination.
3.5	**Method of determination of LD_{50}**	Determined by a modified Behrens-Reed-Muench cumulant method.
3.6	**Further remarks**	The LD_{50} and 95% confidence limits were calculated for the individual sexes and the sexes combined.
		4 RESULTS AND DISCUSSION
4.1	**Mortality**	In the range-finding study, both animals treated at 5000mg/kg bw and the male treated at 3000mg/kg bw died on the day of treatment. All other animals survived the observation period. In the main study, deaths occurred at dose levels of ≥2000mg/kg bw but not at 1000mg/kg bw. All deaths in the main study occurred on the day of treatment. See Table A6.1.1.2-1
4.2	**Clinical signs**	Transient clinical signs of toxicity, on the day of treatment only, were apparent at dose levels of ≥2000mg/kg bw and included hypoactivity, staggering gait, dyspnea, tonic convulsions and tremors.
4.3	**Pathology**	Necropsy and *post mortem* examination revealed no gross lesions in either decedents or survivors killed at the end of the observation period.
4.4	**Body weight**	Survivors treated at 2000 or 3000mg/kg bw gained weight throughout the observation period.
4.5	**LD_{50}**	The acute oral median lethal dose (LD_{50}) and 95% confidence limits were calculated to be 2450 mg/kg bw and 1801-3331 mg/kg bw for males, 2275 mg/kg bw and 1537-3369 mg/kg bw for females and 2371 mg/kg bw and 1884-2983 mg/kg bw for the sexes combined.