European Commission

Draft Renewal Assessment Report prepared according to the Commission Regulation (EU) N° 1107/2009

INDOXACARB

Volume 3 – B.7 (AS)

Rapporteur Member State: France
Co-Rapporteur Member State: Spain

Version History

When	What
2016-12	Initial RAR

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B.7- RESIDUE DATA

B.7.1 - STORAGE STABILITY OF RESIDUES

Previous evaluation:	*Studies submitted and evaluated for the first inclusion of indoxacarb on Annex I (2000)*

Study 1: Storage stability in apples, grapes, tomatoes and lettuce

Author (s)	Year	Title – Source – Company - Report n° GLP compliance - Published or not
Paul J. Desmond	1997	**Title:** A study of the recovery of residues of DPX-KN128/DPX-KN127[1] (formulated as either DPX-JW062 or DPX-MP062) after frozen storage on : grapes, grape wet pomace, wine, apples, lettuce, tomatoes, apple juice and soil; and incurred residue studies on tomatoes, lettuce and wet apple pomace. **Company :** Dupont **Report N°:** No.AMR 3778-96 **GLP compliance :** not applicable **Unpublished**

[1] DPX-KN127 should be IN-KN127

Study design

Grapes, apples, lettuce, and tomatoes were homogenized and fortified with 0.20 mg DPX-JW062/kg. In addition, processed fractions from grapes (wet pomace and wine) were fortified with 0.20 mg DPX-JW062/kg. Furthermore, tomatoes, lettuce, apple juice, and wet apple pomace data were also taken from separately performed residue field studies with incurred residues. The incurred residue studies were conducted as follows:

- treated samples were chosen after analysis of some magnitude of residue study samples
- a single sample was selected and processed and analyzed until multiple analyses gave a standard deviation of less than 20%
- the sample was then subdivided in glass storage bottles which were stored with the magnitude of residue samples
- a subdivided sample was removed and analyzed in replicate after several intervals of frozen storage

Study	Crop/study	Maximum storage interval for frozen storage (months)
AMR 3296-95	Apple wet pomace/incurred	7
AMR 3289-95	Tomatoes/incurred	12
AMR 3286-95	Lettuce/incurred	12

Except the day 0 samples, all of the samples were stored in a freezer at approximately -20°C for 0-553 days. At each specified intervals, sets of four samples (two stored samples, one control freshly fortified and on unfortified control sample) were extracted, cleaned up, and analyzed for DPX-KN128/ IN-KN127 concentrations using GC-MSD.

Analytical method using GC/MS (AMR 3493-95) was used to analyse Indoxacarb (DPX-KN128 and IN-KN127).This analytical method has been fully validated with an acceptable LOQ of 0.01mg/kg in each matrix.

Results

The storage stability by storage period for the different crops is summarized in the tables below (tables 8.2.1-1-8.2.1-11).

Table B.7.1-1: Storage stability by storage period for grapes

Days in freezer storage	control	Fortification (stored samples) (mg/kg[1])	Stored samples Recovery (%)	Fresh fortification (mg/kg)	Fresh Recovery (%)

0	<0.01	0.22, 0.19	100	0.2	100
1	<0.01	0.18, 0.18	86	0.16	80
7	<0.01	0.16, 0.17	79	0.23	115
15	<0.01	0.13, 0.17	71	0.14	70
32	<0.01	0.11, 0.14	**60**	**0.13**	**65**
78	<0.01	0.11, 0.15	**62**	0.17	85
193	<0.01	0.16, 0.13	69	0.18	90
362	<0.01	0.15, 0.14	69	0.18	90
417	<0.01	0.16, 0.14	71	0.2	100
418	<0.01	0.18, 0.18	86	0.19	95
458	<0.01	0.15, 0.19	81	0.19	95
553	<0.01	0.15, 0.21	86	0.21	105

[1] Expressed as the sum of DPX-KN128 and IN-KN127

In table IIIA 8.2.1-1, although the level of residue declined by nearly 40% after 32 days of storage, it was considered that the samples are sufficiently stable over 553 days frozen storage as procedural recovery measured at 32 days was relatively low too (suggesting an analytical problem occurred).

Table B.7.1-2: Storage stability by storage period for wet grape pomace

Days in freezer storage	control	Fortification (stored samples) (mg/kg[1])	Stored samples Recovery (%)	Fresh fortification (mg/kg)	Fresh Recovery (%)
0	<0.01	0.20, 0.23	100	0.21	100
1	<0.01	0.18, 0.21	91	0.21	100
7	<0.01	0.21, 0.20	93	0.20	95
15	<0.01	0.20, 0.22	95	0.21	100
36	<0.01	0.18, 0.21	89	0.21	100
63	<0.01	0.21, 0.21	95	0.18	86
90	<0.01	0.20, 0.19	89	0.21	100
301	<0.01	0.22, 0.23	102	0.23	109

[1] Expressed as the sum of DPX-KN128 and IN-KN127

Based on the results above, the storage stability of DPX-KN128/ IN-KN127 following storage at -20°C is considered to be demonstrated in wet grape pomace for up to 301 days.

Table B.7.1-3: Storage stability by storage period for wine

Days in freezer storage	control	Fortification (stored samples) (mg/kg[1])	Stored samples Recovery (%)	Fresh fortification (mg/kg)	Fresh Recovery (%)
0	<0.01	0.19, 0.24	100	0.21	100
1	<0.01	0.17, 0.19	82	0.20	95
7	<0.01	0.18, 0.20	86	0.20	95
15	<0.01	0.19, 0.19	86	0.21	100
36	<0.01	0.17, 0.21	86	0.20	95
63	<0.01	0.17, 0.16	75	0.18	86
90	<0.01	0.16, 0.16	73	0.18	86
301	<0.01	0.17, **0.1**	**61**	0.24	114

In table IIIA 8.2.1-3, recoveries ranged from 61% to 86%. No decline could be detected for DPX-KN128/ IN-KN127 in wine during 90 days. Residue level measured a 301 days decline by nearly

40%. Since residue level from fresh procedural recoveries at 301 days is relatively high, the storage stability following storage at -20°C is considered to be demonstrated in wine for up to 90 days only.

Table B.7.1-4: Storage stability by storage period for apples

Days in freezer storage	control	Fortification (stored samples) (mg/kg[1])	Stored samples Recovery (%)	Fresh fortification (mg/kg)	Fresh Recovery (%)
0	<0.01	0.13, 0.13	65	0.16	80
1	<0.01	0.16, 0.17	83	0.18	90
7	<0.01	0.14, 0.14	70	0.15	75
22	<0.01	0.18, 0.18	90	0.14	70
30	<0.01	0.12, 0.14	**65**	0.14	70
148	<0.01	0.19, 0.20	98	0.20	100
172	<0.01	0.20, 0.20	100	0.15	75
379	<0.01	0.21, 0.20	103	0.19	95
441	<0.01	0.18, 0.19	93	0.19	95
530	<0.01	0.17, 0.15	80	0.17	85

[1] Expressed as the sum of DPX-KN128 and IN-KN127

In table IIIA 8.2.1-4, due to abnormally low residue levels in samples at t0, it was not possible to compare the residues concentration at each time point to the initial residue concentration. Recovery rates at each storage times were calculated by taking the fortification level of 0.2 mg/kg as a reference.

Although the level of residue declined by nearly 35% after one month of storage, it was considered that the samples are sufficiently stable over 530 days frozen storage as procedural recovery measured at 1 month was relatively low too (suggesting an analytical problem occurred).

Except at 30 days, the residues of DPX-KN128/ IN-KN127 show no significant decrease (>30% as compared to the fortification concentration) in apples after deep frozen storage for at least 530 days.

Table B.7.1-5 Storage stability by storage period for tomatoes

Days in freezer storage	control	Fortification (stored samples) (mg/kg[1])	Stored samples Recovery (%)	Fresh fortification (mg/kg)	Fresh Recovery (%)
0	<0.01	0.16, 0.15	-	0.15	-
1	<0.01	0.17, 0.17	85	0.13	65
7	<0.01	0.19, 0.21	100	0.20	100
65	<0.01	0.20, 0.24	110	0.22	110
107	<0.01	0.16, 0.17	83	0.18	90
206	<0.01	0.20, 0.20	100	0.18	90
272	<0.01	0.20, 0.16	90	0.19	95
366	<0.01	0.14, 0.14	70	0.18	90

[1] Expressed as the sum of DPX-KN128 and IN-KN127

In table IIIA 8.2.1-7, due to relatively low residue levels in samples at t0, it was not possible to compare the residues concentration at each time point to the initial residue concentration. Recovery rates at each storage times were calculated by taking the fortification level of 0.2 mg/kg as a reference.

The residues of DPX-KN128/ IN-KN127 show no significant decrease (>30% as compared to the fortification concentration) in tomatoes after deep frozen storage for at least 366 days.

Table B.7.1-6: Storage stability by storage period for lettuce

Days in freezer storage	control	Fortification (stored samples) (mg/kg[1])	Stored samples Recovery (%)	Fresh fortification (mg/kg)	Fresh Recovery (%)
0	<0.01	0.16, 0.15	100	0.20	100
1	<0.01	0.20, 0.16	116	0.19	90
6	<0.01	0.13, 0.17	97	0.13	75
11	<0.01	0.15, 0.17	103	0.19	80
117	<0.01	0.18, 0.15	106	0.18	83
340	<0.01	0.16, 0.13	94	0.16	73

[1] Expressed as the sum of DPX-KN128 and IN-KN127

The residues of DPX-KN128/ IN-KN127 show no significant decrease (>30% as compared to the fortification concentration) in lettuce after deep frozen storage for at least 340 days.

Incurred residue stability data from tomatoes, lettuce and apple from magnitude of residue studies are presented in the following tables.

Table B.7.1-7 Storage stability by storage period for wet apple pomace[1]

Time (days)	0	9	52	111	202
Commodity	**DPX-KN128/ IN-KN127 [2] (mg/kg)**				
apple pomace	2.7 2.3	2.5 2.1	2.9	2.7	2.3

[1] Obtained from field study (incurred samples)

[2] Expressed as the sum of DPX-KN128 and IN-KN127

Table B.7.1-8 Storage stability by storage period for apple juice[1]

Time (days)	0	36	63	186
Commodity	**DPX-KN128/ IN-KN127 [2] (mg/kg)**			
apple juice	0.17 0.18	0.18 0.21	0.19 0.22	0.18 0.17

[1] Obtained from field study

[2] Expressed as the sum of DPX-KN128 and IN-KN127

Table B.7.1-9 Storage stability by storage period for tomatoes[1]

Time (days)	0	29	90	182	365
Commodity	**DPX-KN128/ IN-KN127 [2] (mg/kg)**				
tomatoes	0.21	0.23	0.21	0.22	0.16

[1] Obtained from field study (incurred samples)

[2] Expressed as the sum of DPX-KN128 and IN-KN127

Table B.7.1-10 Storage stability by storage period for lettuce[1]

Time (days)	0	36	91	183	365
Commodity	**DPX-KN128/ IN-KN127 [2] (mg/kg)**				
lettuce	6.0	4.9	8.3	8.1	5.3

[1] Obtained from field study

[2] Expressed as the sum of DPX-KN128 and IN-KN127

Conclusion:

DPX-KN128/ IN-KN127 levels appear stable under frozen storage conditions (ca. -20°C) for at least 18 months in grapes and apples, 12 months in tomatoes and 11 months in lettuce.

Study 2: Storage stability in maize grains and silage

For dry commodities, storage stability was evaluated after the peer review and demonstrated (in maize grain) for a period of 13 months at -20°C (France, 2011).

Author (s)	Annex point /reference n°	Year	Title – Source – Company - Report n° GLP compliance - Published or not
Guinivan, R. M.Kennedy, C. A. Enriquez, M.	CA, 6.3.1/03	2003	**Title :** Combined decline and magnitude of residues of DPX-KN128 (indoxacarb) together with IN-KN127 in maize (green plant and grain) following applications of DPX-MP062 30 WG – Europe, season 2001 **Source :** DuPont **Company :** DuPont de Nemours and company **Report N°:** DuPont-6006 **GLP compliance :** Yes **Unpublished**

Author (s)	Annex point /reference n°	Year	Title – Source – Company - Report n° GLP compliance - Published or not
Guinivan, R. M.Kennedy, C. A. Enriquez, M.	CA, 6.3.1/04	2003	**Title :** Combined decline and magnitude of residues of DPX-KN128 (indoxacarb) together with IN-KN127 in maize (green plant and grain) following applications of DPX-MP062 30 WG and DPX-MP062 150 SC – Europe, season 2002 **Source :** DuPont **Company :** DuPont de Nemours and company **Report N°:** DuPont-9777 **GLP compliance :** Yes **Unpublished**

Stability/recovery of the analyte after periods of frozen storage was assessed in 2 ways:

- Green plant and silage samples with incurred residues were reanalyzed after various periods of frozen storage (there was no residue found in grain samples so incurred residue analyses after periods of frozen storage could not be conducted).
- Individual portions of control homogenate per matrix were fortified at a level of 0.10 mg/kg for each matrix and stored at approximately -20°C. At each sampling interval for each matrix, two fortified specimens and two controls from frozen storage were taken.

Analytical method using GC/MS (AMR 3493-95) was used to analyse Indoxacarb (DPX-KN128 and IN-KN127, only one signal) in maize (green plant, grain and silage). This analytical method has been fully validated with an acceptable LOQ of 0.01mg/kg in each matrix.

Residue values for treated field samples with incurred residues (green plant and silage) are given below along with the average value of repeat analyses of the same sample after specified periods of additional frozen storage.

Residue (mg/kg)				Recovery (%)
Matrix	**Initial Analysis**	**Repeat Analysis**	**Storage Interval(s) (months)**	
Green plant	0.76	0.93	13	122
Green plant	0.65	0.42	13	120
Green plant	0.12	0.11	13	92
Silage	0.29	0.28, 0.25	8 and 10	96 and 86
Silage	0.27	0.31, 0.29	8 and 10	115 and 107

Incurred residues analysed at intervals of 13 (green plant) and 8 and 10 months (silage) of freezer storage after initial analysis gave essentially the same residue values as originally determined.

Recovery data for control fortifications stored for various intervals in a freezer are given below:

	Percent recovery (%)					
Storage interval	**Grain**		**Green plant**		**Silage**	
	Frozen fortification	**Fresh fortification**	**Frozen fortification**	**Fresh fortification**	**Frozen fortification**	**Fresh fortification**
0 (0) months	97	99	79	78	77	75
2 (1) months	99	99	85	76	41	69
3 (3) months	94	100	68	98	29	90
6 (5) months	**35**	**76**	**18**	**65**	25	80
11 (6) months	90	90	91	81	28	75
13 (10) months	96	98	90	88	19	95

Figures in between brackets correspond storage interval for silage. Values without brackets are for grain/green plant.

RMS comment: recoveries at 6 months for grain and green plant are far below 70% whereas at 11 and 13 months recoveries are close to 100%. The following explanation is given by the laboratory:

> *The low average recoveries for the forth analysis interval for grain and green plant followed by good recovery for two additional time points shows a problem with analysis of the frozen fortified control samples that is not a method or a stability problem. The low recoveries for silage indicate the same non-method problem transferring the samples from freezer storage containers to extraction bottles for analysis. The fresh fortifications run with each set give acceptable recoveries. The fresh fortifications for each analysis set were added directly to controls in the extraction bottles and demonstrated that the method performed well. The good agreement in incurred residue values for the same study samples after various periods of frozen storage and the good recoveries for subsequent analyses of freezer stored fortified controls for grain and forage indicate that there was not a problem with extraction of the residues from freezer stored controls. With good demonstrated extraction efficiency and method performance the only variable that could produce a systematic error would be transfer of frozen fortified control samples from freezer storage containers to extraction bottles. The incurred residue data also demonstrates that the problem exists with fortifications added to control samples in a storage bottle and not with residues that were incorporated into the treated field samples.*

The fresh fortifications at 6 months for grain and whole plant show indeed a lowest level than for the other dates. The laboratory explanation can be considered as acceptable.

Conclusion:

DPX-KN128/ IN-KN127 levels appear stable under frozen storage conditions (ca. -20°C) for at least 13 months in maize grain and in green plant. DPX-KN128/ IN-KN127 is not considered as stable under frozen storage conditions in silage.

Previous evaluation:	*Submitted for the purpose of renewal AIRIII*

Report:	CA, 6.1/01, Guinivan, R.A., Daussin, S., 2008
Title:	Recovery of DPX-MP062 and five metabolites from hen-derived matrices (whole eggs, muscle, fat and liver) after frozen storage.
Document No:	DuPont-19901
Guidelines:	OPPTS 860.1380
GLP	Yes

Materials and method

Samples of hen whole eggs, liver, fat, and muscle were fortified with DPX-MP062 and its 5 metabolites (IN-KB687, IN-KG433, IN-KT319, IN-JU873 and IN-JT333), each at a level of 0.20 mg/kg were stored at approximately -20°C and then analyzed at 5 intervals over 16 months. Residues were extracted from whole eggs

using acidified ethyl acetate, and from liver, muscle and fat using acidified acetonitrile. Following partitioning and purification steps, the residues were quantified by LC/MS/MS analysis.

To prepare samples for fortification, the hen muscle, fat and liver samples were cut into small pieces and wheighted (10g) into 250 mL plastic centrifuge bottles. Egg samples were removed from the shells and and homogenized by rigorous mixing. Samples were stored at approximately -20°C until fortification.

For each stability time point, one control, two freshly fortified and two aged fortified samples of each matrix were analysed. Samples were removed from storage and analysed after approximate intervals of 0, 1, 3, 7, 11 and 16 months.

Results
The analyses of the control samples showed that no residues of any component were present.
The residues of all components showed no significant decrease (>30% as compared to the fortification concentration) in the different matrices after storage deep frozen for at least 16 months.

Table IIIA 0-1: Stability of DPX-MP062, IN-KB687, IN-KG433, IN-KT319, IN-JU873 and IN-JT333 residues in hen, whole egg, liver, fat, and muscle following storage at -20 ± 10°C

Commodity/Matrix	**Approx. storage interval (Months)**	**Residue recovered in mg/kg**					
		Stored (-20°C) forts[a]		**Fresh forts[a]**		**Recovery of stored forts as a % of 0-day[c]**	**Recovery of fresh forts as a % of 0-day[d]**
DPX-MP062							
Whole Egg	0	0.19	0.19	0.21	0.19	**97**	**103**
	1	0.18	0.17	0.16	0.19	**90**	**90**
	3	0.21	0.21	0.21	0.22	**108**	**110**
	7	0.17	0.17	0.16	0.17	**87**	**85**
	11	0.20	0.22	0.23	0.25	**108**	**123**
	16	0.23	0.18	0.23	0.20	**105**	**110**
Liver	0	0.20	0.19	0.19	0.18	**102**	**97**
	1	0.24	0.22	0.21	0.20	**121**	**108**
	3	0.19	0.20	0.21	0.22	**103**	**113**
	7	0.17	0.19	0.17	0.17	**95**	**89**
	11	0.24	0.22	0.24	0.24	**121**	**126**
	16	0.26	0.22	0.26	0.20	**126**	**121**
Fat	0	0.20	0.17	0.19	0.19	**99**	**101**
	1	0.20	0.23	0.16	0.16	**115**	**85**
	3	0.20	0.17	0.19	0.20	**99**	**104**
	7	0.17	0.18	0.17	0.15	**93**	**85**
	11	0.19	0.17	0.16	0.18	**96**	**91**
	16	0.20	0.20	0.17	0.16	**107**	**88**
Muscle	0	0.18	0.18	0.20	0.19	**96**	**104**
	1	0.23	0.23	0.19	0.17	**123**	**96**
	3	0.21	0.19	0.20	0.20	**107**	**107**
	7	0.16	0.15	0.15	0.15	**83**	**80**
	11	0.16	0.15	0.14	0.15	**83**	**77**
	16	0.23	0.21	0.25	0.19	**117**	**117**

Commodity/Matrix	**Approx. storage interval (Months)**	**Residue recovered in mg/kg**			
		Stored (-20°C) forts[a]	**Fresh forts[a]**	**Recovery of stored forts as a % of 0-day[c]**	**Recovery of fresh forts as a % of 0-day[d]**
IN-KB687					

Whole Egg	0	0.18	0.17	0.18	0.18	**99**	**101**
	1	0.18	0.17	0.17	0.17	**99**	**96**
	3	0.19	0.19	0.19	0.19	**107**	**107**
	7	0.17	0.17	0.16	0.18	**96**	**96**
	11	0.18	0.19	0.18	0.17	**104**	**99**
	16	0.19	0.21	0.20	0.20	**113**	**113**
Liver	0	0.18	0.18	0.19	0.20	**96**	**104**
	1	0.19	0.19	0.20	0.19	**101**	**104**
	3	0.19	0.19	0.20	0.20	**101**	**107**
	7	0.18	0.18	0.17	0.16	**96**	**88**
	11	0.20	0.20	0.21	0.18	**107**	**104**
	16	0.19	0.20	0.20	0.21	**104**	**109**
Fat	0	0.18	0.16	0.17	0.19	**97**	**103**
	1	0.18	0.19	0.18	0.17	**106**	**100**
	3	0.18	0.17	0.16	0.18	**100**	**97**
	7	0.18	0.16	0.17	0.16	**97**	**94**
	11	0.16	0.17	0.15	0.17	**94**	**91**
	16	0.17	0.19	0.17	0.17	**103**	**97**
Muscle	0	0.20	0.19	0.18	0.21	**100**	**100**
	1	0.18	0.19	0.20	0.19	**95**	**100**
	3	0.19	0.19	0.20	0.19	**97**	**100**
	7	0.20	0.18	0.17	0.16	**97**	**84**
	11	0.18	0.20	0.16	0.18	**97**	**87**
	16	0.19	0.21	0.22	0.20	**103**	**108**

Commodity/Matrix	**Approx. storage interval (Months)**	**Residue recovered in mg/kg**					
		Stored (-20°C) forts[a]	**Fresh forts[a]**			**Recovery of stored forts as a % of 0-day[c]**	**Recovery of fresh forts as a % of 0-day[d]**
IN-KG433							
Whole Egg	0	0.19	0.19	0.20	0.21	96	104
	1	0.20	0.19	0.19	0.19	99	96
	3	0.20	0.20	0.20	0.21	101	104
	7	0.18	0.18	0.19	0.19	91	96
	11	0.19	0.19	0.18	0.18	96	91
	16	0.23	0.20	0.22	0.18	109	101
Liver	0	0.21	0.20	0.18	0.20	**104**	**96**
	1	0.21	0.21	0.20	0.20	**106**	**101**
	3	0.21	0.20	0.22	0.22	**104**	**111**
	7	0.17	0.17	0.18	0.17	**86**	**89**
	11	0.20	0.19	0.22	0.21	**99**	**109**
	16	0.19	0.19	0.21	0.21	**96**	**106**
Fat	0	0.20	0.18	0.19	0.20	**99**	**101**
	1	0.19	0.21	0.19	0.18	**104**	**96**
	3	0.18	0.18	0.19	0.20	**94**	**101**
	7	0.17	0.17	0.18	0.18	**88**	**94**
	11	0.18	0.18	0.18	0.19	**94**	**96**
	16	0.23	0.23	0.21	0.22	**119**	**112**
Muscle	0	0.19	0.18	0.20	0.21	**95**	**105**
	1	0.21	0.21	0.20	0.19	**108**	**100**
	3	0.19	0.19	0.21	0.20	**97**	**105**
	7	0.15	0.16	0.17	0.17	**79**	**87**
	11	0.17	0.17	0.17	0.18	**87**	**90**
	16	0.17	0.19	0.21	0.20	**92**	**105**

Commodity/Matrix	**Approx. storage interval (Months)**	**Residue recovered in mg/kg**					
		Stored (-20°C) forts[a]	**Fresh forts[a]**			**Recovery of stored forts as a % of 0-day[c]**	**Recovery of fresh forts as a % of 0-day[d]**
IN-KT319							

Whole Egg	0	0.19	0.18	0.19	0.19	**99**	**101**
	1	0.20	0.18	0.19	0.19	**101**	**101**
	3	0.16	0.17	0.19	0.21	**88**	**107**
	7	0.19	0.18	0.18	0.20	**99**	**101**
	11	0.17	0.18	0.17	0.17	**93**	**91**
	16	0.20	0.19	0.19	0.20	**104**	**104**
Liver	0	0.20	0.19	0.20	0.20	**99**	**101**
	1	0.18	0.19	0.20	0.19	**94**	**99**
	3	0.19	0.18	0.20	0.20	**94**	**101**
	7	0.17	0.20	0.21	0.20	**94**	**104**
	11	0.20	0.19	0.21	0.19	**99**	**101**
	16	0.19	0.19	0.24	0.22	**96**	**116**
Fat	0	0.21	0.18	0.19	0.21	**99**	**101**
	1	0.20	0.19	0.18	0.17	**99**	**89**
	3	0.19	0.18	0.18	0.18	**94**	**91**
	7	0.20	0.19	0.18	0.19	**99**	**94**
	11	0.20	0.19	0.17	0.16	**99**	**83**
	16	0.23	0.23	0.21	0.22	**116**	**109**
Muscle	0	0.19	0.19	0.20	0.20	**97**	**103**
	1	0.20	0.19	0.19	0.18	**100**	**95**
	3	0.19	0.19	0.20	0.20	**97**	**103**
	7	0.15	0.16	0.16	0.16	**79**	**82**
	11	0.18	0.18	0.17	0.17	**92**	**87**
	16	0.20	0.20	0.22	0.22	**103**	**113**

Commodity/Matrix	**Approx. storage interval (Months)**	**Residue recovered in mg/kg**					
		Stored (-20°C) forts[a]		**Fresh forts[a]**		**Recovery of stored forts as a % of 0-day[c]**	**Recovery of fresh forts as a % of 0-day[d]**
IN-JU873							
Whole Egg	0	0.18	0.19	0.21	0.20	**95**	**105**
	1	0.20	0.16	0.17	0.20	**92**	**95**
	3	0.20	0.21	0.22	0.23	**105**	**115**
	7	0.18	0.17	0.19	0.17	**90**	**92**
	11	0.19	0.20	0.19	0.19	**100**	**97**
	16	0.23	0.20	0.22	0.16	**110**	**97**
Liver	0	0.21	0.21	0.19	0.20	**104**	**96**
	1	0.25	0.23	0.19	0.21	**119**	**99**
	3	0.20	0.20	0.22	0.24	**98**	**114**
	7	0.18	0.16	0.18	0.16	**84**	**84**
	11	0.21	0.20	0.22	0.21	**101**	**106**
	16	0.20	0.17	0.24	0.21	**91**	**111**
Fat	0	0.20	0.18	0.18	0.20	**100**	**100**
	1	0.21	0.22	0.18	0.16	**113**	**89**
	3	0.20	0.19	0.20	0.20	**103**	**105**
	7	0.20	0.17	0.19	0.17	**97**	**95**
	11	0.18	0.18	0.16	0.18	**95**	**89**
	16	0.21	0.21	0.17	0.19	**111**	**94**
Muscle	0	0.17	0.19	0.21	0.21	**92**	**108**
	1	0.24	0.24	0.19	0.18	**123**	**95**
	3	0.20	0.21	0.20	0.21	**105**	**105**
	7	0.16	0.16	0.17	0.17	**82**	**87**
	11	0.16	0.16	0.15	0.17	**82**	**82**
	16	0.17	0.19	0.22	0.18	**92**	**103**

Commodity/Matrix	**Approx. storage interval (Months)**	**Residue recovered in mg/kg**					
		Stored (-20°C) forts[a]		**Fresh forts[a]**		**Recovery of stored forts as a % of 0-day[c]**	**Recovery of fresh forts as a % of 0-day[d]**
IN-JT333							

Whole Egg	0	0.18	0.17	0.18	0.17	**100**	**100**
	1	0.22	0.21	0.22	0.22	**123**	**126**
	3	0.20	0.18	0.20	0.20	**109**	**114**
	7	0.16	0.15	0.16	0.16	**89**	**91**
	11	0.20	0.20	0.17	0.18	**114**	**100**
	16	0.26	0.20	0.28	0.19	**131**	**134**
Liver	0	0.17	0.20	0.18	0.17	**103**	**97**
	1	0.22	0.21	0.19	0.20	**119**	**108**
	3	0.21	0.22	0.19	0.23	**119**	**117**
	7	0.17	0.18	0.15	0.18	**97**	**92**
	11	0.22	0.22	0.21	0.19	**122**	**111**
	16	0.20	0.19	0.22	0.19	**108**	**114**
Fat	0	0.18	0.16	0.18	0.17	**99**	**101**
	1	0.19	0.22	0.18	0.20	**119**	**110**
	3	0.20	0.17	0.18	0.17	**107**	**101**
	7	0.18	0.16	0.17	0.16	**99**	**96**
	11	0.16	0.17	0.12	0.16	**96**	**81**
	16	0.19	0.19	0.17	0.18	**110**	**101**
Muscle	0	0.16	0.17	0.18	0.17	**97**	**103**
	1	0.18	0.22	0.18	0.14	**118**	**94**
	3	0.20	0.22	0.18	0.22	**123**	**118**
	7	0.15	0.14	0.15	0.14	**85**	**85**
	11	0.15	0.16	0.17	0.11	**91**	**82**
	16	0.18	0.15	0.20	0.17	**97**	**109**

[a] On Day-0 all fortifications are fresh. All fortifications are at 0.2 mg/kg (ppm)
[b] Average stored recovery / average fresh recovery
[c] Average of the 2 stored fortifications per matrix per interval / Average of the 4 fortifications done on day-0 per matrix with the result rounded to the nearest whole percent.
[d] Average of the 2 fresh fortifications per matrix per interval / Average of the 4 fortifications done on day-0 per matrix rounded to the nearest whole percent.
NOTE: All values from report were rounded to two significant figures before inclusion in this table. Additional Note: Crossed out values were changes from original table due to transcription errors in the original table.

Conclusion

The study indicates that DPX-MP062 and its five metabolites are stable at approximately -20°C for at least 16 months in hen matrices (whole egg, liver, fat, and muscle).

B.7.2 - METABOLISM, DISTRIBUTION AND EXPRESSION OF RESIDUES

B.7.2.1 Plants

STUDY 1

Characteristics

reference	:	Scott et al, 1997	application rate	:	500 g DPX-JW062/ha, equal to 250 g DPX-KN128/ha
type of study	:	uptake, distribution, and metabolism	concentration	:	not specified
year of execution	:	1993-1995 (report 1997)	frequency	:	1
test substance	:	[indanone-1-^{14}C]DPX-JW062 or [trifluoromethoxyphenyl ring - ^{14}C]DPX-JW062, radiochem. pur. >95%	vehicle interval area	: : :	SE formulation not applicable Mississippi, USA
plant	:	Cotton	total rate	:	idem application rate
GLP statement	:	Yes	Sampling points	:	DAT 0, 7, 14, 30, 59, and 90 days
guideline	:	no guideline in force			

Study design

Field grown cotton (variety DPL 51) was treated with a single application of DPX-JW062 (indanone-1-^{14}C [IND], and trifluoromethoxyphenyl ring-^{14}C [TMP] radiolabeled) at a rate equivalent to 500 g a.s./ha of DPX-JW062 (a racemic 50:50 mixture of the insecticidally active and the inactive enantiomer). The rate is equal to 250 g as/ha of the bioactive enantiomer DPX-KN128 (ca. 1.7 N). Plant samples were taken at 0, 7, 14, 30, 59 days (at forage stage) after application and at maturity (90 days). Total ^{14}C-residues were determined by liquid

scintillation counting (LSC). HPLC was used to analyse crop extracts while mass spectrometry (MS) was used for identification of significant ^{14}C-residues. Volatiles were determined following UV light exposure for 21 days and trapping in sodium hydroxide or ethylene glycol.

Results

Total residues declined from approximately 7.1-13.6 mg DPX-KN128/IN-KN127 equivalents (IND and TMP labelled)/kg at day 0 to 0.019-0.053 mg eq/kg for mature plants (90 days post application), while seeds contained <0.01 mg eq/kg. More than 90% of the total radioactive residues (TRR) were extracted for all samples with the exception of the 90-day (mature) plant samples where 68.4-86.8% of TRR was extracted. In all samples, DPX-KN128/IN-KN127 represented more than 80% of the TRR, with the exception of mature cotton plant (60.5% TRR).

Volatile compounds evolving from leaves of treated cotton plants constituted ca. 7% of the administered dose and consisted mainly of CO_2 (ca. 4%).

Polar metabolites were found on chromatograms but the concentrations were too low for further analysis.

Table B.7.2-1 : Total Radioactive Residue (ppm, DPX-JW062 equivalents) in cotton, following a single application of ^{14}C-DPX-JW062 of 500 g a.i./ha

Sample (Whole Plant unless indicated)	Label	Avg. Weight of Plants	TRR[1]	TRR Extracted (%)	TRR Hydrolyzed[2] (%)	TRR Unextracted (%)
Day 0	IND[3]	144.0	7.069	6.956 (98.4)	0.028 (0.4)	0.085 (1.2)
	TMP[4]	115.1	13.596	13.229 (97.3)	0.111 (0.8)	0.256 (1.9)
Day 7	IND	94.4	6.345	6.187 (97.5)	0.041 (0.6)	0.117 (1.8)
	TMP	106.8	7.352	7.153 (97.3)	0.061 (0.8)	0.138 (1.9)
Day 14	IND	129.6	2.247	2.164 (96.3)	0.043 (1.9)	0.040 (1.8)
	TMP	127.8	3.285	3.285 (100.0)	----------	----------
Day 30	IND	348.4	0.899	0.855 (95.1)	----------	----------
	TMP	406.7	0.972	0.920 (94.7)	0.027 (2.8)	0.025 (2.6)
Day 59	IND	638.5	0.820	0.757 (92.3)	0.017 (2.1)	0.046 (5.7)
	TMP	787.7	0.501	0.496 (92.6)	----------	----------
Day 90 Plant	IND	142.6[5]	0.019[6]	0.013 (68.4)	----------	----------
	TMP	206.6	0.053[6]	0.046 (86.8)	----------	----------
Day 90 Seed	IND		0.007[6]	<0.001 (NM)[7]	----------	----------
	TMP		0.005[6]	<0.001 (NM)	----------	----------

1 TRR - Total Radioactive Residue, equal to the sum of the TRR extracted + TRR hydrolyzed + TRR unextracted. TRR unextracted = TRR unextracted before hydrolysis (from combustion) - TRR hydrolyzed

2 TRR hydrolyzed from Pronase and acidic hydrolysis

3 IND - [Indanone-1-^{14}C]DPX-JW062

4 TMP - [Trifluoromethoxyphenyl ring ^{14}C]DPX-JW062

5 The plants were allowed to dry down in the field house hence the lower weights

6 From combustion

7 NM - Not Meaningful

Table B.7.2-2: Concentration of DPX-JW062 (ppm) in cotton samples, following a single application of ^{14}C-DPX-JW062 of 500 g a.i./ha

Sample	Label[1]	TRR[2]	% TRR in Extract	% JW062 in Extract[3]	JW062 as % TRR	PPM JW062
Day 0 Plant	IND	7.069	98.4	99.8	98.2	6.942
	TMP	13.596	97.3	99.7	97.0	13.189
Day 7 Plant	IND	6.345	97.5	90.7	88.4	5.611
	TMP	7.352	97.3	96.3	93.7	6.888
Day 14 Plant	IND	2.247	96.3	94.5	91.0	2.045
	TMP	3.285	100.0	90.7	90.7	2.979
Day 30 Plant	IND	0.899	95.1	83.8	79.7	0.716
	TMP	0.972	94.7	85.7	81.2	0.789
Day 59 Plant	IND	0.820	92.3	90.8	83.8	0.687
	TMP	0.501	92.6	89.1	82.5	0.413
Day 90 Plant	IND	0.019	68.4	88.4	60.5	0.011
	TMP	0.053	86.8	97.9	83.7	0.045
Day 90 Seed	IND	0.007	<0.001	NA[4]		
	TMP	0.005	<0.001	NA		

1 IND = [Indanone-1-^{14}C]DPX-JW062
TMP = [Trifluoromethoxyphenyl ring ^{14}C]DPX-JW062

2 TRR = Total Radioactive Residue

3 JW062 as %TRR = [% TRR in Extract/100] x [% JW062 in Extract/100] (from HPLC analysis)

4 NA = Not Applicable

Conclusions

Total residues in mature cotton plants amounted up to 0.053 mg eq/kg, and up to <0.01 mg eq/kg in cotton seed. DPX-KN128/IN-KN127 represented more than 60% of the total residues in mature plants.

STUDY 2

Characteristics

reference	: Scott et al, 1997	application rate	: 625 g/ha, equal to 313 g DPX-KN128/ha
type of study	: uptake, distribution, and metabolism	concentration	: not specified
year of execution	: 1993-1995 (report 1997)	frequency	: 4
test substance	: [indanone-1-14C]DPX-JW062 or [trifluoromethoxyphenyl ring - 14C]DPX-JW062, radiochem. pur. >89%	vehicle interval area	: SE formulation : 10 days : Mississippi, USA
plant	: Cotton	total rate	: 2500 g/ha (1250 g DPX-KN128/ha)
GLP statement	: Yes	Sampling points	: DAT 0, 9, 20, 30 days, and maturity
guideline	: no guideline in force		

Study design

Cotton plants, grown in the field, were treated with four applications of ^{14}C-DPX-JW062 at an exaggerated application rate of 625 g/ha per application for a total of 2500 g i/ha (ca. 8.3N). The purpose of this study was to facilitate isolation of any significant metabolites that may have been at too low a concentration in study 1. Applications were about ten days apart. Samples were taken before and after each application with the exception

of the first application and at maturity. Total ^{14}C-residues were determined by liquid scintillation counting. HPLC was used to analyse crop extracts while mass spectrometry (MS) was used for identification of significant ^{14}C-residues. Chiral HPLC was used to determine whether there was any enantio-selectivity in the uptake or metabolism of DPX-JW062 isomers.

Results

According to the notifier, the results of this study were similar to those in study 1. There were indications of formation of minor metabolites but DPX-KN128/IN-KN127 was the only significant residue.
Chiral analysis of the isolated DPX-KN128/IN-KN127 indicated that it was still racemic with a comparable distribution.

Conclusions

Nothing is concluded in view of the limitations of the study (see guidelines and limitations).

Guidelines and limitations

Technical details from this additional study were not available and, therefore, results were not considered in this evaluation.

STUDY 3

Characteristics

reference	:	Gaddamidi et al, 1997b	application rate	: 500 g/ha, equal to 250 g DPX-KN128/ha
type of study	:	uptake, distribution, and metabolism	concentration	: not specified
year of execution	:	1993-1995 (report 1997)	frequency	: 1
test substance	:	[indanone-1-^{14}C]DPX-JW062 or [trifluoromethoxyphenyl ring - ^{14}C]DPX-JW062, radiochem. pur. >98%	vehicle interval area	: SC formulation : not applicable : Delaware, USA
plant	:	Grapes	total rate	: idem application rate
GLP statement	:	Yes	PHI[1]	: DAT 0, 14, 46, and 66 for grapes 0, 7, 14, 31, 46, and 66 for leaves.
Guideline	:	no guideline in force		

[1] PHI is not applicable. Instead, DAT (days after treatment) are reported.

Study design

Field grown grapes (variety Chardonnay) were treated with a single application of DPX-JW062 (indanone-1-^{14}C, and trifluoromethoxyphenyl ring-^{14}C radiolabelled) at a rate equivalent to 500 g /ha, equal to 250 g/ha of the insecticidally active enantiomer DPX-KN128 (ca 1N). Treated samples, consisting of grape leaves and berries, were taken soon after the application solution had dried (day 0), at various time points throughout the study (7, 14, 31, and 46 DAT), and at maturity (66 DAT). Total ^{14}C- residues were determined by liquid scintillation counting (LSC). HPLC and thin layer chromatography (TLC) were used to analyze crop extracts while mass spectrometry (MS) was used for identification of significant ^{14}C-residues.

Determination of surface ^{14}C-residues:

DPX-JW062 is a lipophilic compound. Rinsing grapes and leaves with water did not remove any surface radioactivity. Therefore, samples were rinsed with acetonitrile to determine the surface radioactive residues.

Extraction of grapes:

Samples of grapes from day 0, 14 and 46 were extracted with acetonitrile. The mature grapes (day 66) were extracted separately using about 50 mL of acetonitrile by homogenizing, centrifuging and decanting the

supernatant. The acetonitrile extracts from the Day-66 grape samples separated into two phases due to high sugar content in the grape juice. Therefore the total extract from each ^{14}C-IND and ^{14}C-TMP test grapes was partitioned separately two times with dichloromethane to extract the radioactivity into the organic phase. The organic phases from two partitions were pooled.

Sample preparation for analysis:
Acetonitrile and dichloromethane/acetonitrile extracts were evaporated *in vacuo* at 40°C to a suitable volume. Radioactivity in the concentrated extracts was determined by analyzing duplicate aliquots by LSC.

Identification of radioactive residues:
Aliquots of each extract containing >0.01 ppm was analysed by HPLC.

Results

The total 14C-residues in the extracts were based on the radioactivity in the concentrated extract. There was a little difference in the amounts of ^{14}C-residues in the total extract and in the concentrated extracts, except for the Day-66 samples (see table 8.1.1-1 & table 8.1.1-2)

Table B.7.2-3 Extraction of [IND-1-^{14}C]DPX-JW062- Radioactivity in the total initial and concentrated extracts

Interval	Grapes Weight (g)	Extr. Vol. (mL)	^{14}C in Aliquot (dpm per vol-mL)	Total ^{14}C-Content dpm (ppm) $	Conc. Volume (mL)	^{14}C in Conc. Aliquot (dpm per vol-mL)	Total ^{14}C in Conc. Solution (dpm)	^{14}C-Residues in the Extract (ppm) $
Day 0	13.80	213.0	138/0.25	117,150 (0.317)	9.4	2863/0.25	107,649	0.291
Day 14	20.64	299.0	177/1.0	52,923 (0.096)	8.6	3210/0.5	55,212	0.100
Day 46	20.08	250.0	74/1.0	18,500 (0.034)	2.3	155/0.02	17,825	0.033
Day 66	197.78	439.0	1438/0.5	℘ 1.263 x 10^6 (0.238)	49.0$^\phi$ 10.8$^\theta$	273/0.25 1551/0.02	53,508§ 836,190$^£$	0.168$^\#$

℘ Day-66 grape CH_3CN extract separated into two phases due to high sugar content. The extract was partitioned with CH_2Cl_2. The total radioactivity before partitioning with $CH_2Cl_2$is shown here.

§ Total ^{14}C content in the concentrated aqueous phase.

ϕ Aqueous phase.

θ CH_2Cl_2 phase.

£ Total ^{14}C content in the concentrated CH_2Cl_2 phase.

\# This residue was derived by adding the ^{14}C-contents from the concentrated aqueous and organic phases.

$ $$ppm = \frac{\text{Total } ^{14}\text{C Content, dpm}}{\text{Grape Weight, g}} \times \frac{1\text{-}\mu\text{g DPX - JW062}}{26{,}800 \text{ dpm}}$$

Table B.7.2.-4: Extraction of [TMP-Ring-14C] DPX-JW062 – Radioactivity in the total initial and concentrated extract

Interval	Grapes Weight (g)	Extr. Vol. (mL)	^{14}C in Aliquot (dpm per vol-mL)	Total ^{14}C-Content dpm (ppm)	Conc. Volume (mL)	^{14}C-in Aliquot (dpm per vol-mL)	Total ^{14}C in Conc. Solution (dpm)	^{14}C-Residues in the Extract (ppm)
Day 0	10.85	212.0	138/0.25	62,330 (0.214)	9.5	321/0.05	64,771	0.223
Day 14	20.51	300.0	108/1.0	32,250 (0.059)	8.4	200/0.05	33,520	0.061
Day 46	27.64	270.0	122/1.0	32,940 (0.044)	2.5	296/0.02	37,000	0.050
Day 66	199.98	444.0	756/0.5	6.713×10^5 ℘ (0.125)	36.0$^{\phi}$ 10.8$^{\theta}$	53/0.25 772/0.02	7,632§ $4.169 \times 10^{5£}$	0.079$^{\#}$

℘ Day-66 grape CH_3CN extract separated into two phases due to high sugar content. The extract was partitioned with CH_2Cl_2. The total radioactivity before partitioning with CH_2Cl_2 is shown here.

§ Total ^{14}C content in the concentrated aqueous phase.

ϕ Aqueous phase.

θ CH_2Cl_2 phase.

£ Total ^{14}C content in the concentrated CH_2Cl_2 phase.

\# This residue was derived by adding the ^{14}C-contents from the concentrated aqueous and organic phases.

The total ^{14}C-residues in/on the grapes of day 0 from were 3.0-3.67 mg eq/kg which decreased to 0.34-0.38 eq/kg in the mature samples (day 66).

Rinse solutions taken to determine the surface residues on grapes and grape leaves, contained 2.70-3.43 mg eq/kg (90.0-93.4 %TRR) on day 0, decreased to 0.20-0.26 mg eq/kg (53.0-75.5 %TRR) in the mature samples.

In washed berries from grapes, total ^{14}C-residues were 0.22-0.29 mg eq/kg at day 0, and were 0.08-0.17 mg eq/kg in the mature samples.

In grape pomace, total 14C-residues at day 0 and at maturity were ca. 0.01 total mg eq/kg.

In leaves, total ^{14}C-residues were 76.5-111 mg eq/kg at day 0, and decreased to 7.6-9.0 mg eq/kg at maturity (day 66).

Analysis of grape rinse solutions and extracts at all sampling intervals indicated that more than 90% of the radioactivity in the samples was due to DPX-KN128/IN-KN127. In mature grape samples, the total extractable residue levels were 0.33- 0.35 mg eq/kg (92.3-94.8 %TRR). No significant metabolites of DPX-JW062 were found in the grapes.

Table B.7.2-5 : Total Radioactive Residue in the grapes from the vine treated with [indanone-1-^{14}C]DPX-JW062 and [TMP-^{14}C]DPX-JW062.

Sample (Day)	[Indanone-1-^{14}C]DPX-JW062 ppm (% TRR [1])				[TMP-^{14}C]DPX-JW062 ppm (%TRR [1])			
	Rinse [2]	Extract [3]	Pomace	Total	Rinse [2]	Extract [3]	Pomace	Total
Day 0	2.70 (90.0)	0.29 (9.7)	0.01 (0.5)	3.00	3.43 (93.5)	0.22 (6.1)	0.01 (0.4)	3.67
Day 14	0.72 (85.3)	0.10 (11.8)	0.02 (2.8)	0.84	0.72 (89.9)	0.06 (7.6)	0.02 (2.5)	0.80
Day 46	0.06 (62.4)	0.03 (35.5)	<0.01 [4] (2.0)	0.09	0.13 (68.6)	0.05 (28.6)	<0.01 [4] (2.9)	0.18
Day 66	0.20 (53.0)	0.17 (44.3)	0.01 (2.6)	0.38	0.26 (75.5)	0.08 (23.0)	<0.01 [4] (1.5)	0.34

[1] Total Radioactive Residues (TRR) are based on the actual raw dpm and not on rounded values in the table.

[2] The grapes were rinsed with acetonitrile to determine the surface residues, since DPX-JW062 is lipophilic. ^{14}C-Residues in the rinse solutions were based on the total rinse solution except for the Day-66 residues which are based on the concentrated rinse solution.

[3] The total ^{14}C-residues shown in these columns are based on the radioactivity in the concentrated extract.

[4] Raw dpm were used to derive the % TRR and <0.01 was not considered as 0.01.

Table B.7.2.-6 : Concentration of DPX-JW062 in the grape extracts and in the surface rinses at various sampling period.

Sampling Period (Days)	[Indanone-1-^{14}C]DPX-JW062 Test Samples ppm (% TRR)			[TMP-Ring-^{14}C]DPX-JW062 Test Samples ppm (% TRR)		
	Surface Residues [1]	Extracted Residues [2]	DPX-JW062 ppm (% TRR) [1]	Surface Residues [1]	Extracted Residues [2]	DPX-JW062 ppm (% TRR) [1]
0	2.70 (89.8)	0.27 (9.0%)	2.97 (98.7)	3.43 (93.6)	0.2 (5.5)	3.63 (99.1)
14	0.72 (85.3)	0.08 (9.0)	0.80 (94.3)	0.72 (89.9)	0.05 (6.0)	0.77 (95.9)
46	0.05 (53.8)	0.03 (31.1)	0.08 (84.9)	0.12 (66.5)	0.05 (25.3)	0.17 (91.8)
66	0.20 (51.6)	0.15 (39.0)	0.35 (92.3%)	0.26 (75.5)	0.08 [3] (19.3)	0.33 (94.8)

[1] The ^{14}C-residues of DPX-JW062 in the surface rinse solutions and extracts were determined by HPLC fraction collection and LSC analysis of the fractions.

[2] ^{14}C in the Day-66 extract was partitioned into organic and aqueous phases. 0.15 ppm in the organic layer was entirely due to DPX-JW062. The aqueous phase which contained 0.02 ppm was not analyzed as it contained sugars from the grapes, making it thick syrup.

[$] The aqueous phase contained a negligible amount of ^{14}C (<1.1% TRR).

Conclusions

Total residues in mature grapes were up to 0.38 mg eq/kg, and ca. 0.01 mg eq/kg in pomace. Up to 75.5 % of the total residues were surface removable in mature grapes. More than 90% of the residue was represented by DPX-KN128/IN-KN127. Mature grapes contained up to 0.35 mg eq/kg of DPX-KN128/IN-KN127.

Guidelines and limitations

The study is suitable for evaluation.

STUDY 4

Characteristics

reference	: Gaddamidi et al, 1997a	application rate	: 500 g as/ha, equal to ca. 250 g DPX-KN128/ha
type of study	: uptake, distribution, and metabolism	concentration	: not specified
year of execution	: 1993-1995 (report 1997)	frequency	: 1
test substance	: [indanone-1-^{14}C]DPX-JW062 or [trifluoromethoxyphenyl ring - ^{14}C]DPX-JW062, radiochem. pur. 98%	vehicle interval area	: SC formulation : not applicable : Delaware, USA
plant	: Lettuce	total rate	: idem application rate
GLP statement	: Yes	PHI[1]	: DAT 0, 7, 14, 21, 28, and 35 days
guideline	: no guideline in force		

[1] PHI is not applicable. Instead, DAT (days after treatment) are reported.

Study design

Lettuce (variety Pritzhead) at the 4/5 leave stage was treated with a single application of DPX-JW062 (indanone-1-^{14}C, and trifluoromethoxyphenyl ring-^{14}C radiolabelled) at a rate of 500 g/ha, equal to 250 g /ha of the insecticidal active enantiomer DPX-KN128. Treated samples were collected after the application solution had dried (day 0), at 7, 14, 21, 28 days after application and at maturity (35 days after application). Control samples (sprayed with blank formulation) were taken at each sampling point. Total ^{14}C-residues were determined by liquid scintillation counting (LSC). HPLC and TLC were used to analyze crop extracts while liquid chromatography/mass spectrometry (LC-MS) was used for identification of significant ^{14}C-residues.

Results

The total ^{14}C-residues in the lettuce samples were 10.8-11.2 mg eq/kg at day 0, which decreased to 0.20-0.47 mg eq/kg in the mature (day 35) samples. More than 83% of the total residue was extractable at day 35. The removable surface ^{14}C-residues decreased with time, from 3.95-5.47 mg eq/kg (36.4-48.9 %TRR) at day 0 to 0.022-0.072 mg eq/kg (10.9-15.3 %TRR) in the mature samples.

Analysis of lettuce rinse solutions and extracts at all sampling intervals found only DPX-KN128/IN-KN127. Concentrations of DPX-KN128/IN-KN127 in the mature (day 35) lettuce samples were 0.191-0.467 mg /kg (94.6- 99.2%TRR).

Table B.7.2-7 : Distribution of the Radioactive Residue (ppm) from lettuce treated at 500 g a.i./ha with [TMP-^{14}C]DPX-JW062

SAMPLING PERIOD DAYS	SURFACE RESIDUES[1] PPM (% TRR)	COMBUSTION ANALYSIS[2] PPM (% TRR)	TOTAL ^{14}C RESIDUES[3] TRR PPM	^{14}C RESIDUES EXTRACTED[4] PPM (% TRR)	UNEXTRACTABLE ^{14}C RESIDUES PPM (% TRR)	MATERIAL BALANCE[5] PPM (% TRR)
0	3.951 (36.4)	6.891 (636)	10.842	6.511 (60.0)	0.052 (0.5%)	10.54 (97.2)
7	2.097 (43.5)	2.724 (56.5)	4.821	2.496 (51.8)	0.082 (1.7)	4.675 (97.0)
14	0.766 (30.2)	1.766 (69.8)	2.532	1.545 (61.0)	0.056 (2.2)	2.367 (93.4)
21	0.289 (22.4)	0.998 (77.6)	1.287	0.936 (72.7)	0.038 (3.0)	1.263 (98.1)
28	0.058 (16.2)	0.301 (83.8)	0.359	0.289 (80.5)	0.013 (3.6)	0.360 (100.3)
35	0.022 (10.9)	0.180 (89.1)	0.202	0.169 (83.7)	<0.01 (4.7)	0.201 (99.3)

1 Surface residues were determined by rinsing lettuce samples with CH_3CN.

2 CH_3CN rinsed lettuce samples were homogenized and sample aliquots were combusted to determine the radioactivity.

3 Total tissue radioactive residues were obtained by combining the residues (ppm) in CH_3CN rinse and from the combustion analysis.

4 Extracted with CH_3CN. The values are from the concentrated extracts.

5 Surface residues + CH_3CN extractable residues + unextracted residues.

Table B.7.2-8 : Concentration of DPX-JW062 in the lettuce extracts and in the surface washes at various sampling period.

SAMPLING PERIOD (DAYS)	[INDANONE-1-^{14}C]DPX-JW062 TEST SAMPLES * PPM (% TRR)			[TMP-^{14}C]DPX-JW062 TEST SAMPLES * PPM (% TRR)		
	SURFACE RESIDUES	EXTRACTED RESIDUES	DPX-JW062 TOTAL[1]	SURFACE RESIDUES	EXTRACTED RESIDUES	DPX-JW062 TOTAL[1]
0	5.467 (48.9)	6.439 (57.6)	11.906 (106.4)	3.951 (36.4)	6.511 (60.0)	10.462 (96.4)
7	2.244 (43.4)	2.898 (56.0)	5.142 (99.4)	2.097 (43.5)	2.496 (51.8)	4.593 (95.3)
14	0.570 (21.5)	2.073 (78.2)	2.643 (99.7)	0.766 (30.2)	1.545 (61.0)	2.311 (91.3)
21	0.379 (26.8)	1.012 (71.6)	1.391 (98.4)	0.289 (22.4)	0.936 (72.7)	1.225 (95.2)
28	0.059 (10.5)	0.473 (83.9)	0.532 (94.3)	0.058 (16.2)	0.289 (80.5)	0.347 (96.7)
35	0.072 (15.3)	0.395 (83.9)	0.467 (99.2)	0.022 (10.9)	0.169 (83.7)	0.191 (94.6)

1 The amounts of [^{14}C]DPX-JW062 were based on the HPLC analysis of surface residues and extracted residues. DPX-JW062 was the only ^{14}C-component in all extracts of IND and TMP test lettuce samples, which integrated to be 100% in all samples in HPLC analysis. This was confirmed by collecting the HPLC fractions, analyzing by LSC, and reconstructing the chromatogram using Day-35 TMP lettuce extract.

* $$\%\ \text{TRR DPX-JW062} = \frac{\text{DPX - JW062 in Surface Residue (ppm)} + \text{DPX - JW062 in the Extract}}{\text{Total Radioactive Residue (TRR)}}$$

Conclusions

Total residues in lettuce were up to 0.47 mg eq/kg in mature samples. Ca. 84% of the total residue was extractable in mature samples. The amount of surface removable residue in mature plants was on average 13%. DPX-KN128/IN-KN127 represented more than 94% of the total residue in mature plants.

Guidelines and limitations

The study is suitable for evaluation.

STUDY 5

Characteristics

reference	: Gaddamidi et al, 1997a	application rate	: 625 g DPX-JW062/ha, equal to ca. 313 g DPX-KN128/ha
type of study	: uptake, distribution, and metabolism	concentration	: not specified
year of execution	: 1993-1995 (report 1997)	frequency	: 4
test substance	: trifluoromethoxyphenyl ring - ^{14}C]DPX-JW062, radiochem. pur. 99%	vehicle interval area	: SC formulation : 7 days : Delaware, USA
plant	: Lettuce	total rate	: ca. 2500 g/ha (1250 g DPX-KN128/ha)
GLP statement	: Yes	PHI[1]	: DAT 0, 7, 14, and 21 days
guideline	: no guideline in force		

[1] PHI is not applicable. Instead, DAT (days after treatment) are reported.

Study design

Lettuce (variety Pritzhead) was treated with 4 applications of DPX-JW062 (trifluoromethoxyphenyl ring-^{14}C radiolabelled) at a total rate of 2500 g/ha, equal to 1250 g/ha of the insecticidal enantiomer DPX-KN128. Treated samples were collected after the application solution had dried (day 0), and at 7, 14, 21, and 28 days after application. Control samples (sprayed with blank formulation) were taken at each sampling point. Total ^{14}C-residues were determined by liquid scintillation counting (LSC). HPLC and TLC were used to analyze crop extracts while liquid chromatography/mass spectrometry (LC-MS) was used for identification of significant ^{14}C-residues.

Results

According to the notifier, the results were similar to those in study 4. No radiolabeled residues other than DPX-KN128/IN-KN127 were detected in the lettuce samples.

Conclusions

Nothing is concluded in view of the limitations of the study (see guidelines and limitations).

Guidelines and limitations

Technical details from this additional study were not available and therefore results were not considered in this evaluation.

STUDY 6

Characteristics

Reference	: Brown et al, 1997	application rate	: 150 g/ha, equal to 75 g DPX-KN128/ha
type of study	: uptake, distribution, and metabolism	concentration	: -
year of execution	: 1995-1997 (report 1997)	frequency	: 4
test substance	: [trifluoromethoxyphenyl ring - ^{14}C]DPX-JW062, radiochem. pur. >98%	vehicle interval area	: WDG formulation : 6-10 days : Delaware, USA

Plant	: Tomato	total rate	: 600 g/ha (300 g DPX-KN128/ha)
GLP statement	: Yes	PHI[1]	: DAT 0, 3, 7, and 14 days
Guideline	: no guideline in force		

[1] PHI is not applicable. Instead, DAT (days after treatment) are reported.

Study design

Tomatoes (variety Heinz 8892) were treated with four applications of DPX-JW062 (trifluoromethoxy-phenyl ring-^{14}C radiolabelled) to a total rate of 600 g/ha, equal to 300 g/ha of the insecticidally active enantiomer DPX-KN128 (ca. 1.3 N). The test substance was applied over the top of the plants, and applications were made approximately 6-10 days apart. Mature tomatoes were harvested 14 days after the final treatment. Tomato leaf samples were taken soon after the application solution dried (day 0). Tomato leaf and fruit samples were collected before and after all applications, and 3, 7, and 14 (final harvest) days after the final application. Total ^{14}C-residues were determined by liquid scintillation counting (LSC). Solvent-rinsed radioactivity was determined following combustion. HPLC and TLC were used to analyze crop extracts, while LC-MS was used for identification of significant ^{14}C-residues. Chiral HPLC analysis was used to determine the enantiomeric ratio of significant ^{14}C-residues.

Results

The total residues in tomato fruit were up to 0.14 mg eq/kg. At harvest, the mature fruit contained 0.08 mg eq/kg. The majority of the radioactivity (>87 %TRR) in the fruit was present as surface dislodgeable residues (acetonitrile rinse). After removal of the surface residues, most fruit samples contained 0.01 mg eq/kg.

In the surface rinse, more than 87% of the TRR was identified as DPX-KN128/IN-KN127. No significant metabolites of DPX-JW062 were found in any of the tomato fruit samples.

Parent compound isolated from leaf extracts from the samples collected before the second application and at harvest, 14 days after final application, were subjected to chiral HPLC analysis, which demonstrated that the two enantiomers remained in a 1:1 ratio.

Table B.7.2-9 : Total Radioactive Residue in tomato fruit treated with [TMP(U)-^{14}C]DPX-JW062

Sampling Interval	[TMP(U)-^{14}C]DPX-JW062 Equivalents %TRR (ppm)			
Day	Surface Dislodgeable[2]	Tissue Extractable	Tissue Unextractable	Total ppm
Before 2nd treatment	95.3 (0.04)	NC[3]	4.7 (<0.01)	0.04
After 2nd treatment	96.7 (0.14)	NC	3.3 (<0.01)	0.14
Before 3rd treatment[4]	88.6 (0.11)	11.2 (0.01)	0.2 (<0.01)	0.12
After 3rd treatment	90.1 (0.08)	NC	9.9 (0.01)	0.09
Before 4th treatment	88.9 (0.05)	NC	11.1 (0.01)	0.06
After 4th treatment	93.8 (0.12)	NC	6.2 (0.01)	0.12
3 Days after 4th treatment	93.1 (0.13)	NC	6.9 (0.01)	0.14
7 Days after 4th treatment	93.0 (0.09)	NC	7.0 (0.01)	0.10
14 Days after 4th treatment	87.3 (0.07)	NC	12.7 (0.01)	0.08

[1] See Appendix 4, Tables 3 and 4 for raw data.

[2] At each sampling point, the entire sample of tomato fruit was rinsed with acetonitrile to determine the surface residues; the rinsed fruit was homogenized and combusted. Only one sample of the rinsed fruit, collected immediately before the 3rd treatment, contained TRR >0.01 ppm.

[3] "NC" means not conducted.

[4] A portion (*ca.* 100 g) of the rinsed fruit was extracted. Calculations to determine %TRR and total ppm were corrected for sample size.

Table B.7.2-10 : Total Radioactive Residue in tomato plant leaves treated with [TMP(U)-^{14}C]DPX-JW062

Sampling Interval	[TMP(U)-^{14}C]DPX-JW062 Equivalents % TRR (ppm)			
Day	Surface Dislodgeable[2]	Tissue Extractable	Tissue Unextractable	Total ppm
0	73.3 (3.28)	21.0 (0.94)	5.7 (0.25)	4.47
Before 2nd treatment	47.5 (2.05)	50.2 (2.16)	2.3 (0.10)	4.31
After 2nd treatment	89.1 (10.11)	10.2 (1.16)	0.7 (0.08)	11.35
Before 3rd treatment	75.3 (5.23)	23.8 (1.65)	0.9 (0.06)	6.94
After 3rd treatment	90.1 (4.72)	9.4 (0.49)	0.5 (0.03)	5.24
Before 4th treatment	87.2 (4.94)	11.7 (0.66)	1.1 (0.06)	5.67
After 4th treatment	83.4 (7.96)	15.6 (1.49)	1.0 (0.10)	9.55
3 Days after 4th treatment	99.7 (8.75)	0.3 (0.03)	<0.1 (<0.01)	8.78
7 Days after 4th treatment	81.8 (4.87)	17.1 (1.02)	1.1 (0.06)	5.95
14 Days after 4th treatment	56.2 (2.38)	41.1 (1.74)	2.7 (0.11)	4.23

1 See Appendix 4, Tables 3 and 4 for raw data.

2 At each sampling point, the entire sample of tomato leaves was rinsed with acetonitrile to determine the surface residues; a portion (typically 50 g) of the rinsed leaves was extracted. Calculations to determine %TRR and total ppm were corrected for sample size.

In tomato leaf samples, total residues ranged up to 11.4 mg eq/kg (after the second treatment). Most of the total residues were surface dislodgeable from tomato leaves, and ranged from 2.05-10.1 mg eq/kg (47.5-89.1 %TRR). A minor amount of total residues was extractable, ranging from 0.03-2.16 mg eq/kg (0.3-50.2 %TRR). The amount of unextractable residue in tissues was <6%.

DPX-KN128/IN-KN127 was the major component in leaf rinses and extracts (>89%).

Table B.7.2-11 : Distribution of [TMP(U)-^{14}C]DPX-JW062 in tomato plant samples (fruit and leaves)

Sampling Interval	Tomato Leaves %TRR (ppm)			Tomato Fruit %TRR (ppm)		
	Surface Rinse	Tissue Extract	[^{14}C]JW062	Surface Rinse	Tissue Extract	[^{14}C]JW062
Day 0	73.3 (3.28)	21.0 (0.94)	94.3 (4.23)	NS[2]	NS	NS
Before 2nd treatment	47.5 (2.05)	50.2 (2.16)	97.7 (4.21)	95.3 (0.04)	NC[2]	95.3 (0.04)
After 2nd treatment	89.1 (10.11)	10.2 (1.16)	99.3 (11.27)	96.7 (0.14)	NC	96.7 (0.14)
Before 3rd treatment	75.3 (5.23)	23.8 (1.65)	97.1 (6.74)	88.6 (0.11)	11.2 (0.01)	99.8 (0.12)
After 3rd treatment	90.1 (4.72)	9.4 (0.49)	99.5 (5.21)	90.0 (0.08)	NC	90.1 (0.08)
Before 4th treatment	87.2 (4.94)	11.7 (0.66)	98.9 (5.61)	88.9 (0.05)	NC	88.9 (0.05)
After 4th treatment	83.4 (7.96)	15.6 (1.49)	99.0 (9.46)	93.8 (0.11)	NC	93.8 (0.11)
3 Days after 4th treatment	99.7 (8.75)	0.3 (0.03)	99.9 (8.77)	93.1 (0.13)	NC	93.1 (0.13)
7 Days after 4th treatment	81.8 (4.87)	8.6 (0.51)	89.6 (5.33)	93.0 (0.09)	NC	93.0 (0.09)
14 days after 4th treatment	56.2 (2.38)	41.1 (1.74)	97.3 (4.12)	87.3 (0.07)	NC	87.3 (0.07)

[1] Summary of chromatographic data provided in Tables 1 thru 4 in Appendix 4 of this report.

[2] "NS" means not sampled; "NC" means not conducted.

Conclusions

Total residues in mature tomato fruits amounted up to 0.08 mg eq/kg. More than 87% of the total residues in the fruit was surface-dislodgeable and consisted almost entirely of the DPX-KN128/IN-KN127.

In leaves, total residues amounted up to 11.4 mg eq/kg. A majority of the total residue (47.5-99.7%) was surface-dislodgeable and a minority of the non-dislodgeable residue (0.3-50.2 %) was extractable from the fruit. DPX-KN128/IN-KN127 was the major component of the residue (>89%).

Chiral HPLC analysis of the residues in tomatoes showed that the enantiomers remained in a 1:1 ratio.

Guidelines and limitations

The study is suitable for evaluation.

B.7.2.2 - Poultry

STUDY 1

Characteristics

Reference	: [redacted] 1997	exposure	: 5 consecutive days
type of study	: absorption, distribution, excretion, and metabolism	dose	: equal to 10 (and 65)[1] mg/kg diet
year of execution	: 1994-1997 (report 1997)	vehicle	: none
test substance	: [indanone-1-^{14}C]DPX-JW062 or [trifluoromethoxyphenyl ring -^{14}C]DPX-JW062, purity >95%	GLP statement	: yes
Route	: oral	guideline	: no guideline in force
Species	: laying hen (white leghorn)		
group size	: 5		

[1] No data were reported of the study performed with the high dose level.

Study design

Groups of laying hens (White leghorn) were dosed with one of two radiolabeled forms of DPX-JW062, in capsule form, once per day for five consecutive days at a dose of 10 mg/kg diet (ca. 50 N). Eggs and excreta were sampled daily. Eggs were separated into white and yolk. Muscle (thigh and breast), fat, liver, skin with fat, gizzard, gastrointestinal tract with contents, and blood samples were taken at sacrifice, within 24 hours after the last dosing. Total ^{14}C -residues were determined by liquid scintillation counting (LSC). DPX-KN128/IN-KN127 and metabolites were isolated by HPLC and their chemical nature was characterised by HPLC (retention time matching with standards), LC/MS and LC/NMR.

Results

The total recovery of the administered radioactive dose was approximately 89.3-89.7%. The majority of the radioactivity was found in excreta (87.0-87.6%) with a relatively rapid elimination rate.

The residue levels in organs, tissues, and excreta are shown in table 8.2.2-1.

Table B.7.2-12: Distribution of 14C-residues in various matrices of laying hens following an oral dose of 10 mg DPX-JW062/kg diet for 5 consecutive days

Matrix	Total tissue levels	
	mg eq/kg	% of dose
Excreta	ND	87.0-87.6

Matrix	Total tissue levels	
	mg eq/kg	% of dose
Egg white	0.02-0.10	0.10-0.21
Egg yolk	0.01-0.33	0.18-0.19
Liver	0.11-0.15	0.07-0.09
Muscle (breast and thigh)	0.02-0.04	0.16-0.18
Skin with fat	0.21-0.25	0.16
Fat	0.46-0.51	0.84-0.88
Gizzard	0.08-0.13	0.04-0.07
TOTAL	ND	89.3-89.7

ND, not determined

Eggs: In egg white, 90.6-98.2 %TRR was extractable and 1.82-9.45 %TRR remained unextracted. In egg yolk, 78.5-94.1 %TRR was extractable and 5.9-21.5 %TRR remained unextracted.

In egg white, 32.3-39.5 %TRR, and in egg yolk 61.3-80.9 %TRR was characterised and identified.

Multiple components were observed in egg white, with none exceeding 0.02 mg eq/kg. IN-MK638 and IN-KB687 were detected in egg white at the level of <0.01 and 0.01 mg eq/kg, respectively.

Metabolites identified in egg yolk were IN-KG433, IN-KT319, IN-JU873, 5-OH-JT333, Metabolite F, DPX-KN128/IN-KN127, IN-JT333, IN-MK638, and IN-KB687. None of these individual components was above 0.05 mg eq/kg. The 120h egg yolk pellet (0.07 mg eq/kg) was further characterised by protease digestion followed by 6M HCI acid hydrolysis. Upon protease treatment 0.03 mg eq/kg was released, which was not further identified. After acid treatment, all the components were <0.01 mg eq/kg.

Muscle: in thigh and breast muscle, 86.6-93.5 %TRR was extractable and 6.49-13.4 %TRR remained unextracted.

A total of 58.4-78.5 %TRR was characterised and identified in thigh and breast muscle.

Metabolites identified in thigh and breast muscle were IN-KG433, IN-KT319, IN-JU873/ 5-OH-JT333, Metabolite F, DPX-KN128/IN-KN127, IN-JT333, IN-MK638, and IN-KB687. None of the individual components occurred above a concentration of 0.01 mg eq/kg.

Skin and fat: in skin with fat, and fat, more than 98 %TRR was extractable.

A total of 76.9-92.0 %TRR was characterised and identified in skin with fat and fat.

The major residue component in skin with fat, and fat was metabolite F at about 0.19-0.22 mg eq/kg in fat, and at 0.04-0.06 mg eq/kg in skin with fat (37.8-45.3 %TRR and 16.2-29.3 %TRR, respectively).

Other metabolites identified in skin with fat and fat were IN-KG433/IN-MN969 (0.01-0.03 mg eq/kg), IN-KT319 (0.01-0.03 mg eq/kg), IN-JU873 (0.01-0.02 mg eq/kg), 5-OH-JT333 (0.03-0.08 mg eq/kg), IN-JT333 (0.03-0.09 mg eq/kg), IN-MK638 (0.01 mg eq/kg), and IN-KB687 (0.01 mg eq/kg). DPX-KN128/IN-KN127 was present in levels of 0.02-0.04 mg/kg.

Chiral analysis was performed on both the enantiomer pairs DPX-KN128/ IN-KN127 and the metabolite IN-JT333 (i.e., enantiomer pairs IN-KN125/IN-KN124). For DPX-KN128/IN-KN127 the ratios for the bioactive/inactive components were 2.8-3.2/1, and for the metabolite 1.8-2.1/1. The results indicate enrichment of the active enantiomers in fat for both DPX-KN128/IN-KN127 and the metabolite IN-JT333.

Liver: 51.4-65.0 %TRR was extractable and 35.0-48.6 %TRR remained unextracted.

A total of 36.6-46.9 %TRR was directly characterised and identified in the liver.

Metbolites identified in the liver were IN-KG433/ IN-MN969/ IN-KT319 (0.01mg eq/kg), IN-JU873/

5-OH-JT333 (0.02-0.03 mg eq/kg), Metabolite F (0.01 mg eq/kg), IN-MK638 (0.01 mg eq/kg), and IN-KB687 (0.01 mg eq/kg). DPX-KN128/IN-KN127 was present at a level of 0.01 mg/kg. The insecticidally and toxicologically relevant metabolite IN-JT333 was not detectable (<0.006 mg eq/kg).

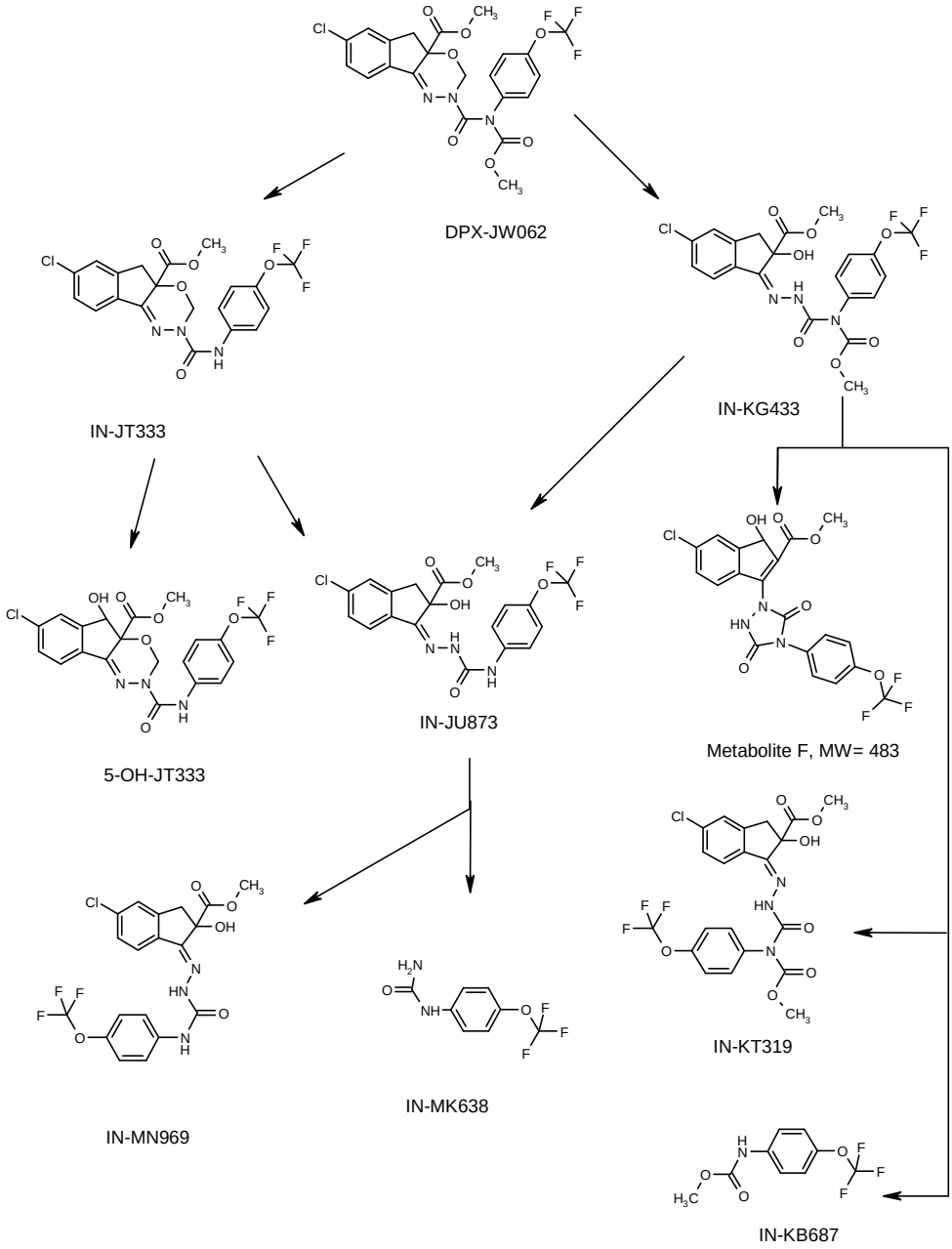
Protease treatment of the unextracted material released a further 20.2-28.8%, while strong acid treatment (6M HCl) released ca. 41%. Identification of the residues revealed no component above 0.01 mg eq/kg.

Gizzard: 71.1-81.9 %TRR was extractable, and 18.1-29.0 %TRR remained unextracted.
A total of 50-7-56.3%TRR characterised and identified in the gizzard.
Metbolites identified in the gizzard were IN-KG433/ IN-MN969/ IN-KT319/ 5-OH-JT333 isomer (0.01mg eq/kg), IN-JU873/5-OH-JT333 (0.01 mg eq/kg), Metabolite F (0.01 mg eq/kg), IN-MK638 (0.01 mg eq/kg), and IN-KB687 (0.01 mg eq/kg). DPX-KN128/IN-KN127 was present at a level of 0.02 mg eq/kg.

Summary of metabolic pathways

The metabolism of DPX-JW062 in the hen involves the opening of the oxadiazine ring to form IN-KG433 and related isomer IN-KT319. IN-KG433 was the major metabolite in the excreta and was found in all tissues. IN-KG433 appears to be further metabolised via hydration/rehydration steps to yield metabolite F and/or forms IN-JU873. The N-carboxymethoxy group is also metabolised on the parent compound to yield IN-JT333, which is further oxidised in the 5-position and/or opens the oxidiazine ring to form IN-JU873 and related isomer IN-MN969. Cleaved products IN-KB687 and IN-MK638 are also found in small amounts.

Proposed metabolic pathway in laying hens



Conclusions

DPX-JW062 is very extensively metabolised in the laying hen. The metabolism in the hen mainly involves three types of conversions, the opening of the oxadiazine ring to form IN-KG433, which is further metabolised, the loss of N-carboxymethoxy moiety to form IN-JT333, and hydroxylation.

Transfer of residues to eggs and tissues is relatively low. Highest residue levels are found in fat, skin with fat, and egg yolk. An extensive number of metabolites is found in eggs and tissues, including the insecticidally and toxicologically relevant component IN-JT333. DPX-KN128/IN-KN127 is present in small amounts. Metabolite F is a major residue component of eggs, fat, and skin with fat, and is not found in rats, ruminants or plants**.**

In Article 12 of indoxacarb (EFSA Journal 2011;9(8):2343) EFSA is of the opinion that further information on the identity of metabolite F, which might be present in significant amounts in poultry, is still required. In the absence of such information, the residue definition for risk assessment in poultry should be considered as tentative. RMS agrees.

Nevertheless, the general metabolic pathways appeared comparable in rodents and ruminants. Chiral analysis indicates enrichment of the active enantiomers in fat for both DPX-KN128/IN-KN127 and the metabolite IN-JT333.

Guidelines and limitations

It is noted that residues in egg white were only partly identified (in total ca. 36%).
Further characterisation of the residues in egg-white, and the kidneys is not required because no significant residues are expected in poultry considering the exaggerated dose rate, and because of the anticipated TMDI for poultry.
The study is suitable for evaluation.

B.7.2.3 - Lactating ruminants

STUDY 2

Characteristics

reference	: [redacted] 1997	exposure	: 5 consecutive days (via capsules)
type of study	: absorption, distribution, excretion, and metabolism	dose	: 10 mg/kg diet
year of execution	: 1994-1997 (report 1997)	vehicle	: D-glucose
test substance	: [indanone-1-^{14}C]DPX-JW062 and [trifluoromethoxyphenyl ring -^{14}C]DPX-JW062[1], purity >99%	GLP statement	: Yes
route	: oral	guideline	: no guideline in force
species	: lactating cow (Friesian)		
group size	: 2		

[1] Ratio DPX-KN128/ IN-KN127 = 1:1

Study design

Two adult lactating Friesian cows (480-490 kg) were dosed each with one of the two radiolabeled forms of DPX-JW062 once per day for five consecutive days at a dose equal to 10 mg/kg diet (ca. 9 N). Urine and feces were collected daily from each animal. Milk was collected daily from each animal in the morning and afternoon. Milk from the morning collection following the final dose was separated into skim milk and cream. At 23.5 hours after the final dose, the animals were sacrificed and liver, kidneys, bile, gastrointestinal contents, muscle samples, and fat samples were collected. Total ^{14}C -residues were determined by liquid scintillation counting (LSC) as the sum of extracted and unextracted residues. HPLC and TLC were used to analyze extracts while HPLC retention time matching and LC-MS were used for characterisation and identification of significant ^{14}C-residues. Chiral HPLC analysis was used to determine the enantiomeric ratio of DPX-KN128 and IN-KN127.

Results

Urinary and fecal excretion was the major elimination route for DPX-JW062 accounting for 72.6-80.0% of the total administered dose. Fecal excretion represented 53.3-60.2% and urinary excretion 19.3-19.8% of the total dose after 5 days. In tissues, 0.9% of the administered dose was found, and in the milk 0.7-0.8%. The total tissue burden (including milk) accounted for 1.6-1.7% of the total dose, after 5 days.

The residue levels in organs, tissues, and excreta are presented in table 8.2.3-1.

Table B.7.2-13 Distribution of ^{14}C-residues in organs and tissues of lactating cows following oral doses of 10 mg DPX-JW062/kg diet for 5 consecutive days

Matrix	Total tissue levels

	mg eq/kg	% of dose
Urine	ND	19.3-19.8
Feces	ND	53.3-60.2
Milk	0.13-0.18	0.7-0.8
Liver	0.537-0.689	0.447-0.517
Kidneys	0.288-0.365	0.03-0.05
Muscle		
Foreleg	0.04-0.05	0.005-0.006
Rump	0.03-0.04	0.004
Fat		
Omental	0.65-0.80	0.08-0.09
Perirenal	1.1	0.06-0.09
Subcutaneous	0.03-0.06	0.003-0.005
TOTAL	ND	74.3-81.6

ND, not determined

Milk: total residue levels ranged from 0.13-0.18 mg eq/kg in whole milk, 1.74 mg eq/kg in cream, and 0.086-0.123 in skimmed milk after 5 days.

In total, 52.9-90.4 %TRR in milk was extractable and 9.6-47.1 %TRR remained unextracted.

A total of 45.6-77.2 %TRR in milk was characterised and identified.

The major radiolabeled residue in milk was unchanged DPX-KN128/IN-KN127 (0.028 mg eq/kg). IN-JT333, an insecticidally active metabolite, was not observed (<0.01 mg eq/kg). lN-MP819, a non-chiral, insecticidally inactive compound, was found in low concentrations (0.016- 0.023 mg eq/kg). No other residue component was present at a concentration higher than 0.01 mg eq/kg. Chiral HPLC analysis of isolated DPX-KN128/IN-KN127 indicated a ratio of DPX-KN128 to IN-KN127 of about 2: 1.

Muscle: in foreleg muscle, 80.5 %TRR was extractable while 19.5 %TRR remained unextracted.

A total of 53.7-57.0 %TRR in foreleg muscle was characterised and identified.

The DPX-KN128/IN-KN127 represented 28.7-37% of the TRR, equivalent to 0.01-0.02 mg/kg. IN-JT333 was not detected and neither were any other metabolites (<0.01 mg eq/kg).

Liver: 54.7-58.3 %TRR was extractable before protease hydrolysis, and 41.7-45.3 %TRR was unextracted. After protease treatment of the liver, an additonal 23.3-26.5 %TRR was extractable. A total of 15.2-22.0 %TRR remained unextractable after protease hydrolysis.

A total of 25.5-41.1 %TRR in liver was characterised and identified.

DPX-KN128/IN-KN127 was the major radiolabeled residue, at a level of 0.038- 0.079 mg/kg. IN-JT333 was not detected (<0.01 mg eq/kg). Hydroxylated parent 5-HO-DPX-JW062 (diastereomers) and the glucuronide of hydroxylated parent were the only metabolites with concentrations higher than 0.01 mg eq/kg. 5-HO-DPX-JW062 was present at 0.030-0.063 mg eq/kg. The glucuronide of 5-OH-DPX-JW062 was present at 0.019-0.024 mg eq/kg. The sum of IN-MF014 and IN-MN470, metabolites containing only the TMP label, accounted for 0.060 mg eq/kg. Several unknown components were present in levels up to 0.038-0.052 mg/kg.

Kidneys: 70.4-85.8 %TRR was extractable before protease hydrolysis, and 14.2-29.6 %TRR remained unextracted. After protease treatment of the kidneys, an additonal 9.9-18.9 %TRR was extractable. A total of 4.3-10.7%TRR remained unextractable after protease hydrolysis.

A total of 48.2-74.3 %TRR in the kidneys was characterised and identified.

DPX-KN128/IN-KN127 represented 0.153-0.177 mg/kg. Chiral analysis of isolated DPX-JW062 indicated a ratio of about 2:1-2.5: 1 for DPX-KN128 versus IN-KN127. IN-JT333 was not detected (<0.01 mg eq/kg). 5-

HO-DPX-JW062 diastereomers were tentatively identified by retention time matching and accounted for 0.023-0.037 mg eq/kg. Several unknown components were present in levels up to 0.034-0.043 mg eq/kg.

Fat: in perirenal fat, 94.0-97.1 %TRR was extractable while 2.9-6.0 %TRR remained unextracted.

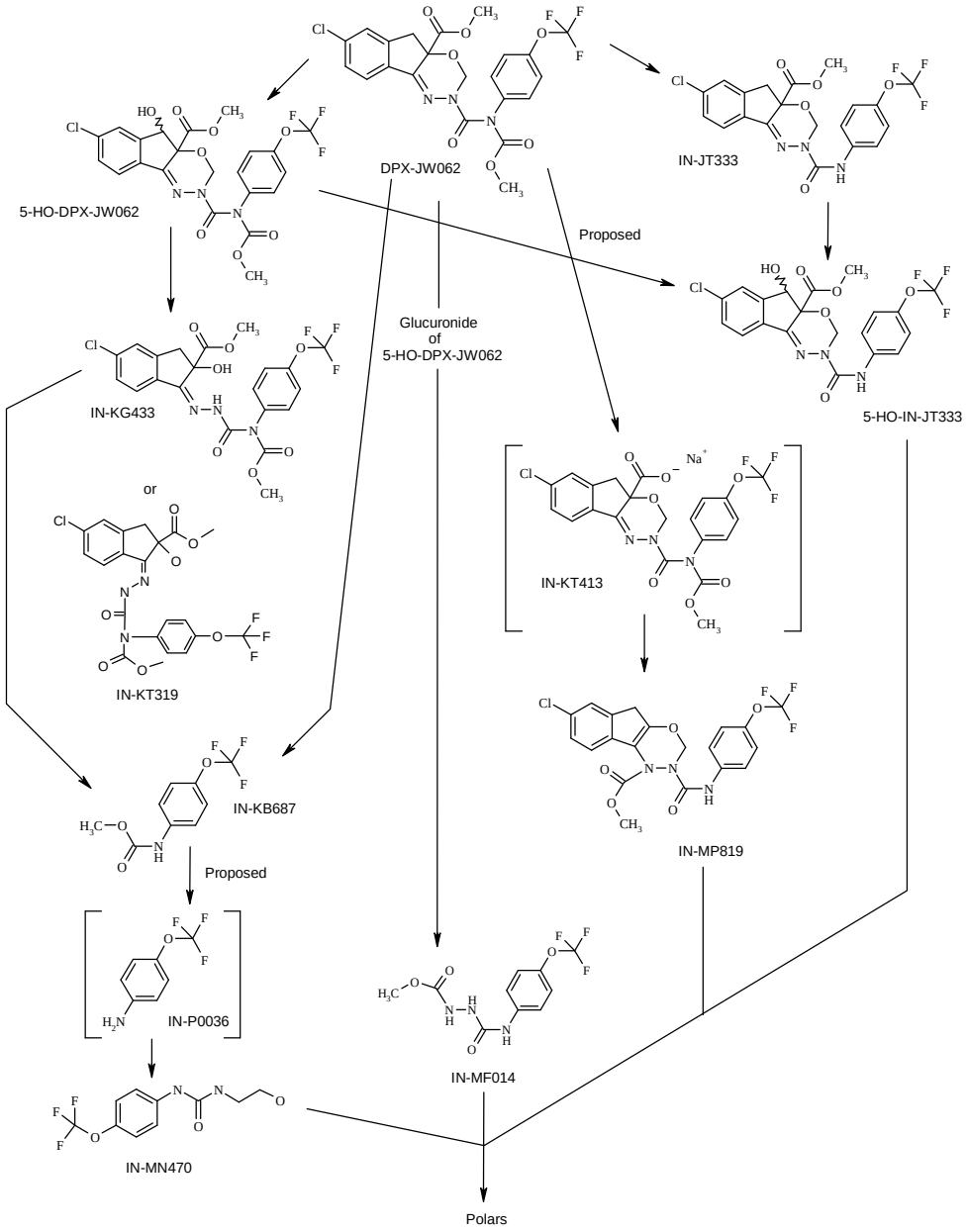
A total of 72.7-86.4 %TRR in perirenal fat was characterised and identified.

DPX-KN128/IN-KN127 represented about 0.72-0.89 mg/kg. INJT333 was present at concentrations of 0.06 mg -0.08 mg eq/kg.

Summary of metabolic pathways

The metabolism of DPX-JW062 in the cow proceeded by several pathways. Hydrolysis at the carbomethoxy group of DPX-JW062 leads to formation of IN-JT333, a metabolite also found in the rat and poultry metabolism studies. The formation of IN-MP819, found in milk, is thought to be due to rearrangement of IN-KT413, the free acid of DPX-JW062. The oxadiazine ring of DPX-JW062 opens to form IN-KG433 and its geometrical isomer IN-KT319. Parent and IN-JT333 were also hydroxylated in the indanone ring to form the diastereomeric pair of 5-OH-DPX-JW062 and 5-HO-IN-JT333. HO-DPX-JW062 can then be conjugated with glucuronic acid to form the glucuronide. Finally, the oxadiazine ring was cleaved leading to IN-KB687 and IN-MF014. IN-KB687 can then form the ethanolamine adduct IN-MN470. IN-KB687, IN-MF014, and IN-MN470 contained the TMP ring only. Metabolism of DPX-JW062 in the cow is consistent with rat and poultry metabolism.

Proposed metabolic pathway in lactating cow:



DPX-JW062 is extensively metabolised in the lactating cow. The general metabolic pathway involves hydrolysis of the carbomethoxy group, oxidation of the indanone ring, cleavage of the oxidiazine ring, and conjugation. Transfer of residues to milk and tissues is relatively low. Highest residue levels are found in fat. DPX-KN128/IN-KN127 is the major residue component in all tisssues, organs, and excreta. The insecticidally and toxicologically relevant metabolite IN-JT333 is present as a minor component in fat only.

Chiral analyses indicate some enrichment of the insecticidally active component DPX-KN128 (from 50% to ca. 70%).

Guidelines and limitations

It is noted that residues in foreleg muscle were only partly identified (in total ca. 55%). In the liver residues were also only partially identified (in total ca. 33%). This is partly due to the fact that the residues released by protease treatment of the liver were not further identified. Further identification of the residues in foreleg muscle and liver is not required because no significant residues are expected in ruminants considering the exaggerated dose rate, and because of the anticipated TMDI for cattle.

The study is suitable for evaluation.

B.7.2.4 - Pigs

No studies were submitted on the metabolism, distribution, and expression of residues in pigs.

B.7.2.5 - Fish

According to Commission Regulation 283/2013, metabolism studies in fish may be required where the plant protection product is used in crops whose parts or products, also after processing, are fed to fish and where residues in feed may occur from the intended applications. The exact conditions under which such a study should be performed are further described in the Working document of the EU Commission SANCO/11187/2013, rev. 3 on the nature of pesticide residues in fish. The document specifies that the accumulation of compounds with low lipophilicity via the diet is known to be negligible and that fish metabolism studies are therefore only required for active substances with a log POW equal or greater than 3. The log POW for indoxacarb (DPX-KN128) is 4.65. However, no EU guidelines are available for now.

B.7.3 - MAGNITUDE OF RESIDUE TRIALS IN PLANTS

B.7.3.1 - Maize

B.7.3.1.1 - Identification of critical GAPs

Indoxacarb is intended for uses on maize and the representative critical GAP is reported in the table below.

Table B.7.3-1: Critical GAP for indoxacarb on maize

Crop	Region	Outdoor/ Protected	Application	Number of applications (days interval)	Rate (g as/ha)	BBCH at last application/ PHI
Maize	EU (North and South)	Outdoor	Hydraulic ground directed boom	2 (20days)	37.5	BBCH 34-77

A total of 21 supervised residue trials were conducted on maize grain on over more than two growing seasons in southern and northern Europe. Some of these trials were initially assessed in the EFSA Journal 2011;9(8):2343.
Among these trials, 17 (9SEU and 8 NEU) residue trials were considered suitable to assess the magnitude of indoxacarb in maize grains, and 16 (12 SEU and 4 NEU) residue trials are available to assess the magnitude of residue in maize forage/silage.
In DuPont-9777 study, four trials were carried out both with the DPX-MP062 30WG and DPX-MP062 150SC formulation, at each time the more critical residue data was selected.
As regards forage, residue data were selected at PHI 14 on green plant allowing 2 weeks (14 days) for the maize to develop from BBCH 69 (last treatment) to BBCH 86 (mid to late dough stage when maize is typically used as forage[1].

[1] The OECD Overview document (2009) gives the following definition: Corn forage (field and pop). Cut sample (whole aerial portion of the plant) at late dough/early dent stage (black ring/layer stage for corn only).Growth stages of mono-and dicotyledonous plants from the BBCH monograph, Federal Biological Research Centre for Agriculture and Forestry, 2001 gives the following growth stage descriptions for maize:BBCH 85 Dough stage: kernels yellowish to yellow (variety dependent),about 55% dry matter, BBCH 87 Physiological maturity: black dot/layer visible at base of kernels, about 60% dry matter. Allowing 2 weeks (14 days) for the maize to develop from BBCH 69 (last treatment) to BBCH 86 (mid to late dough stage when maize is typically used as forage) the 14 day forage data is compiled from DuPont-35172 for the evaluations in this table as the data best representative of field corn forage as described by the OECD overview document.

B.7.3.1.2 - Residues resulting from supervised trials

Previous evaluation:	*Studies not submitted to the EU for the first time and listed under "Documents Submitted" and already assessed in EFSA Journal 2011;9(8):2343.*

DuPont-6006 and DuPont-9777

Author (s)	Annex point /reference n°	Year	Title – Source – Company - Report n° GLP compliance - Published or not
Guinivan, R. M.Kennedy, C. A. Enriquez, M.	CA, 6.3.1/03	2003	**Title :** Combined decline and magnitude of residues of DPX-KN128 (indoxacarb) together with IN-KN127 in maize (green plant and grain) following applications of DPX-MP062 30 WG – Europe, season 2001 **Source :** DuPont **Company :** DuPont de Nemours and company **Report N°:** DuPont-6006 **GLP compliance :** Yes **Unpublished**

Acceptability	Test guideline	Deviations
Yes	European Union Directive 91/414/EEC, Residue Chemistry	**None** Study dates May 2001 to June 2003

Author (s)	Annex point /reference n°	Year	Title – Source – Company - Report n° GLP compliance - Published or not
Guinivan, R. M.Kennedy, C. A. Enriquez, M.	CA, 6.3.1/04	2003	**Title :** Combined decline and magnitude of residues of DPX-KN128 (indoxacarb) together with IN-KN127 in maize (green plant and grain) following applications of DPX-MP062 30 WG and DPX-MP062 150 SC – Europe, season 2002 **Source :** DuPont **Company :** DuPont de Nemours and company **Report N°:** DuPont-9777 **GLP compliance :** Yes **Unpublished**

Acceptability	Test guideline	Deviations
Yes	European Union Directive 91/414/EEC, Residue Chemistry	**None** Study dates May 2002 to June 2003

Materials and method

The purpose of this study was to determine the decline and magnitude of residues of DPX-KN128/IN-KN127 in maize (green plant and grain) specimens, following treatment with DPX-MP062 30WG, a water-dispersible granule formulation containing 30% DPX-KN128 insecticidal active ingredient, under maximum use pattern in Europe. In addition, for four of the sites, additional green plant was harvested, chopped, and ensiled for 3 weeks to produce silage for residue analysis.

During the season 2001, 2 magnitudes of residue and 5 decline tests were carried out in Europe in Greece, Italy, Spain and France.
Additionally, 6 magnitudes of residue and 4 decline tests were carried out in Europe during the 2002 season in Greece, Italy, France and Germany.

Maize was treated twice at growth stages BBCH 55 and BBCH 73-77, with an interval of 2 weeks to one month, at a rate of approximately 37.5 g DPX-KN128/ha
Sampling was realized according to EU Guidelines, appendix B. The samples were frozen and kept under –18°C until analyzed.
Specimens were stored at about -20°C or below for periods less than 11 months for green plant/grain and 10 months for silage, respectively.

Analytical method (GC/MSD, AMR 3493-95 Suplement I) using GC/MS was used to analyse Indoxacarb (DPX-KN128 and IN-KN127, only one signal) in maize (green plant, grain and silage). This analytical method has been fully validated with an acceptable LOQ of 0.01mg/kg in each matrice.

Results

Details of the application and residue information are summarised in the following table.
For the second study, only data related to the use of the formulation WG are reported.
No residue of Indoxacarb at or above the limit of quantification of the method was found in any of the untreated samples.

Summary of data from residue trials

SOUTHERN RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)

Content of a.i. (g/kg or g/l) : 300 g/kg
Formulation (e.g. WP) : WG
Commercial product (name) : DPX-MP062 30 WG (Steward)
Applicant :

Active ingredient : DPX-KN128 (as Indoxacarb)
Crop / crop group : Maize

Indoors / outdoors : Outdoor
Other a. s. in formulation (common name and content) : None
Residues calculated as : DPX-KN128/IN-KN127

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1) Sowing or planting 2) Flowering 3) Harvest	Application rate per treatment			Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
			kg a.s./ha	Water l/ha	kg a.s./hl						
	(a)	(b)				(c)		(a)		(d)	(e)
SOUTH ZONE											
DuPont-6006 57300 Nea Malgara Greece	Maize/Goldylan	/	0.0359	672	0.005	2 treatments 18 Jul.2001	BBCH 75	Green plant	0.80 0.62 0.46 <u>0.44</u> 0.42	0 3 7 14 21	
								Grain	<u><0.01*</u> <0.01 <0.01 <u><0.01</u> <0.01	0 7 14 27 43	
DuPont-6006 20072 Castiglione d'Adda Italy	Maize/Balka	/	0.0392	707	0.006	2 treatments 3 Aug.2001	BBCH 77	Green plant	0.20 0.29 0.28 0.14 0.20	0 3 7 14 25	
								Grain	<u><0.01*</u> <0.01 <0.01 <u><0.01</u> <0.01	0 7 14 28 40	Silage of plant harvested at 25 days PHI
								Silage	<u>0.28</u>	46	

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1) Sowing or planting 2) Flowering 3) Harvest	Application rate per treatment kg a.s./ha	Water l/ha	kg a.s./hl	Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
	(a)	(b)				(c)		(a)		(d)	(e)
DuPont-6006 20090 Caleppio di Settala Italy	Maize/Lycia	/	0.0381	688	0.006	2 treatments 2 Aug.2001	BBCH 73	Green plant Grain Silage	0.11 <0.01 0.10	33 47 54	 Silage of plant harvested at 33 days PHI
DuPont-6006 20060 Mulazzano Italy	Maize/Madera	/	0.0372	672	0.006	2 treatments 21 Aug.2001	BBCH 74	Green plant Grain Silage	0.26 <0.01 0.16	21 31 42	 Silage of plant harvested at 21 days PHI
DuPont-6006 02620 Minaya Spain	Maize/Brasco	/	0.0383	627	0.006	2 treatments 23 Aug.2001	BBCH 77	Green plant Grain Silage	0.65 0.15 0.12 0.11 <0.01* <0.01 <0.01 <0.01 <0.01 0.037	0 3 7 14 0 7 14 28 48 35	 Silage of plant harvested at 14 days PHI
DuPont-6006 32130 Noilhan South France	Maize/Voxxan	/	0.0386	299	0.013	2 treatments 20 Aug.2001	BBCH 77	Green plant Grain 	0.51 0.57 0.49 0.048 0.028 <0.01* <0.01 <0.01 <0.01 <0.01	0 3 7 14 30 0 7 14 28 44	
DuPont-9777 57200 Profitis Greece	Maize/Sigma	/	0.0381	710	0.005	2 treatments 12 Aug.2002	BBCH 75	Green plant Grain	0.069 <0.01	18 32	
DuPont-9777 20090 Caleppio di Settala Italy	Maize/Tevere	/	0.0380	687	0.006	2 treatments 13 Aug.2002	BBCH 77	Green plant Grain	0.14 0.16 0.16 0.094 0.041 <0.01	0 3 7 14 21 36	

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1) Sowing or planting 2) Flowering 3) Harvest	Application rate per treatment			Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
			kg a.s./ha	Water l/ha	kg a.s./hl						
	(a)	(b)				(c)		(a)		(d)	(e)
DuPont-9777 32220 Lombez South France	Maize/LG 3457	/	0.0415	428	0.010	2 treatments 22 Aug.2002	BBCH 75	Green plant Grain	0.11 <u>≤0.01</u>	21 40	

NORTHERN RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)

Active ingredient : DPX-KN128 (as Indoxacarb)
Crop / crop group : Maize

Content of a.i. (g/kg or g/l) : 300 g/kg
Formulation (e.g. WP) : WG/SC
Commercial product (name) : DPX-MP062 30 WG/DPX-MP062 150SC
Applicant :

Indoors / outdoors : Outdoor
Other a. s. in formulation
(common name and content) : None
Residues calculated as : DPX-KN128/IN-KN127

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1) Sowing or planting 2) Flowering 3) Harvest	Application rate per treatment			Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
			kg a.s./ha	Water l/ha	kg a.s./hl						
	(a)	(b)				(c)		(a)		(d)	(e)
NORTH ZONE											
DuPont-6006 37390 Charentilly North France	Maize/DK 295	/	0.0408	528	0.008	2 treatments 27 Aug.2001	BBCH 75	Green plant Grain	0.72 0.30 0.21 <u>0.18</u> 0.15 <u><0.01*</u> <0.01 <0.01 <u><0.01</u> <0.01	0 3 7 14 25 0 7 14 28 45	
DuPont-9777 51240 Marson North France	Maize/Pandora	/	0.0405	418	0.010	2 treatments 29 Aug.2002	BBCH 77	Green plant Grain	0.28 <u><0.01</u>	28 46	

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety	Date of 1) Sowing or planting 2) Flowering 3) Harvest	Application rate per treatment			Dates of treatments or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
			kg a.s./ha	Water l/ha	kg a.s./hl						
	(a)	(b)				(c)		(a)		(d)	(e)
DuPont-9777 37340 Ambillou North France	Maize/Monumental	/	0.0375	483	0.008	2 treatments 23 Aug.2002	BBCH 75	Green plant Grain	0.22 <0.01	11 53	
DuPont-9777 51220 Brimont North France	Maize/Franki	/	0.0400	413	0.010	2 treatments 23 Jul.2002	BBCH 77	Green plant Grain	0.33 0.48 0.34 <0.26> 0.26 <0.010	0 3 7 14 28 46	
DuPont-9777 5597 Hüffelden-Nauheim Germany	Maize/Sagitta	/	0.0397	410	0.010	2 treatments 24 Aug.2002	BBCH 75	Green plant Grain	0.39 0.26 0.19 <0.22> 0.14 <0.01	0 3 7 14 20 65	
DuPont-9777 88524 Uttenweiler Germany	Maize/Palermo	/	0.0399	411	0.010	2 treatments 13 Aug.2002	BBCH 73-75	Green plant Grain	0.069 <0.01	11 53	
DuPont-9777 30872 Garbsen Germany	Maize/Ravenna	/	0.0388	400	0.010	2 treatments 13 Aug.2002	BBCH 74	Green plant Grain	0.35 0.22 0.19 0.12 <0.14> <0.01	0 3 7 14 29 61	
DuPont-9777 06386 Hinsdorf Germany	Maize/DK 298	/	0.0388	400	0.010	2 treatments 20 Aug.2002	BBCH 75	Green plant Grain	0.21 <0.01	26 50	

Remarks: (a) According to CODEX Classification / Guide
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (Label pre-harvest interval, PHI, underline)
(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

*** data on maize grain were also selected at PHI 0 (BBCH 77- immature grain) in order to extrapolate to sweet corn.**

Previous evaluation:	*Study submitted to the EU for the first time in this submission and listed under "Documents Submitted".*

DuPont-35172

Report:	CA, 6.3.1/01, Aitken A., 2014
Title:	Determination of the Decline of Residues of DPX-KN128 (Indoxacarb) along with IN-KN127 in Maize Forage Following Applications of DPX-MP062 30WG - Southern Europe – 2012
Document No:	DuPont-35172
Guidelines:	OECD Principles of Good Laboratory Practices ENV/MC/CHEM(98)17,OECD, Paris, 1998 Application of the GLP Principles to field studies ENV/JM/MONO(99)22
GLP	Yes

Acceptability	**Deviations**
Yes	No

Table B.7.3-2 Summary of global information on study 1

Comparative trials (between formulations, with and adjuvant/safener/synergist)	DPX-MP062-613 30 WG (300 g a.s./kg)
Number of applications	2
Dose (g as/ha)	37.5 g a.s./ha
Mode of application	Foliar spray
PHI (days) and/or growth stage (BBCH)	-0, 0, 7, 14, 21, 28 DALA
Analytical method (Code +Type)	AMR 4271-96 "Testing of DFG Method S 19 for the determination of residues of KN128 along with KN127 in crops which might be treated with DPX-MP062"
LoQ (mg/kg)	0.01 mg/kg

Table B.7.3-3 Summary of the study 1 trials

N° Trial		35172/01	35172/02	35172/03	35172/04	35172/05
North/South/Indoor		S	S	S	S	S
Decline (D)/Harvest (H) trial?		D	D	D	D	D
Formulation		WG	WG	WG	WG	WG
Equivalence between formulations		Y	Y	Y	Y	Y
Accordance with intended GAP		Y(1)	Y(1)	Y(1)	Y(1)	Y(1)
Correct sampling		Y	Y	Y	Y	Y
Samples frozen within 24h		Y	Y	Y	Y	Y
Storage period (in days)	Sample	<12 months	<13 months (375 d)	<12 months	<13 months (385 d)	<12 months
	Extract	≤1	≤1	≤1	≤1	≤1
Storage T° <-18°C		Y	Y	Y	Y	Y
Validated analytical method		Y	Y	Y	Y	Y
Negative controls		Y	Y	Y	Y	Y
Considered trial		Y	Y	Y	Y	Y
Remarks						

(1) 10 days interval between the two applications instead of 20 indicated.

Table B.7.3-4 Summary of data from residue trials for study 1

RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)
Notifier: E. I. du Pont de Nemours and Company
address 1 Wilmington, Delaware 19898, U.S.A.
address 2
address 3

Active ingredient : indoxacarb
Crop / crop group : Maize forage
Submission date :
Page :

Content of a.i. (g/kg or g/l) : 300 g a.i./kg
Formulation (e.g. WP) : WG
Commercial product (name) : STEWARD
Applicant : Foliar application using a boom sprayer

Indoors / outdoors : Outdoor
Other a. s. in formulation (common name and content) :
Residues calculated as : DPX-KN128/IN-KN127

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety (a)	Date of 1)Sowing or planting 2)Flowering 3) Harvest (b)	Application rate per treatment			Dates of treatments or no. of treatments and last date (c)	Growth stage at last treatment or date	Portion analysed (a)	Residues (mg/kg)	PHI (days) (d)	Remarks (e)
			kg a.s./ha	Water hl/ha	**g** a.s./hl						
DuPont-35172 Termens, Catalunya, 25670, Spain	Maize / PR 33Y-74	1. 20 Apr 12 2. NR 3. 21 Jul 12 28 Jul 12 04 Aug 12 11 Aug 12 18 Aug 12	38.43 38.74	511 517	7.52 7.49	A1 = 11 Jul 12 A2 = 21 Jul 12	61 69	Maize forage	0.37 0.61 0.82 <u>0.32</u> 0.080 0.13	-0 +0 7 14 21 28	
DuPont-35172 Tocina, Andalucia, 41340, Spain	Maize / MAS 58	1. 20 Feb 12 2. NR 3. 22 Jun 12 29 Jun 12 06 Jul 12 13 Jul 12 20 Jul 12	37.52 37.82	500 503	7.50 7.52	A1= 12 Jun 12 A2= 22 Jun 12	65 69	Maize forage	0.16 1.2 0.86 <u>0.77</u> 0.16 0.17	-0 +0 7 14 21 28	

DuPont-35172 Cervesina, 27050, Lombardia, Italy	Maize / Grizly	1. 27 Mar 12 2. NR 3. 23 Jul 12 30 Jul 12 06 Aug 12 13 Aug 12 20 Aug 12	38.13 38.74	510 517	7.48 7.49	A1 = 13 Jul 12 A2 = 23 Jul 12	67 69	Maize forage	0.19 1.9 0.30 <u>0.14</u> 0.081 0.057	-0 +0 7 14 21 28	
DuPont-35172 Graffignana 26813, Lombardia, Italy	Maize / Antiss	1. 25 Mar 12 2. NR 3. 23 Jul 12 30 Jul 12 06 Aug 12 13 Aug 12 20 Aug 12	37.82 39.04	502 521	7.49 7.49	A1 = 13 Jul 12 A2 = 23 Jul 12	67 69	Maize Forage	0.20 0.71 0.27 0.30 0.31 <u>0.34</u>	-0 +0 7 14 21 28	
DuPont-35172 Sandrans, Rhône Alpes, 01990, South France	Maize / Octet	1. 07 May 12 2. NR 3. 06 Aug 12 13 Aug 12 20 Aug 12 27 Aug 12 03 Sep 12	36.30 36.91	486 492	7.47 7.50	A1 = 27 Jul 12 A2 = 06 Aug 12	65 69	Maize Forage	0.099 0.84 0.36 <u>0.18</u> 0.12 0.087	-0 +0 7 14 21 28	

Remarks:
(a) According to CODEX Classification / Guide
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (Label pre-harvest interval, PHI, underline)
(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

B.7.3.1.4 - Conclusion on supporting data for the uses on maize

Maize is considered as a major crop in northern and southern parts of Europe.

8 residue trials conducted on maize in northern zone of EU and 9 residue trials conducted in southern zone of EU are available; they were conducted in accordance with the intended GAP. At harvest, residue levels of indoxacarb were always below the LOQ of 0.01mg/kg.

16 residue trials (4 NEU and 12 SEU) conducted on maize forage/silage in accordance with the intended GAP are available. Residue levels in forage/silage ranged from 0.14 mg/kg to 0.26 mg/kg in northern zone and from 0.048 mg/kg to 0.77 mg/kg in southern zone.

As a consequence, the proposed EU critical GAP on maize is adequately covered by available residue trials.

B.7.3.2 - Sweet corn

B.7.3.2.1 - Identification of critical GAPs

Indoxacarb is intended for uses on sweet corn and the representative critical GAP is reported in the table below.

Table B.7.3-5 Critical GAP for indoxacarb on sweet corn

Crop	Region	Outdoor/ Protected	Application	Number of applications (days interval)	Rate (g as/ha)	BBCH at last application/ PHI
Maize, sweet corn	EU (North and South)	Outdoor	Hydraulic ground directed boom	2 (20days)	37.5	BBCH 34-77

B.7.3.2.2 - Residues resulting from supervised trials

Previous evaluation:	*Submitted for the purpose of renewal AIRIII*

DuPont-13320

Report:	CA, 6.3.2/01, Giammarrusti, L., De Paoli, M., 2003
Title:	Decline of Residues of DPX-KN128 (lndoxacarb) together with IN-KN127 in Sweet Com Following Application of DPX-MP062 30WG - Italy, Season 2003
Document No:	DuPont- 13320
Guidelines:	OECD Principles of Good Laboratory Practices ENV/MC/CHEM(98)17,OECD, Paris, 1998 Application of the GLP Principles to field studies ENV/JM/MONO(99)22
GLP	Yes

Acceptability	Deviations
Yes	None

Table B.7.3-6 Summary of global information on study 1

Comparative trials (between formulations, with and adjuvant/safener/synergist)	DPX-MP062 30 WG (75% DPX-KN128 / 25% IN-KN127)
Number of applications	3 (10 days interval)
Dose (g as/ha)	37.5 g a.s./ha
Mode of application	Ground directed boom spraying
PHI (days) and/or growth stage (BBCH)	0, 1, 3, 5 and 7 days
Analytical method (Code +Type)	Testing of DFG Method S19 for the determination of Residues of KN128 along with KN127 in crops witch may be treated with DPX-MP062", DuPont Report No. AMR 4271-96.
LoQ (mg/kg)	0.01 mg/kg

Table B.7.3-7 Summary of the study 1 trials

N° Trial		1	2
North/South/Indoor		S	S
Decline (D)/Harvest (H) trial?		D	D
Formulation		WG	WG
Equivalence between formulations		Y	Y
Accordance with intended GAP		Y(1)	Y(1)
Correct sampling		Y	Y
Samples frozen within 24h		Y	Y
Storage period (in days)	Sample	<3 months	<3 months
	Extract	<1 day	<3 days
Storage T° <-18°C		Y	Y

Validated analytical method	Y	Y
Negative controls	Y	Y
Considered trial	Y	Y
Remarks		

(1) 3 applications instead of two intended however as all results are below the LOQ, trials were taken into account.

Table B.7.3-8 Summary of data from residue trials for study 1

RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)
Notifier: DuPont de Nemours Italiana
address 1 Via A. Volta, 16 – 20093 Cologno M.se

Active ingredient : indoxacarb
Crop / crop group : Sweet corn

Content of a.i. (g/kg or g/l) : 300 g a.i./kg
Formulation (e.g. WP) : WG
Commercial product (name) : STEWARD
Applicant : Ground Foliar application overhead

Indoors / outdoors : Outdoor
Other a. s. in formulation
(common name and content) :
Residues calculated as : DPX-KN128/IN-KN127

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety (a)	Date of 1)Sowing or planting 2)Flowering 3) Harvest (b)	Application rate per treatment			Dates of treatments or no. of treatments and last date (c)	Growth stage at last treatment or date	Portion analysed (a)	Residues (mg/kg)	PHI (days) (d)	Remarks (e)
			kg a.s./ha	Water hl/ha	kg a.s./hl						
DuPont-13320 I Vaccari 29100 Piacenza	Sweet corn Royalty F1	16/06/2003	38.62 37.38 38.42	n.r.	826 800 822	29/07/2003 08/08/2003 18/08/2003	59 65 75	cob	<0.01 <0.01 <0.01 <0.01 <0.01	0 1 3 5 7	
DuPont-13320 Gerbido di Mortizza 29100 Piacenza	Sweet corn Royalty F1	20/06/2003	37.09 39.20 39.06	n.r.	794 838 836	29/07/2003 08/08/2003 18/08/2003	59 65 75	cob	<0.01 <0.01 <0.01 <0.01 <0.01	0 1 3 5 7	

Remarks:
(a) According to CODEX Classification / Guide
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (Label pre-harvest interval, PHI, underline)
(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included
Note: All entries to be filled in as appropriate

B.7.3.2.3 - Conclusion on supporting data for the uses on sweet corn

Sweet corn is considered as a minor crop in northern and southern parts of Europe. 2 residue trials conducted on sweet corn in southern zone of EU are available; they were conducted in accordance with the intended GAP.
Indoxacarb 150 g/L EC uses on sweet corn are also supported by residue data from the field corn (maize) trials discussed above. The EU document "Guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs", SANCO 7525/VI/95 - rev.9, March 2011, allows for extrapolation of immature maize data to sweet corn. The milk stage for maize is BBCH 73–79 (Growth stages of mono-and dicotyledonous plants, BBCH monograph, Federal Biological Research Centre for Agriculture and Forestry, 2001). As stated above the final treatment in studies DuPont-6006 and DuPont 9777 were between BBCH 73 and 77, and therefore 0-day sampling in the maize field trials represents sampling at the milk stage, which is also representative of sweet corn. Finally, 6 trials conducted in southern Europe and 1 trial conducted in northern Europe are considered suitable to assess residue levels in sweet corn according to the intended GAP.
Residue levels of indoxacarb are below the LOQ of 0.01 mg/kg.
The available data package for grain can be used to derive an MRL on sweet corn.

B.7.3.3 - Lettuce

B.7.3.3.1 - Identification of critical GAPs

Indoxacarb is intended for uses on lettuce and the representative critical GAP is reported in the table below.

Table B.7.3-9 Critical GAP for indoxacarb on lettuce

Crop	Region	Outdoor/ Protected	Application	Number of applications (days interval)	Rate (g as/ha)	BBCH at last application/ PHI
Lettuce	EU	outdoor	Hydraulic ground directed boom	4 (7d)	37.5	BBCH 13-49 Seed crops BBCH 13-59 PHI:1 day

B.7.3.3.2 - Residues resulting from supervised trials

15 supervised residue trials were conducted on lettuce between 1998 and 2014 in Southern and Northern Europe. In DuPont-33518 study, four trials were carried out both with the DPX-MP062 30WG and DPX-KN128 30 WG formulation, at each time the more critical residue data was selected.

Some of them were initially assessed in the first inclusion of indoxacarb on Annex I.

Previous evaluation:	*Studies submitted and evaluated for the first inclusion of indoxacarb on Annex I (2000)*

Dupont-2577 and AMR 5006-98

Report:	CA, 6.3.3, Kennedy, C.M., Enriquez, M.A., Gasser, F., Larcinese, J.P., Belgaid, R, 2000
Title:	Combined decline and magnitude of residues of DPX-KN128 (indoxacarb) together with IN-KN127 in leaf vegetables (field lettuce) following applications of DPX-MP062 30WG – Southern Europe, season 1999.
Document No:	DuPont-2577
Guidelines:	/
GLP	Yes

Report:	CA, 6.3.3, Kennedy, C.M., Enriquez, M.A., Larcinese, J-P., Mattou, H., 1999
Title:	Combined Decline And Magnitude Of Residues Of DPX-KN128 (Indoxacarb) Together With IN-KN127 In Leaf Vegetables (Lettuce) Following Applications Of DPX-MP062 30WG Southern Europe – Season 1998
Document No:	Report AMR 5006-98
Guidelines:	/
GLP	Yes

A total of 10 residue trials were conducted over 2 growing seasons. These trials were conducted according to a more critical GAP (6 applications instead of 4 applications requested in the framework of this renewal, therefore they were not taken into account).
The two studies were conducted in 1999 using DPX-MP062-171 (30WG) as test substance.

Commodity	**Source**	**EU zone**	**Evaluation** GAP Residue levels (mg/kg)
Lettuce	Monograph	South (10)	Trials GAP: **6 x 37.5 kg as/ha, PHI 1d** 0.16 ; 0.19 ; 0.25 ; 0.39 ; 2x0.52 ; 0.55 ; 0.86 ; 0.89 ; 1.6

1	2	3	4			5	6	7	8	9	10
Report-No. Location incl. Postal code and date	Commodity/ Variety (a)	Date of 1)Sowing or planting 2)Flowering 3) Harvest (b)	Application rate per treatment			Dates of treatments or no. of treatments and last date (c)	Growth stage at last treatment or date	Portion analysed (a)	Residues (KN128+ KN127) (mg/kg)	PHI (days) (d)	Remarks (e)
			kg a.s./ha (KN128)	Water l/ha	kg a.s./hl (KN128)						
ADDITIONAL TRIALS											
Anachoma-Iona, Thessaloniki, Greece (S), 1999	Lettuce/ Romana	1. 03-10-99 3. 13-01-00 3. 14-01-00 3. 16-01-00 3. 18-01-00 3. 20-01-00	0.0355	393	0.009	6 13-01-00	BBCH 43	Leaves	0.44 1.71 1.64 1.24 0.92 0.60	-1h +2h 1 3 5 7	6-7 d **Du Pont-2577** WG30 Residue Analysis Method : GC/MSD, AMR 3493-95 Supplement 1, February 15, 1996
El Pilar de la Horadada, Alicante, Spain (S), 1999	Lettuce/ Iceberg-Legion	1. 15-10-99 3. 10-12-99 3. 11-12-99 3. 13-12-99 3. 15-12-99 3. 17-12-99	0.0391	519	0.008	6 10-12-99	BBCH 47	Leaves	0.34 1.27 0.52 0.39 0.12 0.05	-1h +2h 1 3 5 7	6-7 d **Du Pont-2577** WG30 Residue Analysis Method : GC/MSD, AMR 3493-95 Supplement 1, February 15, 1996
Pulpi, Almeria, Spain (S), 1999	Lettuce/ Iceberg	1. 09-09-99 3. 29-10-99	0.0378	510	0.007	6 28-10-99	BBCH 48	Leaves	0.39	1	6-8 d **Du Pont-2577** WG30 Residue Analysis Method : GC/MSD, AMR 3493-95 Supplement 1, February 15, 1996
Monteux, Vaucluse, 84170, France (S), 1999	Lettuce/ Christine	1. 18-08-99 3. 28-09-99 3. 29-09-99 3. 01-10-99 3. 03-10-99 3. 05-10-99	0.0374	470	0.008	6 28-09-99	BBCH 48	Leaves	0.27 0.95 0.86 0.75 0.45 0.39	-1h +2h 1 3 5 7	7 d **Du Pont-2577** WG30 Residue Analysis Method : GC/MSD, AMR 3493-95 Supplement 1, February 15, 1996
Graveson, Bouches du Rhône, 13690, France (S), 1999	Lettuce/ Bougy	1. 21-08-99 3. 30-09-99	0.0357	443	0.008	6 29-09-99	BBCH 49	Leaves	0.52	1	6-8 d **Du Pont-2577** WG30 Residue Analysis Method : GC/MSD, AMR 3493-95 Supplement 1, February 15, 1996
TRIALS FROM THE 1st ADDENDUM (February 2001)											

Contrada da Pigno, Italy (S) 1998	Lettuce/ Grintaus	1. 20-10-1998 3. 30-12-1998	0.036	800	0.005	6 29-12-1998	BBCH 47-48	Heads	0.89	1	7 d **5006-98** WG30 Residue Analysis Method : GC/MSD, AMR 3493-95 Supplement 1, February 15, 1996
Caleppio di Settala, Italy (S) 1998	Lettuce/ Iceberg	1. 17-04-1998 3. 08-06-1998 3. 09-06-1998 3. 11-06-1998 3. 13-06-1998 3. 15-06-1998	0.036	800	0.005	6 08-06-1998	BBCH 49	Heads	0.21 0.16 0.10 0.06 0.03	0 1 3 5 7	7 d **5006-98** WG30 Residue Analysis Method : GC/MSD, AMR 3493-95 Supplement 1, February 15, 1996
Utrera, Spain (S) 1998	Lettuce/ Mikel RZ	1. 19-09-1998 3. 03-11-1998 3. 04-11-1998 3. 06-11-1998 3. 08-11-1998 3. 10-11-1998	0.037	608	0.006	6 03-11-1998	BBCH 45	Heads	0.41 0.25 0.18 0.15 0.06	0 1 3 5 7	7 d **5006-98** WG30 Residue Analysis Method : GC/MSD, AMR 3493-95 Supplement 1, February 15, 1996
Almussafes, Spain (S) 1998	Lettuce/ Mikel R2	1. 23-05-1998 3. 09-07-1998	0.038	876	0.004	6 08-07-1998	BBCH 49	Heads	0.19	1	7 d **5006-98** WG30 Residue Analysis Method : GC/MSD, AMR 3493-95 Supplement 1, February 15, 1996
Alleins, France (S), 1998	Lettuce/ Divina	1. 08-05-1998 3. 16-06-1998 3. 17-06-1998 3. 19-06-1998 3. 21-06-1998 3. 23-06-1998	0.039	524	0.008	6 16-06-1998	BBCH 49	Heads	0.83 0.55 0.36 0.24 0.20	0 1 3 5 7	7 d **5006-98** WG30 Residue Analysis Method : GC/MSD, AMR 3493-95 Supplement 1, February 15, 1996

Remarks:
(a) According to CODEX Classification / Guide
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (Label pre-harvest interval, PHI, underline)
(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

Previous evaluation:	*Submitted for the purpose of renewal AIRIII*

Study 1- DuPont-19688

Report:	KCA 6.3.1/11, Old, J., Hansford, R.J., Ward, L., 2007
Title:	Determination of magnitude of residues of DPX-KN128 (indoxacarb) together with IN-KN127 in lettuce and broccoli/cauliflower following applications of DPX-MP062-30WG and DPX-KN128-15EC - Europe 2006
Document No:	DuPont-19688
Guidelines:	Directive 91/414/EEC (1991)
GLP	Yes

Acceptability	Deviations
Yes	Previous field history, crop husbandry records, or meteorological data were supplied by farmer co-operators and non-GLP facilities Study dates May 2006 to August 2007

Material and method:
The field program was conducted in 2006 at one location in Italy and one location in France (SEU). Six foliar applications of DPX-MP062 30WG or Explicit® EC were made at side-by-side bridging trials to lettuce at a target rate of 35.5 g DPX-KN128 a.s./ha each (equivalent to 0.125 kg/ha of DPX- P062 30WG or 0.250 kg/ha of Explicit® EC) when the crops were at BBCH growth stages 15–16, 19, 45, 47, 47–49, and 49.

A total of two residue trials were conducted over one
growing season (2006). A summary of these lettuce studies is given below. Specimens of lettuce were collected at sampling. A minimum of 12 heads per plot weighing >1.0 kg was collected in each case. One control specimen and one treated specimen at sampling per plot, for lettuce were submitted for analysis.

Specimens were analysed for residues following procedures described in DuPont Report No. AMR 4271-96, "Testing of DFG Method S19 for the determination of residues of KN128 along with KN127 in crops which might be treated with DPX-MP062." The detection was performed with LC/MS/MS as described in the report DUP-0602V, "Validation of multi-residue method DFG S19 (L 00.00-34) for the determination of residues of DPX-MP062 (DPX-KN128 (Indoxacarb) and IN-KN127) in grass."

The experimentally determined Limit of Quantification (LOQ) was 0.010 mg/kg.
These residues trials were not taken into account since they were conducted according to a more critical GAP.

Table B.7.3-10 Summary of data from residue trials for study 1

RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)

Active ingredient : Indoxacarb (isomer S)
Crop / crop group : Lettuce

Content of a.i. (g/kg or g/l) :
Formulation (e.g. WP) : EC or WG (side by side bridging)
Commercial product (name) : EXPLICIT EC or DPX-MP062 30WG (side by side bridging)
Applicant :

Indoors / outdoors : Outdoor
Other a. s. in formulation (common name and content) :
Dupont Solutions SAS : Sum of indoxacarb and its enantiomer R.

Residue trial summary for Lettuce and salad plants

Trial No./ Location/ Year	*Commodity/ Variety*	*Date of 1.Sowing or planting 2.Flowering 3. Harvest*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			g a.s./ ha	*Water (l/ha)*	*g a.s./hl*				*DPX-KN128+ IN-KN127*		
DuPont-19688;2006, Italy, Triginto di Mediglia, Lombardia,(SEU)	Lettuce / Lollo *Open leaf*	1.28 May 06 2 NR 3. 12 Jul 06	36.91 37.81 37.21 38.42 37.51 38.12	496 506 497 515 504 511	0.007 0.007 0.007 0.007 0.007 0.007	08 Jun 06 14 Jun 06 21 Jun 06 28 Jun 06 05 Jul 06 11 Jul 06	BBCH 16 BBCH 19 BBCH 45 BBCH 47 BBCH 49 BBCH 49	Heads	1.7	1	**WG**

Residue trial summary for Lettuce and salad plants

Trial No./ Location/ Year	*Commodity/ Variety*	*Date of 1.Sowing or planting 2.Flowering 3. Harvest*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			g a.s./ ha	*Water (l/ha)*	*g a.s./hl*				*DPX-KN128+ IN-KN127*		
DuPont-19688, Triginto di Mediglia, Lombardia 20060 Italy	Lettuce / Lollo *Open leaf*	1.28 May 06 2 NR 3. 12 Jul 06	36.77 37.37 38.58 38.43 36.92 37.98	489 498 513 511 491 505	0.008 0.008 0.008 0.008 0.008 0.008	08 Jun 06 14 Jun 06 21 Jun 06 28 Jun 06 05 Jul 06 11 Jul 06	BBCH 16 BBCH 19 BBCH 45 BBCH 47 BBCH 49 BBCH 49	Heads	1.1	1	**EC**
DuPont-19688, Lucernay, Rhone Alpes, 69480 France	Lettuce/ Feuille de Chêne	1. 04 Sep 06 2. NR 3. 27 Oct 06	37.81 36.00 36.91 39.02 37.21 39.33	506 480 492 520 497 523	0.007 0.008 0.008 0.008 0.007 0.008	21 Sep 2006 28 Sep 2006 05 Oct 2006 13 Oct 2006 20 Oct 2006 26 Oct 2006	BBCH 15 BBCH 19 BBCH 45 BBCH 47 BBCH 47-49 BBCH 49	Heads	1.4	1	**WG**
DuPont-19688, Lucernay, Rhone Alpes, 69480 France	Lettuce/ Feuille de Chêne	1. 04 Sep 06 2. NR 3. 27 Oct 06	38.13 38.73 36.92 35.86 36.31 35.86	509 516 493 479 485 478	0.007 0.008 0.007 0.007 0.007 0.008	21 Sep 2006 28 Sep 2006 05 Oct 2006 13 Oct 2006 20 Oct 2006 26 Oct 2006	BBCH 15 BBCH 19 BBCH 45 BBCH 47 BBCH 47-49 BBCH 49	Heads	0.43	1	**EC**

(a) According to BAYER codes
(b)Only if relevant

(c) High or low volume spraying, spreading, dusting etc., overall, broadcast, type or equipment used must be indicated

(e) BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4

(f) Minimum number of days after last application (Label pre-harvest interval, PHI, underline): DBLA = days before last application, DALA = days after last application

(g) Remarks may include: climatic conditions; reference to analytical method; Information concerning the metabolites included, the method of storage, storage stability, analysis date

Residues calculated as DPX-KN128

Study 2- DuPont-33518

Report:	KCA 6.3.1/10, Lakaschus, S., Amann, S.; 2012
Title:	Determination of Magnitude of Residues of DPX-KN128 (Indoxacarb) Together with IN-KN127 in Lettuce Following Applications of DPX-MP062 30WG and DPX-KN128 30WG - Europe, 2011
Document No:	DuPont-33518 Eurofins S11-00926
Guidelines:	European Communities Guidelines for the Generation of Data Concerning Residues, as Provided in Annex II, Part A, Section 6 and Annex III, Part A, Section 8 of EC Commission Directive 91/414/EEC. SANCO/825/00 rev.8.1 (16/11/2010) Guidance Document on Pesticide Residue Analytical Methods
GLP	Yes

Acceptability	**Deviations**
Yes	None

Table B.7.3-11 Summary of global information on study 2

Comparative trials (between formulations, with and adjuvant/safener/synergist)	1/ DPX-MP062 30WG: Indoxacarb (DPX-KN128) 30g a.s./100g 2/ DPX-KN128 30WG: Indoxacarb (DPX-KN128) 30g a.s./100g
Number of applications	6 (RTI:7 days)
Dose (g as/ha)	1/ DPX-MP062 : 37,5 g a.s./ha 2/ DPX-KN128 : 37,5 g a.s./ha
Mode of application	Foliar Treatment
PHI (days) and/or growth stage (BBCH)	PHI : 1 day
Analytical method (Code +Type)	- Testing of DFG Method S19 for the determination of residue of KN128 along with KN127 in crops which might be treated with DPX-MP062. Dupont Report AMR 4271-96, 1997 - Confirmation of the Stability of DPX-KN128 (Indoxacarb) and IN-KN127 on Crops for which European Maximum Residue Limits are Proposed - Independent Laboratory Validation of the Analytical Residue Method AMR 4271-96 for the Determination of Residues of DPX-KN128 and IN-KN127 in Plant Material which might be Treated with DPX-MP062.
LoQ (mg/kg)	KN128 (indoxacarbe) 0,01 mg/kg (LOD: 0,003 mg/kg

Table B.7.3-12 Summary of the study 2 trials

N° Trial		DuPont-33518 / 1	DuPont-33518 / 2	DuPont-33518 / 3	DuPont-33518 / 4
North/South/Indoor		N	S	S	S
Decline (D)/Harvest (H) trial?		H	H	H	H
Formulation		WG	WG	WG	WG
Equivalence between formulations		Y	Y	Y	Y
Accordance with intended GAP		Y(1)	Y	Y	Y
Correct sampling		Y	Y	Y	Y
Samples frozen within 24h		Y	Y	Y	Y
Storage period (in days)	Sample	< 8 months	< 7 months	< 7 months	< 4 months
	Extract	1-9 days	1-3 days	1-9 days	3 days
Storage T° <-18°C		Y	Y	Y	Y
Validated analytical method		Y	Y	Y	Y
Negative controls		Y	Y	Y	Y

Considered trial	N	N	N	N
Remarks				

(1) PHI: Some deviations on the RTI 7+-1 can be 9 days in some trials. Number of applications (6 applications) is more critical than the requested one (4 applications).

These trials were not taken into account. However, according to the results, residues levels with the racemic mixture would be higher than using only the active ingredient.

Table B.7.3-13 Summary of data from residue trials for study 2

RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)

Content of a.i.	(g/kg or g/l)	: 30g a.s./100g	Active ingredient	:	indoxacarb
Formulation	(e.g. WP)	: WG	Crop / crop group	:	lettuce
Commercial product	(name)	:	Indoors / outdoors	:	outdoor
Applicant		:	Other a. s. in formulation (common name and content)	:	none
			Residues calculated as	:	DPX-KN128 + IN-KN127

Residue trial summary for Lettuce and salad plants											
Trial No./ Location/ Year	*Commodity/ Variety*	*Date of 1.Sowing or planting 2.Flowering 3. Harvest*	*Application rate per treatment*			*Dates of treatment or no. of treatments and last date*	*Growth stage at last treatment or date*	*Portion analyzed*	*Residues (mg/kg)*	*PHI (days)*	*Remarks*
			g a.s./ ha	*Water (l/ha)*	*g a.s./hl*				*DPX-KN128+IN-KN127*		
Northern Europe											
Sulniac 56250 - France (1)	Leaf lettuce/ Altadis	1. 11/05/2011 2. NR 3. 06/07/2011	35.6 36.4 35.6 39.7 24.0 34.7	-	-	31/05/2011 07/06/2011 16/06/2011 22/06/2011 28/06/2011 05/07/2011	BBCH 16 BBCH 19 BBCH 19 BBCH 41 BBCH 43 BBCH 49	Leaf lettuce	0.65	1 DALA/	**DPX-MP062 WG**
Sulniac 56250 - France (1)	Leaf lettuce/ Altadis	1. 11/05/2011 2. NR 3. 06/07/2011	38.7 36.1 34.5 40.3 19.3 39.5			31/05/2011 07/06/2011 16/06/2011 22/06/2011 28/06/2011 05/07/2011	BBCH 16 BBCH 19 BBCH 19 BBCH 41 BBCH 43 BBCH 49	Leaf lettuce	0.23	1 DALA	**DPX-KN128 WG**
Southern Europe											
Elne 66200 - France (2)	Head lettuce/ Forlina	1. 26/06/2011 2. NR 3. 05/08/2011	38.0 37.5 39.3 39.0 37.5 36.3			01/07/2011 08/07/2011 15/07/2011 22/07/2011 29/07/2011 04/08/2011	BBCH 18 BBCH 19 BBCH 42 BBCH 42 BBCH 42 BBCH 49	Head lettuce	0.29	1 DALA	**DPX-MP062 WG**
Elne 66200 - France (2)	Head lettuce/ Forlina	1. 26/06/2011 2. NR 3. 05/08/2011	38.3 38.0 39.0 37.8 38.0 36.0			01/07/2011 08/07/2011 15/07/2011 22/07/2011 29/07/2011 04/08/2011	BBCH 18 BBCH 19 BBCH 42 BBCH 42 BBCH 42 BBCH 49	Head lettuce	0.15	1 DALA	**DPX-KN128 WG**
Elne 66200 - France (3)	Leaf lettuce/ Kitare	1. 26/06/2011 2. NR 3. 05/08/2011	38.7 38.7 38.2 39.0 39.3 38.0			01/07/2011 08/07/2011 15/07/2011 22/07/2011 29/07/2011 04/08/2011	BBCH 19 BBCH 41 BBCH 42 BBCH 42 BBCH 42 BBCH 49	Leaf lettuce	0.60	1 DALA	**DPX-MP062 WG**

Elne 66200 - France (3)	Leaf lettuce/ Kitare	1. 26/06/2011 2. NR 3. 05/08/2011	37.8 37.8 39.0 37.5 38.3 38.7			01/07/2011 08/07/2011 15/07/2011 22/07/2011 29/07/2011 04/08/2011	BBCH 19 BBCH 41 BBCH 42 BBCH 42 BBCH 42 BBCH 49	Leaf lettuce	0.42	1 DALA	**DPX-KN128 WG**
Nea Magnisia 57008 - Greece (4)	Leaf lettuce/ Manchester	1. 03/09/2011 2. NR 3. 25/10/2011	36.3 39.0 36.0 39.0 39.0 39.3			21/09/2011 28/09/2011 05/10/2011 12/10/2011 18/10/2011 24/10/2011	BBCH 37 BBCH 41 BBCH 43 BBCH 44 BBCH 47 BBCH 49	Leaf lettuce	1.4	1 DALA	**DPX-MP062 WG**
Nea Magnisia 57008 - Greece (4)	Leaf lettuce/ Manchester	1. 03/09/2011 2. NR 3. 25/10/2011	36.0 38.5 38.7 38.3 38.5 37.0			21/09/2011 28/09/2011 05/10/2011 12/10/2011 18/10/2011 24/10/2011	BBCH 37 BBCH 41 BBCH 43 BBCH 44 BBCH 47 BBCH 49	Leaf lettuce	0.93	1 DALA	**DPX-KN128 WG**

(a) According to BAYER codes
(b) Only if relevant

(c) High or low volume spraying, spreading, dusting etc., overall, broadcast, type or equipment used must be indicated

(e) BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4

(f) Minimum number of days after last application (Label pre-harvest interval, PHI, underline): DBLA = days before last application, DALA = days after last application

(g) Remarks may include: climatic conditions; reference to analytical method; Information concerning the metabolites included, the method of storage, storage stability, analysis date

Residues calculated as DPX-KN128

Study 3- DuPont-35819

Report:	KCA 6.3.1/12, Spence, C.M.; 2014
Title:	Determination of Magnitude and Decline of Residues of DPX-KN128 (Indoxacarb) along with IN-KN127 in Lettuce Following Applications of DPX-KN128 30WG – Europe – Initiated 2012
Document No:	DuPont-35819
Guidelines:	OECD Test Guideline 509, OECD Guideline for the Testing of Chemicals: Crop Field Trial, 07 September 2009. European Communities Guidelines for the Generation of Data Concerning Residues, as Provided in Annex II, Part A, Section 6 and Annex III, Part A, Section 8 of EC Commission Directive 91/414/EEC. SANCO/825/00 rev.8.1 (16/11/2010) Guidance Document on Pesticide Residue Analytical Methods
GLP	Yes

Acceptability	**Deviations**
Yes	None

TableB.7.3-14 Summary of global information on study 3

Comparative trials (between formulations, with and adjuvant/safener/synergist)	1/ DPX-KN128-298 WG : indoxacarb 300 g/kg
Number of applications	4 (RTI:7 days)
Dose (g as/ha)	1/ DPX-KN128 : 37,5 g a.s./ha
Mode of application	Foliar Treatment
PHI (days) and/or growth stage (BBCH)	PHI : - 0,1,3,7,10,14 (Decline) - 1 and 3 (Harvest)
Analytical method (Code +Type)	- Testing of DFG Method S19 for the determination of residue of KN128 along with KN127 in crops which might be treated with DPX-MP062. Dupont Report AMR 4271-96, 1997 - Confirmation of the Stability of DPX-KN128 (Indoxacarb) and IN-KN127 on Crops for which European Maximum Residue Limits are Proposed - Independent Laboratory Validation of the Analytical Residue Method AMR 4271-96 for the Determination of Residues of DPX-KN128 and IN-KN127 in Plant Material which might be Treated with DPX-MP062.
LoQ (mg/kg)	KN128 (indoxacarbe) 0,01 mg/kg (LOD = 0,003mg/kg)

Table B.7.3-15 Summary of the study 3 trials

N° Trial		DuPont-35819 / 1	DuPont-35819 / 2	DuPont-35819 / 3	DuPont-35819 / 4	DuPont-35819 / 5	DuPont-35819 / 6	DuPont-35819 / 7	DuPont-35819 / 8
North/South/Indoor		N	N	N	N	S	S	S	S
Decline (D)/Harvest (H) trial?		D	D	H	H	D	D	H	H
Formulation		WG	WG	WG	WG	WG	WG	WG	WG
Equivalence between formulations		Y	Y	Y	Y	Y	Y	Y	Y
Accordance with intended GAP		Y	Y	Y	Y	Y	Y	Y	Y
Correct sampling		Y	Y(2)	Y	Y	Y	Y	Y	Y
Samples frozen within 24h		Y	Y	Y	Y	Y	Y	Y	Y
Storage period (in days)	Sample	< 10 months	< 11 months	< 11 months	< 10 months	< 9 months	< 10 months	< 10 months	< 9 months
	Extract	< 1 day	1 day	< 1 day	< 1 day	< 1 day	1 day	< 1 day	< 1 day
Storage T° <-18°C		Y(1)	Y	Y	Y	Y	Y	Y(1)	Y
Validated analytical method		Y	Y	Y	Y	Y	Y	Y	Y
Negative controls		Y	Y	Y	Y	Y	Y	Y	Y
Considered trial		Y	Y	Y	Y	Y	Y	Y	Y
Remarks		Some deviations in the sprayer			Some deviations in the sprayer				

(1) Some temperature variations occurred during the storage up to -5°C but the trial is still considered as valid.
(2) Variation in the DALA duration during the sampling. At PHI 8/11 and 15 instead of PHI 7/10/14

N° Trial		DuPont-35819 / 9	DuPont-35819 / 10	DuPont-35819 / 11	DuPont-35819 / 12	DuPont-35819 / 13	DuPont-35819 / 14	DuPont-35819 / 15	DuPont-35819 / 16
North/South/Indoor		N	N	N	N	N	N	N	N
Decline (D)/Harvest (H) trial?		D	D	H	H	D	D	H	H
Formulation		WG	WG	WG	WG	WG	WG	WG	WG
Equivalence between formulations		Y	Y	Y	Y	Y	Y	Y	Y
Accordance with intended GAP		Y(1)	Y	Y	Y	Y	Y	Y	Y
Correct sampling		N(2)	Y	N(2)	Y	Y	Y	Y	N(4)
Samples frozen within 24h		Y	Y	Y	Y	Y	Y	Y	
Storage period (in days)	Sample	< 11 months	< 11 months	< 10 months	< 9 months	< 5 months	< 5 months	< 5 months	< 6 months
	Extract	< 1 day	< 1 day	1 day	1 day	2 days	1 day	< 1 day	< 1 day
Storage T° <-18°C		Y	Y	Y	Y(3)	Y	Y	Y	
Validated analytical method		Y	Y	Y	Y	Y	Y	Y	Y
Negative controls		Y	Y	Y(5)	Y	Y	Y	Y	Y
Considered trial		N	N	N	N	Y	Y	Y	Y
Remarks		Lamb lettuce	Lamb lettuce	Lamb lettuce	Lamb lettuce		No records for the past use on this site	No records for the past use on this site	

(1) RTI of 5 days instead of 7 (+-1)

(2) Some spare samples are missing due to a poor crop yield

(3) Some variations in the temperature during the shipment

(4) One sample is only up to 1kg instead of 2kg.

(5) Untreated sample analysed at a residue level of 0.005 mg/kg (LOD: 0.003 < LOQ = 0.01)

N° Trial		DuPont-35819 / 17	DuPont-35819 / 18	DuPont-35819 / 19
North/South/Indoor		S	S	S
Decline (D)/Harvest (H) trial?		D	D	H
Formulation		WG	WG	WG
Equivalence between formulations		Y	Y	Y
Accordance with intended GAP		Y	Y	Y
Correct sampling		Y	Y	Y
Samples frozen within 24h		Y	Y	Y
Storage period (in days)	Sample	< 7 months	< 6 months	< 5 months
	Extract	3 days	1 day	1 day
Storage T° <-18°C		Y(1)	Y	Y
Validated analytical method		Y	Y	Y
Negative controls		Y	Y	Y
Considered trial		Y	Y	Y
Remarks				

(1) Frozen shipping temperature has been up to -2.5°C during sometimes instead of -18°C

Table B.7.3-16 Summary of data from residue trials for study 3

RESIDUES DATA SUMMARY FROM SUPERVISED TRIALS (SUMMARY)
(Application on agricultural and horticultural crops)

Content of a.i.	(g/kg or g/l)	:	300 g/kg
Formulation	(e.g. WP)	:	WG
Commercial product	(name)	:	
Applicant		:	

Active ingredient	:	indoxacarb
Crop / crop group	:	lettuce
Indoors / outdoors	:	outdoor
Other a. s. in formulation (common name and content)	:	none
Residues calculated as	:	DPX-KN128 + IN-KN127

Residues expressed as DPX-KN128 plus IN-KN127 in field lettuce from supervised trials

GAP is general for all countries: Four foliar applications of DPX-KN128 30WG at 37.5 g a.s./ha each to lettuce as a post-emergence insecticide								
GLP and trial details	**Crop**	**Country**	**Application rate (g a.s./ha)**	**Crop growth stage**	**Commodity or matrix**	**PHI (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-35819-1; study to GLP, study carried out in 2012	Open leaf field lettuce	UK Gedney Marsh, Holbeach, Lincolnshire	37.25 (99% of GAP) 36.31 (97% of GAP) 36.31 (97% of GAP) 38.81 (103% of GAP)	BBCH 47 BBCH 47–48 BBCH 47–48 BBCH 49	Mature leaves	-0	0.18	Lettuce leaves mean recovery = 82%, 90%, and 99%, RSD = 13%, 16%, and 6.9% (n = 20, 20, and 8 in 0.01, 0.10, and 1.0 ppm, respectively)
						+0	0.51	
			38.50 (103% of GAP) 37.87 (101% of GAP) 36.62 (98% of GAP) 36.93 (98% of GAP)	BBCH 47 BBCH 46–48 BBCH 47–48 BBCH 48–49		1	<u>0.59</u>	
			36.62 (98% of GAP) 38.50 (103% of GAP) 38.19 (102% of GAP) 38.50 (103% of GAP)	BBCH 47 BBCH 43 BBCH 46 BBCH 48		3	0.32	
			40.69 (109% of GAP) 38.50 (103% of GAP) 37.25 (99% of GAP) 38.19 (102% of GAP)	BBCH 19 BBCH 47 BBCH 47–48 BBCH 47–48		7	0.24	
			39.75 (106% of GAP) 36.93 (98% of GAP) 37.87 (101% of GAP) 36.00 (96% of GAP)	BBCH 19 BBCH 47 BBCH 43 BBCH 46		10	0.12	
			36.93 (98% of GAP) 39.13 (104% of GAP) 37.56 (100% of GAP) 37.25 (99% of GAP)	BBCH 13–15 BBCH 19 BBCH 47 BBCH 47–48		14	0.071	

Residues expressed as DPX-KN128 plus IN-KN127 in field lettuce from supervised trials (continued)

GAP is general for all countries: Four foliar applications of DPX-KN128 30WG at 37.5 g a.s./ha each to lettuce as a post-emergence insecticide								
GLP and trial details	**Crop**	**Country**	**Application rate (g a.s./ha)**	**Crop growth stage**	**Commodity or matrix**	**PHI (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-35819-2; study to GLP, study carried out in 2012	Open leaf field lettuce	Germany Goch-Nierswalde, Kleve	36.56 (97% of GAP) 37.56 (100% of GAP) 38.06 (101% of GAP) 38.06 (101% of GAP)	BBCH 18 BBCH 41 BBCH 45 BBCH 49	Mature leaves	-0	0.14	Lettuce leaves mean recovery = 82%, 90%, and 99%, RSD = 13%, 16%, and 6.9% (n = 20, 20, and 8 in 0.01, 0.10, and 1.0 ppm, respectively)
						+0	0.84	
			39.06 (104% of GAP) 39.06 (104% of GAP) 37.56 (100% of GAP) 37.06 (99% of GAP)	BBCH 17 BBCH 37–39 BBCH 45 BBCH 47–49		1	<u>0.45</u>	
			39.06 (104% of GAP) 39.06 (104% of GAP) 39.06 (104% of GAP) 36.56 (97% of GAP)	BBCH 17 BBCH 33 BBCH 43 BBCH 47		3	0.24	
			39.06 (104% of GAP) 38.56 (103% of GAP) 38.56 (103% of GAP) 38.56 (103% of GAP)	BBCH 16 BBCH 18 BBCH 41 BBCH 45		8	0.16	
			38.56 (103% of GAP) 38.06 (101% of GAP) 38.06 (101% of GAP) 38.06 (101% of GAP)	BBCH 15 BBCH 17 BBCH 33 BBCH 43		11	0.067	
			38.06 (101% of GAP) 37.56 (100% of GAP) 38.06 (101% of GAP) 38.06 (101% of GAP)	BBCH 15 BBCH 16 BBCH 18 BBCH 41		15	0.044	

Residues expressed as DPX-KN128 plus IN-KN127 in field lettuce from supervised trials (continued)

GAP is general for all countries: Four foliar applications of DPX-KN128 30WG at 37.5 g a.s./ha each to lettuce as a post-emergence insecticide								
GLP and trial details	**Crop**	**Country**	**Application rate (g a.s./ha)**	**Crop growth stage**	**Commodity or matrix**	**PHI (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-35819-3; study to GLP, study carried out in 2012	Open leaf field lettuce	France Lorgies, Nord-Pas de Calais	36.62 (98% of GAP) 37.25 (99% of GAP) 39.44 (105% of GAP) 37.87 (101% of GAP)	BBCH 46 BBCH 47 BBCH 48 BBCH 48–49	Mature leaves	1	0.14	Lettuce leaves mean recovery = 82%, 90%, and 99%, RSD = 13%, 16%, and 6.9% (n = 20, 20, and 8 in 0.01, 0.10, and 1.0 ppm, respectively)
			38.81 (103% of GAP) 36.31 (97% of GAP) 35.68 (95% of GAP) 36.31 (97% of GAP)	BBCH 46 BBCH 47 BBCH 48 BBCH 48–49		3	0.17	
DuPont-35819-4; study to GLP, study carried out in 2012	Open leaf field lettuce	Czech Republic Český Těšín, Moravskoslezský kraj	36.23 (97% of GAP) 36.98 (99% of GAP) 37.30 (99% of GAP) 39.05 (104% of GAP)	BBCH 45 BBCH 46–47 BBCH 47–48 BBCH 48–49	Mature leaves	1	0.85	
			35.82 (96% of GAP) 37.08 (99% of GAP) 37.80 (101% of GAP) 36.12 (96% of GAP)	BBCH 45 BBCH 46 BBCH 47 BBCH 48		3	0.42	

Residues expressed as DPX-KN128 plus IN-KN127 in field lettuce from supervised trials (continued)

GAP is general for all countries: Four foliar applications of DPX-KN128 30WG at 37.5 g a.s./ha each to lettuce as a post-emergence insecticide								
GLP and trial details	**Crop**	**Country**	**Application rate (g a.s./ha)**	**Crop growth stage**	**Commodity or matrix**	**PHI (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-35819-5; study to GLP, study carried out in 2012	Open leaf field lettuce	Spain Benavent de Segria, Catalunya	37.87 (101% of GAP) 37.25 (99% of GAP) 38.50 (103% of GAP) 37.87 (101% of GAP)	BBCH 45 BBCH 47 BBCH 47 BBCH 49	Mature leaves	-0	0.17	Lettuce leaves mean recovery = 82%, 90%, and 99%, RSD = 13%, 16%, and
						+0	0.77	

Residues expressed as DPX-KN128 plus IN-KN127 in field lettuce from supervised trials (continued)

			38.81 (103% of GAP) 37.56 (100% of GAP) 37.87 (101% of GAP) 37.87 (101% of GAP)	BBCH 45 BBCH 47 BBCH 47 BBCH 49		1	<u>0.53</u>	6.9% (n = 20, 20, and 8 in 0.01, 0.10, and 1.0 ppm, respectively)
			37.87 (101% of GAP) 37.56 (100% of GAP) 37.87 (101% of GAP) 37.56 (100% of GAP)	BBCH 45 BBCH 47 BBCH 47 BBCH 49		3	0.44	
			37.56 (100% of GAP) 38.19 (102% of GAP) 37.87 (101% of GAP) 38.50 (103% of GAP)	BBCH 44 BBCH 45 BBCH 47 BBCH 47		7	0.14	
			37.87 (101% of GAP) 36.93 (98% of GAP) 38.81 (103% of GAP) 37.87 (101% of GAP)	BBCH 44 BBCH 45 BBCH 47 BBCH 47		10	0.14	
			38.50 (103% of GAP) 37.25 (99% of GAP) 37.87 (101% of GAP) 37.25 (99% of GAP)	BBCH 44 BBCH 44 BBCH 45 BBCH 47		14	0.084	

Residues expressed as DPX-KN128 plus IN-KN127 in field lettuce from supervised trials (continued)

GAP is general for all countries: Four foliar applications of DPX-KN128 30WG at 37.5 g a.s./ha each to lettuce as a post-emergence insecticide								
GLP and trial details	**Crop**	**Country**	**Application rate (g a.s./ha)**	**Crop growth stage**	**Commodity or matrix**	**PHI (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-35819-6; study to GLP, study carried out in 2012	Open leaf field lettuce	Greece Chalkidona, Thessaloniki	37.40 (100% of GAP) 37.60 (100% of GAP) 37.60 (100% of GAP) 37.56 (100% of GAP)	BBCH 32 BBCH 37 BBCH 41 BBCH 49	Mature leaves	-0	0.084	Lettuce leaves mean recovery = 82%, 90%, and 99%, RSD = 13%, 16%, and 6.9% (n = 20, 20, and 8 in 0.01, 0.10, and 1.0 ppm, respectively)
						+0	0.22	
			37.69 (101% of GAP) 37.64 (100% of GAP) 37.35 (100% of GAP) 37.56 (100% of GAP)	BBCH 32 BBCH 35/37 BBCH 41 BBCH 43/49		1	<u>0.67</u>	
			37.27 (99% of GAP) 37.52 (100% of GAP) 37.52 (100% of GAP) 37.52 (100% of GAP)	BBCH 19/32 BBCH 35 BBCH 41 BBCH 43/49		3	0.14	
			37.14 (99% of GAP) 37.52 (100% of GAP) 37.48 (100% of GAP) 37.52 (100% of GAP)	BBCH 19 BBCH 32 BBCH 37 BBCH 41		7	0.11	
			37.48 (100% of GAP) 37.48 (100% of GAP) 37.43 (100% of GAP) 37.64 (100% of GAP)	BBCH 19 BBCH 19/32 BBCH 35 BBCH 41		10	0.065	
			37.56 (100% of GAP) 37.39 (100% of GAP) 37.85 (101% of GAP) 37.60 (100% of GAP)	BBCH 16/17 BBCH 19 BBCH 32 BBCH 37		14	0.015	

Residues expressed as DPX-KN128 plus IN-KN127 in field lettuce from supervised trials (continued)

GAP is general for all countries: Four foliar applications of DPX-KN128 30WG at 37.5 g a.s./ha each to lettuce as a post-emergence insecticide								
GLP and trial details	**Crop**	**Country**	**Application rate (g a.s./ha)**	**Crop growth stage**	**Commodity or matrix**	**PHI (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-35819-7; study to GLP, study carried out in 2012	Open leaf field lettuce	France Lucenay, Rhone Alpes	37.25 (99% of GAP) 37.56 (100% of GAP) 38.50 (103% of GAP) 37.56 (100% of GAP)	BBCH 47 BBCH 47 BBCH 49 BBCH 49	Mature leaves	1	<u>0.80</u>	Lettuce leaves mean recovery = 82%, 90%, and 99%, RSD = 13%, 16%, and 6.9% (n = 20, 20, and 8 in 0.01, 0.10, and 1.0 ppm, respectively)
			38.50 (103% of GAP) 38.19 (102% of GAP) 37.25 (99% of GAP) 38.50 (103% of GAP)	BBCH 47 BBCH 47 BBCH 49 BBCH 49		3	0.65	
DuPont-35819-8; study to GLP, study carried out in 2012	Open leaf field lettuce	Spain Aguadulce, Andalucia	37.25 (99% of GAP) 39.13 (104% of GAP) 38.81 (103% of GAP) 36.93 (98% of GAP)	BBCH 33 BBCH 39 BBCH 39 BBCH 49	Mature leaves	1	<u>0.29</u>	
			38.19 (102% of GAP) 38.19 (102% of GAP) 38.50 (103% of GAP) 37.87 (101% of GAP)	BBCH 33 BBCH 35 BBCH 39 BBCH 49		3	0.23	

Residues expressed as DPX-KN128 plus IN-KN127 in field lettuce from supervised trials (continued)

GAP is general for all countries: Four foliar applications of DPX-KN128 30WG at 37.5 g a.s./ha each to lettuce as a post-emergence insecticide								
GLP and trial details	**Crop**	**Country**	**Application rate (g a.s./ha)**	**Crop growth stage**	**Commodity or matrix**	**PHI (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-35819-9; study to GLP, study carried out in 2012	Field **Lambs lettuce**	Austria Rohrau, Lower Austria	36.25 (97% of GAP) 37.17 (99% of GAP) 37.83 (101% of GAP) 39.20 (105% of GAP)	BBCH 16 BBCH 16 BBCH 16 BBCH 16–18	Mature leaves	-0	0.54	Lettuce leaves mean recovery = 82%, 90%, and 99%, RSD = 13%, 16%, and 6.9% (n = 20, 20, and 8 in 0.01, 0.10, and 1.0 ppm, respectively)
						+0	3.6	
			36.20 (97% of GAP) 38.15 (102% of GAP) 39.25 (105% of GAP) 38.88 (104% of GAP)	BBCH 16 BBCH 16 BBCH 16 BBCH 16		1	3.2	
			36.95 (99% of GAP) 36.25 (97% of GAP) 36.12 (96% of GAP) 37.38 (100% of GAP)	BBCH 14–16 BBCH 16 BBCH 18 BBCH 18–20		3	1.7	
			35.67 (95% of GAP) 36.87 (98% of GAP) 38.63 (103% of GAP) 37.28 (99% of GAP)	BBCH 14 BBCH 16 BBCH 18 BBCH 18		7	0.53	
			35.70 (95% of GAP) 37.75 (101% of GAP) 38.50 (103% of GAP) 36.60 (98% of GAP)	BBCH 12–14 BBCH 14–16 BBCH 16 BBCH 16		9	0.29	
			35.67 (95% of GAP) 37.70 (101% of GAP) 39.33 (105% of GAP) 39.33 (105% of GAP)	BBCH 12 BBCH 14 BBCH 16 BBCH 18		14	0.053	

Residues expressed as DPX-KN128 plus IN-KN127 in field lettuce from supervised trials (continued)

GAP is general for all countries: Four foliar applications of DPX-KN128 30WG at 37.5 g a.s./ha each to lettuce as a post-emergence insecticide								
GLP and trial details	**Crop**	**Country**	**Application rate (g a.s./ha)**	**Crop growth stage**	**Commodity or matrix**	**PHI (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-35819-10; study to GLP, study carried out in 2012	Field **Lambs lettuce**	Germany Goch-Nierswalde, Kleve	38.56 (103% of GAP) 38.06 (101% of GAP) 37.06 (99% of GAP) 39.06 (104% of GAP)	BBCH 18 BBCH 39 BBCH 45 BBCH 49	Mature leaves	-0	0.67	Lettuce leaves mean recovery = 82%, 90%, and 99%, RSD = 13%, 16%, and 6.9% (n = 20, 20, and 8 in 0.01, 0.10, and 1.0 ppm, respectively)
						+0	2.7	
			39.06 (104% of GAP) 38.56 (103% of GAP) 36.56 (97% of GAP) 38.56 (103% of GAP)	BBCH 17 BBCH 37 BBCH 45 BBCH 47–49		1	<u>1.5</u>	
			37.06 (99% of GAP) 38.06 (101% of GAP) 37.56 (100% of GAP) 38.06 (101% of GAP)	BBCH 17 BBCH 33 BBCH 41 BBCH 47		3	0.96	
			39.06 (104% of GAP) 37.56 (100% of GAP) 37.06 (99% of GAP) 38.56 (103% of GAP)	BBCH 16 BBCH 18 BBCH 39 BBCH 45		8	0.70	
			39.06 (104% of GAP) 38.56 (103% of GAP) 37.06 (99% of GAP) 38.56 (103% of GAP)	BBCH 15 BBCH 17 BBCH 33 BBCH 41		11	0.64	
			38.06 (101% of GAP) 38.06 (101% of GAP) 38.06 (101% of GAP) 38.06 (101% of GAP)	BBCH 15 BBCH 16 BBCH 18 BBCH 39		15	0.29	

Residues expressed as DPX-KN128 plus IN-KN127 in field lettuce from supervised trials (continued)

GAP is general for all countries: Four foliar applications of DPX-KN128 30WG at 37.5 g a.s./ha each to lettuce as a post-emergence insecticide								
GLP and trial details	**Crop**	**Country**	**Application rate (g a.s./ha)**	**Crop growth stage**	**Commodity or matrix**	**PHI (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-35819-11; study to GLP, study carried out in 2012	Field **Lambs lettuce**	Czech Republic Uherský Ostroh, Zlinsky kraj	36.98 (99% of GAP) 36.33 (97% of GAP) 36.00 (96% of GAP) 38.35 (102% of GAP)	BBCH 15 BBCH 16 BBCH 16–17 BBCH 16–18	Mature leaves	1	4.9	Lettuce leaves mean recovery = 82%, 90%, and 99%, RSD = 13%, 16%, and 6.9% (n = 20, 20, and 8 in 0.01, 0.10, and 1.0 ppm, respectively)
			36.68 (98% of GAP) 38.22 (102% of GAP) 36.72 (98% of GAP) 36.45 (97% of GAP)	BBCH 15 BBCH 16 BBCH 16–17 BBCH 16–18		3	3.6	
DuPont-35819-12; study to GLP, study carried out in 2012	Field **Lambs lettuce**	France Verlinghem, Nord-Pas de Calais	36.00 (96% of GAP) 38.50 (103% of GAP) 36.62 (98% of GAP) 36.31 (97% of GAP)	BBCH 47 BBCH 47–48 BBCH 48 BBCH 48–49	Mature leaves	1	1.2	
			35.68 (95% of GAP) 38.81 (103% of GAP) 37.87 (101% of GAP) 37.25 (99% of GAP)	BBCH 47 BBCH 47–48 BBCH 48 BBCH 48–49		3	1.1	

Residues expressed as DPX-KN128 plus IN-KN127 in field lettuce from supervised trials (continued)

GAP is general for all countries: Four foliar applications of DPX-KN128 30WG at 37.5 g a.s./ha each to lettuce as a post-emergence insecticide								
GLP and trial details	**Crop**	**Country**	**Application rate (g a.s./ha)**	**Crop growth stage**	**Commodity or matrix**	**PHI (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-35819-13; study to GLP, study carried out in 2012	Open leaf field lettuce	France Douai, Nord-Pas de Calais	39.44 (105% of GAP) 39.13 (104% of GAP) 39.13 (104% of GAP) 36.62 (98% of GAP)	BBCH 45 BBCH 46 BBCH 48 BBCH 49	Mature leaves	-0	0.034	Lettuce leaves mean recovery = 82%, 90%, and 99%, RSD = 13%, 16%, and 6.9% (n = 20, 20, and 8 in 0.01, 0.10, and 1.0 ppm, respectively)
						+0	0.31	
			36.31 (97% of GAP) 37.56 (100% of GAP) 35.68 (95% of GAP) 38.50 (103% of GAP)	BBCH 45 BBCH 46 BBCH 48 BBCH 48		1	<u>0.29</u>	
			35.06 (93% of GAP) 35.37 (94% of GAP) 36.31 (97% of GAP) 38.19 (102% of GAP)	BBCH 44 BBCH 46 BBCH 47 BBCH 48		3	0.18	
			35.68 (95% of GAP) 35.68 (95% of GAP) 35.68 (95% of GAP) 37.56 (100% of GAP)	BBCH 41–42 BBCH 45 BBCH 46 BBCH 48		8	0.055	
			36.00 (96% of GAP) 36.93 (98% of GAP) 36.00 (96% of GAP) 36.62 (98% of GAP)	BBCH 19 BBCH 44 BBCH 46 BBCH 47		10	0.045	
			38.19 (102% of GAP) 36.93 (98% of GAP) 38.81 (103% of GAP) 36.31 (97% of GAP)	BBCH 16–18 BBCH 41–42 BBCH 45 BBCH 46		15	0.013	

Residues expressed as DPX-KN128 plus IN-KN127 in field lettuce from supervised trials (continued)

GAP is general for all countries: Four foliar applications of DPX-KN128 30WG at 37.5 g a.s./ha each to lettuce as a post-emergence insecticide

GLP and trial details	Crop	Country	Application rate (g a.s./ha)	Crop growth stage	Commodity or matrix	PHI (days)	Residues found (mg/kg)	Recovery data
DuPont-35819-14; study to GLP, study carried out in 2013	Open leaf field lettuce	Belgium Wytschate, Hainaut	36.62 (98% of GAP) 37.87 (101% of GAP) 39.44 (105% of GAP) 38.50 (103% of GAP)	BBCH 16–17 BBCH 44 BBCH 48 BBCH 48–49	Mature leaves	-0	0.14	Lettuce leaves mean recovery = 82%, 90%, and 99%, RSD = 13%, 16%, and 6.9% (n = 20, 20, and 8 in 0.01, 0.10, and 1.0 ppm, respectively)
						+0	0.19	
			36.31 (97% of GAP) 36.93 (98% of GAP) 37.56 (100% of GAP) 36.62 (98% of GAP)	BBCH 16–17 BBCH 44 BBCH 48 BBCH 48–49		1	<u>0.27</u>	
			37.87 (101% of GAP) 36.62 (98% of GAP) 37.87 (101% of GAP) 38.19 (102% of GAP)	BBCH 16–17 BBCH 43 BBCH 44 BBCH 48		3	0.19	
			37.56 (100% of GAP) 36.93 (98% of GAP) 36.93 (98% of GAP) 36.62 (98% of GAP)	BBCH 16 BBCH 16–17 BBCH 44 BBCH 48		7	0.072	
			36.31 (97% of GAP) 38.19 (102% of GAP) 36.62 (98% of GAP) 38.81 (103% of GAP)	BBCH 15 BBCH 16–17 BBCH 43 BBCH 44		10	0.067	
			37.25 (99% of GAP) 38.19 (102% of GAP) 37.25 (99% of GAP) 36.00 (96% of GAP)	BBCH 14 BBCH 16 BBCH 16–17 BBCH 44		14	0.043	

Residues expressed as DPX-KN128 plus IN-KN127 in field lettuce from supervised trials (continued)

GAP is general for all countries: Four foliar applications of DPX-KN128 30WG at 37.5 g a.s./ha each to lettuce as a post-emergence insecticide								
GLP and trial details	**Crop**	**Country**	**Application rate (g a.s./ha)**	**Crop growth stage**	**Commodity or matrix**	**PHI (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-35819-15; study to GLP, study carried out in 2013	Open leaf field lettuce	UK Freuchie, Fife	37.87 (101% of GAP) 39.44 (105% of GAP) 37.87 (101% of GAP) 37.25 (99% of GAP)	BBCH 37 BBCH 39 BBCH 41 BBCH 47	Mature leaves	1	<u>0.28</u>	Lettuce leaves mean recovery = 82%, 90%, and 99%, RSD = 13%, 16%, and 6.9% (n = 20, 20, and 8 in 0.01, 0.10, and 1.0 ppm, respectively)
			37.25 (99% of GAP) 37.87 (101% of GAP) 37.87 (101% of GAP) 36.31 (97% of GAP)	BBCH 37 BBCH 39 BBCH 41 BBCH 45		3	0.19	
DuPont-35819-16; study to GLP, study carried out in 2013	Open leaf field lettuce	Poland Urbanowice, Gościęcin, Opeln	39.0 (104% of GAP) 38.7 (103% of GAP) 39.3 (105% of GAP) 36.9 (98% of GAP)	BBCH 41 BBCH 42 BBCH 43 BBCH 44	Mature leaves	1	<u>0.18</u>	
			39.0 (104% of GAP) 38.7 (103% of GAP) 39.3 (105% of GAP) 36.6 (98% of GAP)	BBCH 41 BBCH 42 BBCH 43 BBCH 44		3	0.11	

Residues expressed as DPX-KN128 plus IN-KN127 in field lettuce from supervised trials (continued)

GAP is general for all countries: Four foliar applications of DPX-KN128 30WG at 37.5 g a.s./ha each to lettuce as a post-emergence insecticide								
GLP and trial details	**Crop**	**Country**	**Application rate (g a.s./ha)**	**Crop growth stage**	**Commodity or matrix**	**PHI (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-35819-17; study to GLP, study carried out in 2013	Open leaf field lettuce	Spain Utrera, Andalucia	36.93 (98% of GAP) 38.19 (102% of GAP) 37.87 (101% of GAP) 38.19 (102% of GAP)	BBCH 34 BBCH 37 BBCH 45 BBCH 49	Mature leaves	-0	0.016	Lettuce leaves mean recovery = 82%, 90%, and 99%, RSD = 13%, 16%, and 6.9% (n = 20, 20, and 8 in 0.01, 0.10, and 1.0 ppm, respectively)
						+0	0.10	
			37.56 (100% of GAP) 36.93 (98% of GAP) 38.19 (102% of GAP) 37.25 (99% of GAP)	BBCH 34 BBCH 37 BBCH 45 BBCH 49		1	<u>0.060</u>	
			37.25 (99% of GAP) 38.50 (103% of GAP) 36.93 (98% of GAP) 38.19 (102% of GAP)	BBCH 33 BBCH 34 BBCH 39 BBCH 47		3	0.028	
			36.93 (98% of GAP) 37.87 (101% of GAP) 37.25 (99% of GAP) 36.62 (98% of GAP)	BBCH 19 BBCH 34 BBCH 37 BBCH 45		7	0.017	
			37.25 (99% of GAP) 36.93 (98% of GAP) 38.19 (102% of GAP) 37.56 (100% of GAP)	BBCH 16 BBCH 33 BBCH 34 BBCH 39		10	0.003	
			38.19 (102% of GAP) 37.25 (99% of GAP) 38.19 (102% of GAP) 37.25 (99% of GAP)	BBCH 15 BBCH 19 BBCH 34 BBCH 37		14	ND	

Residues expressed as DPX-KN128 plus IN-KN127 in field lettuce from supervised trials (continued)

GAP is general for all countries: Four foliar applications of DPX-KN128 30WG at 37.5 g a.s./ha each to lettuce as a post-emergence insecticide								
GLP and trial details	**Crop**	**Country**	**Application rate (g a.s./ha)**	**Crop growth stage**	**Commodity or matrix**	**PHI (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-35819-18; study to GLP, study carried out in 2013	Open leaf field lettuce	Italy Torrevecchia Pia, Lombardia	37.56 (100% of GAP) 39.13 (104% of GAP) 38.50 (103% of GAP) 37.56 (100% of GAP)	BBCH 17 BBCH 41 BBCH 47 BBCH 49	Mature leaves	-0	0.051	Lettuce leaves mean recovery = 82%, 90%, and 99%, RSD = 13%, 16%, and 6.9% (n = 20, 20, and 8 in 0.01, 0.10, and 1.0 ppm, respectively)
						+0	0.71	
			36.93 (98% of GAP) 38.50 (103% of GAP) 37.25 (99% of GAP) 38.50 (103% of GAP)	BBCH 17 BBCH 41 BBCH 47 BBCH 49		1	<u>0.35</u>	
			36.62 (98% of GAP) 37.87 (101% of GAP) 36.62 (98% of GAP) 37.87 (101% of GAP)	BBCH 15 BBCH 19 BBCH 42 BBCH 47		3	0.16	
			37.87 (101% of GAP) 38.19 (102% of GAP) 37.87 (101% of GAP) 35.68 (95% of GAP)	BBCH 14 BBCH 17 BBCH 41 BBCH 47		7	0.079	
			36.31 (97% of GAP) 37.56 (100% of GAP) 38.81 (103% of GAP) 37.25 (99% of GAP)	BBCH 14 BBCH 15 BBCH 19 BBCH 42		10	0.032	
			36.62 (98% of GAP) 36.93 (98% of GAP) 36.93 (98% of GAP) 38.81 (103% of GAP)	BBCH 13 BBCH 14 BBCH 17 BBCH 41		14	0.011	

Residues expressed as DPX-KN128 plus IN-KN127 in field lettuce from supervised trials (continued)

GAP is general for all countries: Four foliar applications of DPX-KN128 30WG at 37.5 g a.s./ha each to lettuce as a post-emergence insecticide								
GLP and trial details	**Crop**	**Country**	**Application rate (g a.s./ha)**	**Crop growth stage**	**Commodity or matrix**	**PHI (days)**	**Residues found (mg/kg)**	**Recovery data**
DuPont-35819-19; study to GLP, study carried out in 2013	Open leaf field lettuce	Greece Nea Magnisia, Thessaloniki	37.86 (101% of GAP) 37.79 (101% of GAP) 37.49 (100% of GAP) 37.59 (100% of GAP)	BBCH 14/17 BBCH 19/33 BBCH 33/35 BBCH 39	Mature leaves	1	<u>0.36</u>	Lettuce leaves mean recovery = 82%, 90%, and 99%, RSD = 13%, 16%, and 6.9% (n = 20, 20, and 8 in 0.01, 0.10, and 1.0 ppm, respectively)
			37.63 (100% of GAP) 37.69 (101% of GAP) 37.49 (100% of GAP) 37.53 (100% of GAP)	BBCH 14/17 BBCH 19/33 BBCH 35/39 BBCH 49		3	0.28	

B.7.3.3.3 - Conclusion on supporting data for the uses on lettuce

Lettuce is considered as a major crop in northern and southern parts of Europe. 8 residue trials conducted on lettuce in northern zone of EU and 7 residue trials conducted in southern zone of EU are available; some of the trials were conducted with a more critical GAP (6 applications instead of 4).
Residue levels of indoxacarb ranged from 0.06 mg/kg to 0.85 mg/kg.
RMS believes the available data package for lettuce is sufficient to derive suitable values for risk assessment. However, according to the guidelines, 1 additional residue trial conducted in southern Europe could be requested.
Furthermore, several "bridging trials" have been submitted in order to compare different formulations in applications on lettuce. However, beyond the formulation, different technical specifications were also compared, since side-by-side trials were conducted with either DPX-KN128 or DPX MP062 (racemic mixture). Residue levels using the racemic mixture were higher than those obtained with the active ingredient (DPX-KN128).

B.7.4 - FEEDING STUDIES

B.7.4.1 - Poultry

The dietary burden calculations show sufficient poultry exposure to warrant a feeding study. EFSA evaluated a poultry feeding study reviewed by JMPR (Food and Agriculture Organization of the United Nations), 2009. Indoxacarb. In: Pesticide residues in food – 2009) consisting of 4 groups of laying hens, each consisting of ten animals which were dosed for 28 consecutive days with indoxacarb (as R and S isomers) at levels of 1.75, 7, 21 and 70 mg/kg in the diet (equivalent to 0.11, 0.44, 1.33 and 4.42 mg/kg b.w). This study is summarized below.

DuPont-8305

Report:	CA, 6.4.1/01, [redacted] 2004
Title:	Magnitude of residues of indoxacarb (as DPX MP062) in laying hen tissue and eggs: a feeding study conducted to EPA guidelines
Document No:	DuPont-8305 [redacted] Project 200491
Guidelines:	OECD Principles of Good Laboratory Practice (as revised in 1997), published in ENV/MC/CHEM (98) 17, Paris, 1998 United Kingdom Good Laboratory Practice Regulations 1999, Statutory Instrument No. 3106
GLP	Yes

Acceptability	Deviations
Yes	None

Materials and method
This study determined the magnitude and distribution of residues of indoxacarb as DPX-MP062 in the whole eggs, egg white and yolk (selected samples), muscle, skin with fat, liver, and abdominal fat pad samples of laying hens following treatment with DPXMP062 (DuPont Code No. DPX-MP062).
DPX-MP062 contains 75% DPX-KN128 (indoxacarb) and 25% IN-KN127 the insecticidally inactive isomer of indoxacarb. Target treatment levels were 1.75 ppm, 7.0 ppm, 21.0 ppm, and 70.0 ppm of DPXMP062 in relation to the daily food consumption.
The 7.0 ppm DPX-MP062 dose level is considered to be the maximum theoretical dietary burden. The 1.75 ppm dose level is included as this is considered to be a more realistic feed level of DPX-MP062.

Four treatment groups and one control group were established for this study. The control group and 1.75, 7.0, 21.0, and 70.0 ppm treatment groups each contained ten animals. The laying hens were dosed by a gelatine capsule given by balling gun daily. Animals were sacrificed on Study Day 29 at ca 23 hours after administration of the last capsule and muscle, liver, abdominal fat pad and skin with fat samples were collected. Sampling facilities include a cleaning phase for eggs with a clean damp towel, carcasses were also cleaned and plucked free.

Sample collection:

Egg collection:	Twice daily – pm eggs from one day were pooled with am eggs from the next day on a daily basis for 28 days. Egg samples from the depuration group were collected from Day 28 until Day 56.
Interval from last dose to sacrifice:	*ca*. 23 hours; 27 days and *ca*. 23 hours for depuration group
Tissues harvested and analysed:	Liver, muscle (approximately equal quantities of leg and breast), abdominal fat pad, and skin with fat

Tissue samples taken at sacrifice and egg samples (whole eggs and eggs divided into whites and yolks) collected at various intervals over the 28 day dosing period were analyzed for residues of DPX-MP062 (combined amounts of DPX-KN128 and IN-KN127) and 5 metabolites.

Storage stability:
Samples were stored at *ca*. -20°C (-4°F) for a maximum of 12.6 months for eggs and 9.9 months for tissues. Freezer storage stability data demonstrated that residues of DPX-MP062 and metabolites are stable in fortified samples of eggs, fat, muscle, liver, and skin at approximately -20°C for periods of storage for samples in this study.

Analysis:
The analytical procedure used for analysis of DPX-MP062 and its hen metabolites was based on the method reported in DuPont Report n° AMR 12739 "Analytical method for the determination of DPX-MP062 and metabolites IN-KB687, IN-KG433, IN-KT319, IN-JU873 and IN-JT333 in poultry skin, liver, muscle, fat and eggs".

The method involved extraction of the residue with acidified acetonitrile. Each sample extract was cleaned-up using water/hexane partitioning and a solid phase extraction cartridge. All six analytes were quantified in a single injection. Two ions were monitored for each analyte. Residues were determined using liquid chromatography with detection and quantitation by LC/MS/MS. The LOQ of this method was 0.010 mg/kg (ppm) for all analytes in all matrices. The LOD of this method was 0.003 mg/kg (ppm) for all analytes in all matrices. Results are reported per analyte. Recovery data for fortifications run concurrently with the treated samples ranged from 84–102% (DPX-MP062), 92–103% (IN-KT319), 89–96% (IN-KG433), 71–92% (IN-JU873), 78–90% (IN-JT333), and 89-101% (IN-KB687). All standard deviations and relative standard deviations for the recovery data were less than 20%.

Results
Residues of all analytes in whole eggs increased throughout the first 7 days of dosing. Residues reached a plateau in eggs for five analytes between 7 and 12 days. IN-JT333 residues reached a plateau after approximately 14 to 21 days.

Residues in eggs were dose-dependent and were predominantly IN-KG433 (see **Table IIIA 8.4.1-1**). In the 1.75 ppm dose group, the maximum residues of IN-KT319, IN-KG433, and IN-JU873 were 0.016, 0.020, and 0.013 ppm, respectively. In the 7 ppm dose group, residues of DPX-MP062, IN-JT333, IN-KT319, IN-KG433, IN-JU873, and IN-KB687 were 0.020, 0.020, 0.059, 0.10, 0.035, and 0.016 ppm, respectively. In the 21 ppm dose group, residues of DPX-MP062, IN-JT333, IN-KT319, IN-KG433, IN-JU873, and IN-KB687 were 0.060, 0.050, 0.18, 0.30, 0.12, and 0.041 ppm, respectively. In the 70 ppm dose group, residues of DPX-MP062, IN-JT333, IN-KT319, IN-KG433, IN-JU873, and IN-KB687 were 0.28, 0.18, 0.54, 0.95, 0.50, and 0.14 ppm, respectively. All other residues were <LOQ.

The highest residues in egg yolk and egg white were IN-KG433 and IN-JU873. Residues of IN-JT333, IN-JU873, and IN-KB687 were much lower in egg white than in egg yolk. At the 7 ppm dietary dose rate, all average residues were 0.12 ppm or less. By Day 36 of the study (7 days of depuration), there were essentially no detectable residues in egg white. Yolk residues were non-detectable by Day 43 for all residues except IN-JT333. IN-JT333 residues were non-quantifiable by Day 50 and non-detectable by Day 56.

The highest tissue residue was IN-JT333 in fat. Other residues were highest in fat and skin (skin has a large fat content). After IN-JT333 the highest residues were for IN-KG433, IN-JU873, IN-KT319, DPX-MP062, and IN-KB687 in decreasing order of magnitude. The highest residues were for IN-JT333, IN-KG433, IN-JU873, IN-KT319, DPX-MP062, and IN-KB687 in decreasing order of magnitude (see **Table IIIA 8.4.1-2:**).

In the 7 ppm dose group, average residues of analytes present in fat >LOQ were: DPX-MP062, 0.044 ppm; IN-JT333, 0.20 ppm; IN-KT319, 0.040 ppm; IN-KG433, 0.079 ppm; and IN-JU873, 0.065 ppm. In the 70 ppm dose group, the average residues >LOQ were: DPX-MP062, 0.63 ppm; IN-JT333, 1.7 ppm; IN-KT319, 0.25 ppm; IN-KG433, 0.69 ppm; IN-JU873, 0.82 ppm; and IN-KB687, 0.042 ppm.

In the 7 ppm dose group, there were no average residues of analytes present in muscle >LOQ. In the 70 ppm dose group, the average residues >LOQ were: IN-JT333, 0.018 ppm; IN-KT319, 0.017 ppm; IN-KG433, 0.024 ppm; and IN-JU873, 0.045 ppm.

In the 7 ppm dose group, average residues of analytes present in liver >LOQ were: IN-KG433, 0.019 ppm; and IN-JU873, 0.019 ppm. In the 70 ppm dose group, the average residues >LOQ were: IN-JT333, 0.057 ppm; IN-KT319, 0.031 ppm; IN-KG433, 0.23 ppm; and IN-JU873, 0.17 ppm.

In the 7 ppm dose group, average residues of analytes present in skin >LOQ were: IN-JT333, 0.037 ppm; IN-KG433, 0.024 ppm; and IN-JU873, 0.022 ppm. In the 70 ppm dose group, the average residues >LOQ were: DPX-MP062, 0.20 ppm; IN-JT333, 0.43 ppm; IN-KT319, 0.12 ppm; IN-KG433, 0.23 ppm; IN-JU873, 0.12 ppm; and IN-KB687, 0.014 ppm.

Following withdrawal of the dose, residues declined. By 10 days post-last dose, all analytes were <LOQ in eggs except IN-JT333. The IN-JT333 levels reached non-quantifiable levels by Day 45, and all analytes were non-detectable (less than 0.003 ppm) by Day 52. There were no quantifiable residues in tissue depuration samples with one exception. There was a detectable residue for IN-JT333 in the fat depuration group. The depuration group was dosed at 70 ppm, so there is very little chance that fat would have a detectable residue for a 7 ppm dietary dose (1× dose rate). There were no other detectable residues in tissue depuration samples.

Table IIIA 0-1:
Residues of DPX-MP062 and metabolites in eggs

Analyte	Sampling point	Highest residue value for each analyte in whole eggs after residues of each individual analyte had reached a plateau			
		1.75 ppm	7 ppm (ratio[a])	21 ppm (ratio[a])	70 ppm (ratio[a])
		Residue (ppm)			
DPX-MP062	18 days	0.0046	0.020 (4.3)	0.060 (3.0)	0.28 (4.7)
IN-JT333	21 days	0.0089	0.020 (2.2)	0.050 (2.5)	0.18 (3.6)
IN-KT319	18 days	0.016	0.059 (3.7)	0.18 (3.1)	0.54 (3.0)
IN-KG433	23 days	0.020	0.10 (5.0)	0.30 (3.0)	0.95 (3.2)
IN-JU873	21 days	0.013	0.035 (2.7)	0.12 (3.4)	0.50 (4.2)
IN-KB687	18 days	0.0051	0.016 (3.1)	0.041 (2.6)	0.14 (3.4)

[a] The ratio given is for the residue at that dose divided by the residue for the next lowest dose. Therefore, there is no ratio for the 1.75 ppm dietary dosing group. Theoretical ratios based on target dietary dose levels are 4 (7 ppm/1.75 ppm), 3 (21 ppm/7 ppm), and 3.3 (70 ppm/21 ppm).

Table IIIA 0-2:
Residues of DPX-MP062 and metabolites in tissues

Dose level (ppm)	Matrix	DPX-MP062	IN-JT333	IN-KT319	IN-KG433	IN-JU873	IN-KB687
		Residue (ppm)					
7	Fat	0.044	0.20	0.040	0.079	0.065	0.0058
70		0.63	1.7	0.25	0.69	0.82	0.042
7	Muscle	<0.003	<0.003	<0.003	0.0034	<0.003	<0.003
70		0.0051	0.018	0.017	0.024	0.045	<0.003
7	Liver	<0.003	0.0049	0.0039	0.019	0.019	<0.003
70		<0.003	0.057	0.031	0.23	0.17	0.0038
7	Skin	0.0086	0.037	0.0080	0.024	0.022	<0.003
70		0.20	0.43	0.12	0.23	0.12	0.014

B.7.4.2 - Ruminants

The available feeding study on ruminants was evaluated in the initial DAR. Summary of this study is reported hereafter.

DuPont-AMR 3820-96

Characteristics

reference	: [redacted] 1997	exposure	: 28 consecutive days (via capsules)
type of study	: livestock feeding	dose	: 7.5, 22.5, or 75 mg/kg diet
year of execution	: 1996-1997	vehicle	: not specified
test substance	: DPX-MP062, batch DPX-MP062-51A, purity 94.5%	GLP statement	: Yes
route	: oral	guideline	: no guideline in force
species	: lactating cow (Holstein)		
group size	: 3 or 4 (high dose group)		

Study design
Groups of adult lactating Holstein cows were orally dosed twice per day with capsules containing DPX-MP062 at doses equivalent to 7.5, 22.5 or 75 mg/kg in the diet, for 28 consecutive days. Milk samples were collected daily from each morning and afternoon milking beginning on the day before the first dosing and continuing until the morning of sacrifice for each animal. Skimmed milk and cream samples were prepared from whole milk samples collected on days 14, 21, and 28. All animals except a depuration animal were sacrificed on day 29 between 14 and 22 hours after the last dose, and tissue samples were collected. The depuration animal was sacrificed 15 days after the last dose (day 43). Samples were analyzed for KNI28/KNI27 and IN-JT333 by analytical method AMR 3337-95 which is an HPLC-UV column switching method. The limit of quantitation (LOQ) for both analytes was 0.010 ppm in milk (whole milk, skimmed milk, and cream) and tissues (muscle, fat, liver and kidney).

Results
In whole milk, residues of DPX-KN128/IN-KN127 reached a plateau by the 14th day of dosing. Plateau levels at day 14 were ca. 0.020 mg/kg (max. 0.026 mg/kg) in milk from the low dose group; ca. 0.053 mg/kg in milk from the middle dose group, and ca. 0.18 mg/kg in milk from the high dose group. Quantifiable residues (0.010 mg/kg) of the metabolite IN-JT333 were observed in two milk samples from the high dose treatment group. Levels of IN-MP819, an insecticidally inactive compound, were <0.01 mg/kg in the low dose level animals and ranged from 0.018 to 0.032 mg/kg in the high dose level animals on day 18.

Residues of DPX-KNI28/IN-KN127 were reduced in skimmed milk in comparison to residues observed in whole milk samples collected on the same day. Residues of DPX-KNI28/IN-KN127 and IN-JT333 concentrated in cream at all three treatment levels, at levels of 0.21 (max. 0.25), 0.58, and 2.0 mg/kg, respectively, in comparison to the whole milk samples. The mean DPX-KNI28/IN-KN127 and IN-JT333 residues in milk, skimmed milk, and cream were proportional to the dosing level.

The mean DPX-KNI28/IN-KN127 levels in muscle were below the LOD in the low dose and middle dose group, and 0.066 mg/kg in the high dose group. In liver the DPX-KNI28/IN-KN127 levels were below the LOD in the low dose and middle dose group, and 0.018 mg/kg in the high dose group. In the kidneys, the DPX-KNI28/IN-KN127 levels were below the LOD in the low dose group, 0.017 mg/kg in the middle dose group, and 0.039 mg/kg in the high dose group. Fat contained the highest levels of DPX-KNI28/IN-KN127; a level of 0.22 mg/kg was found in the low dose group, 0.45 mg/kg in the middle dose group, and 1.9 mg/kg in the high dose group.

Levels of IN-JT333 above the LOD were only found in fat at the two highest dose groups and amounted to 0.030 mg/kg and 0.080 mg/kg, respectively.

The decline of residues in one animal of the high dose group was determined following cesssation of dosing. Eleven days after the final dose (at day 40), no residue levels above the LOD of DPX-KN128/IN-KN127 or IN-JT333 in milk were found. Fifteen days after the final dose, no residue levels above the LOD in muscle, liver, or kidney samples were observed.

In fat, residues of DPX-KN128/KNI27 and IN-JT333 had decreased to about 0.08 mg/kg and <0.01 mg/kg, respectively.

Conclusions
Following an intake of 7.5 mg/kg diet, plateau levels of DPX-KN128/KNI27 in whole milk are reached in ca. 2 weeks. Detectable levels of DPX-KN128/KNI27 are found in whole milk, cream, and significant levels are found in fat. No detectable levels of DPX-KN128/KNI27 are observed in skimmed milk, muscle, liver or the kidneys. Only in fat, detectable levels of IN-JT333 are present at this feeding level.

At higher intake levels, DPX-KN128/KNI27 levels increase proportional with the intake dose in whole milk, skimmed milk, cream, muscle, fat, liver, and the kidneys. IN-JT333 is found in fat and cream in detectable levels, that also increase proportional with the intake dose.

It is noted that the low feeding dose of 7.5 mg/kg diet represents ca. 58 x the TMDI (for both dairy and beef cattle), and including pome fruit ca. 21 and 9 x the TMDI, for dairy cattle and beef cattle, respectively (see section B.6.15). On the basis of the anticipated TMDI, it is estimated that DPX-KN128/KNI27 levels will be <LOD in milk, skimmed milk, cream, meat, fat, and edible offals.

If the use on pome fruit is considered, in cream DPX-KN128/KNI27 is expected to be at levels around the LOD. In fat, DPX-KN128/KNI27 levels are expected to be around the LOD in dairy cattle, and ca. 0.024 in beef cattle.

Levels of IN-JT333 are expected to be <LOD in all tissues and milk (products), with or without including the use on pome fruits.

Guidelines and limitations
No guidelines are currently in force. The study is suitable for evaluation.

B.7.4.3 - Pigs

Regarding swine matrices, as the metabolic fate of indoxacarb residues in rodents and ruminants is considered to be similar; the metabolism findings in ruminants can be extrapolated to pigs.

B.7.4.4 - Fish

As the log POW for indoxacarb (DPX-KN128) is 4.65, fish metabolism and feeding studies may be required. However, no EU guidelines are available for now.
Furthermore, residue level in grains of maize which could be fed to fish, are all under the LOQ, therefore, fish would not be significantly exposed through their diets. No data are required (see also section IIIA 8.2.5).

B.7.5 - EFFECTS OF PROCESSING

B.7.5.1 - Nature and magnitude of the residues in processed commodities

Previous evaluation:	*Studies submitted and evaluated for the first inclusion of indoxacarb on Annex I (2000, 2005)*

In the original Annex II dossier (2000), effect of processing on the nature of the residue and on the residue level has been described respectively for hydrolytic conditions and for grapes, apples, tomatoes through six processing studies presented hereafter.

Report:	KCA 6.5.1/01; Ferraro, P.S., McEuen, S.F. (1996)
Title:	Hydrolysis of DPX-JW062 (a racemic mixture of DPX-KN128 and DPX-KN127[1]) in buffer solutions of pH 5, 7, and 9
Report No:	AMR 2789-93
Guidelines:	**SETAC, U.S. EPA 161-1**
GLP/GEP:	**Yes / partially meets the current guideline (OECD 507)**

Report:	KCA 6.5.1/02; Spare, W.C. (1999)
Title:	Hydrolysis of DPX-JW062 (a racemic mixture of DPX-KN128 and DPX-KN127[1]) in buffer solutions of pH 5, 7, and 9
Report No:	AMR 2789-93, supplement No. 1
Guidelines:	**EU Working Document 7035/VI/95 Rev. 5-22.7.1997, U.S. EPA 161-1**
GLP/GEP:	**Yes / partially meets the current guideline (OECD 507)**

Report:	KCA 6.5.3/01; Guinivan, R.A.; Enriquez, M.A.; Tzanos, D.; Schelling-Schiavo, M. (1997)
Title:	Magnitude of KN128 Together with KN127 Residues in Tomato Products Derived From Tomatoes Grown in Europe with Applications of DPX-JW062 WG - Season 1995 (Analysis by GC/MSD)
Report No:	AMR 3390-95
Guidelines:	**Not applicable**
GLP/GEP:	**Yes / partially meets the current guideline (OECD 508)**

Report:	KCA 6.5.3/02; Guinivan, R.A.; Weidenauer, M.; Mollard, L. (1997)
Title:	Magnitude of DPX-KN128 Together with IN-KN127 Residues in Grape Products Derived From Grapes Grown in Europe with Applications of DPX-JW062 WG - Season 1995 (Analysis by GC/MSD)
Report No:	AMR 3388-95
Guidelines:	**91/414/EEC**
GLP/GEP:	**Yes / partially meets the current guideline (OECD 508)**

[1] DPX-KN127 should be IN-KN127

Report:	KCA 6.5.3/03; Zietz, E. (1997)
Title:	Magnitude of DPX-KN128 Together with IN-KN127 Residues in Apple Products Derived From Apples Grown in Europe with Applications of DPX-JW062 WG - Season 1995 (Analysis by GC/MSD)
Report No:	AMR 3389-95
Guidelines:	**91/414/EEC**
GLP/GEP:	**Yes / partially meets the current guideline (OECD 508)**

Report:	KCA 6.5.3/04; Zietz, E., Simpson, W. (1997)
Title:	Magnitude of Residues of DPX-KN128 Together with IN-KN127 in Apple Products Derived From Apples Grown in Europe Following Applications of DPX-MP062 WG - Season 1996
Report No:	AMR 4016-96
Guidelines:	**91/414/EEC**
GLP/GEP:	**Yes / partially meets the current guideline (OECD 508)**

In the addendum to the monograph (2005), effect of processing on the residue level has been described for peaches. This study is summarized hereafter.

Report:	KCA 6.5.3/04; Kennedy, C.M., Enriquez, M.A., Majdi, R., Matni, H. (2001)
Title:	Magnitude of residues of DPX-KN128 (indoxacarb) together with IN-KN127 in processed fractions of peaches (stone fruit) following applications of DPX-MP062 30WG - southern Europe, season 2000
Report No:	DuPont-4310
Guidelines:	**91/414/EEC**
GLP/GEP:	**Yes / partially meets the current guideline (OECD 508)**

All these studies are summarized above contributes to the understanding of processing. As these studies support crops not in the representative GAP, they are therefore not relied upon.

Conclusion
As no residues were found in maize and sweet corn grain at the intended maximum application rate, no studies on the effects of processing on the nature of the residue were considered necessary. Also lettuce is not a crop that undergoes processing.

B.7.6 - RESIDUES IN ROTATIONAL CROPS

B.7.6.1. - Metabolism in rotational crops

In the original Annex II dossier (2000), a metabolism in rotational crops study has been described. This study partially meets the current guideline (OECD 502) as no guideline was in force when the study was carried out.
Since EFSA stated that occurrence of indoxacarb residues in rotational crops was already investigated during the peer review of indoxacarb and as it was concluded that significant residues in rotational crops are not expected, no new study is required.

Previous evaluation:	*Studies submitted and evaluated for the first inclusion of indoxacarb on Annex I (2000)*

Report:	CA, 6.6.1; Freeman, C.J., Terranova, A.J. (1997)
Title:	Accumulation of residues in confined rotational crops (carrots, lettuce, wheat, and soybeans) using field aged soil after treatment with [^{14}C]DPX-JW062, a racemic mixture of DPX-KN128 and IN-KN127
Report No:	AMR 4029-96
Guidelines:	**U.S. EPA 860.1900 (1996)**
GLP/GEP:	**Yes / partially meets the current guideline (OECD 502)**
Deviations from the current guidelines	Further quantitative information is missing, e.g., on absolute levels of components in the various peaks (in mg eq/kg). Qualitative and quantitative details are missing on the characterization and identification of residues after treatment of the wheat straw organic extract by -glucosidase, and wheat straw pellets by cellulase, alkali, acid, and combustion. The soil aging periods were 36, 90 and 125 days instead of 7-30, 60-270 and 270-300 days.

Study design

Pots containing sandy loam soil were treated with a single application of either one of the radiolabelled forms of DPX-JW062 at a rate of 0.60 kg DPX-JW062/ha (equal to 0.30 kg DPX-KN128/ha). Soils were aged 30, 90, and 120 days in the field, and then transferred to a greenhouse. The soils were allowed to dry inside for another 5-6 days before planting the seeds for each crop. The following crops (varieties) were grown in the greenhouse at each aging period: hybrid carrot (Fontana); spring wheat (Katepawa); lettuce (Prizehead); and soybeans (A2242). Duplicate pots were planted for each radiolabel/rotational interval /crop.

Soil samples were taken at application, immediately prior to planting, and at maturity for each crop. For the wheat and soybean crops, immature plants were taken to represent forage samples. All remaining crops were harvested at maturity. The crop fractions harvested for analysis were carrot roots and tops; lettuce leaves; wheat forage, grain, and straw; and soybean seed, forage, and straw.

Total 14C-residues were determined by combustion LSC. Crop parts containing residues >0.01 mg eq/kg were extracted and analysed by HPLC. Metabolites were identified by LC/MS and LC/NMR.

Results

Soil residues decreased from 0.56 mg eq/kg at application (day 0) to 0.25-0.34 mg eq/kg (ranges for the indanone- and trifluoromethoxyphenyl labelled-moieties) after aging for 36 days. These concentrations remained about the same for soil aged 90 to 125 days (0.24-0.36 mg eq/kg).

Distribution of Total ^{14}C-residues in rotational crops are shown in the table below:

Table B.7.6-1 Distribution of Total 14C-residues in rotational crops

Part of plant	Rotational Interval	Total radioactive residues (mg as eq/kg)			
	(DAT)	Lettuce	Carrots	Soybean	Wheat
Leaves	36 90 125	0.01-0.03[1] 0.01 0.01			
Roots	36 90 125		0.01-0.02 0.01 0.01		
Tops	36 90 125		0.03-0.07 0.04 0.01		
Forage	36 90 125			0.06-0.13 0.03-0.08 0.02-0.05	0.14 0.04-0.07 0.02-0.05
Grain	36 90 125				0.04-0.24 0.01-0.04 0.01-0.03
Seed	36 90 125			0.03-0.08 0.02-0.06 0.02-0.03	
Straw	36 90			0.07-0.14 0.06-0.16	0.43-0.49 0.12-0.15

	125			0.08-0.17	0.12-0.15

[1] Ranges refer to the indanone- and trifluoromethoxyphenyl labelled-moieties

In the following table, distribution of extracted and bound residues are presented.

Table B.7.6-2 Distribution of extracted and bound residues in rotational crops at day-36 plant back interval

		Day-36 rotational interval								
		Percent (ppm) total [^{14}C] DPX-JW062-derived residues								
		carrots		lettuce	Spring wheat			soybean		
		tops	roots	Leaves	Forage	Straw	Grain	Forage	Hay	Seed
total [^{14}C] Residues	IND	(0.03)	(0.01)	(0.01)	(0.14)	(0.49)	(0.24)	(0.06)	(0.07)	(0.03)
	TMP	(0.07)	(0.02)	(0.03)	(0.14)	(0.43)	(0.04)	(0.13)	(0.14)	(0.08)
Extracted residues	IND	72.2 (0.02)	75.2 (0.01)	75.5 (0.01)	61.6 (0.09)	70 (0.34)	73.7 (0.16)	59.3 (0.03)	71.7 (0.05)	59.6 (0.02)
	TMP	65.0 (0.04)	51.1 (0.01)	67.5 (0.02)	60.1 (0.08)	60.1 (0.26)	65.4 (0.03)	71.3 (0.09)	71.2 (0.10)	87.6 (0.07)
Bound residues	IND	27.8 (<0.01)	24.8 (<0.01)	24.5 (<0.01)	38.4[2] (0.05)	30 (0.15)	26.3[3] (0.06)	40.7 (0.02)	28.3 (0.02)	40.4 (0.01)
	TMP	35.0 (0.02)	48.9 (0.01)	32.4 (0.01)	39.9[2] (0.06)	39.9 (0.17)	34.6 (0.01)	28.7 (0.04)	28.8 (0.04)	12.4 (0.01)

[1] TRR: extracted + bound residues.
[2] Due to low recovery of the sample pellet (post-extraction), additional characterization was not done.
[3] The extracted pellet was inadvertedly discarded; however, exhaustive extraction (enzyme, acid and base) would most likely remove only a portion of the bound residues. The concentration of the remaining bound residues and any extractable residue in the aqueous extracts would be below the criteria (0.05 ppm) for characterization.

Table B.7.6-3 Distribution of extracted and bound residues in rotational crops at day-90 plant back interval

		Day-90 rotational interval								
		Percent (ppm) total [^{14}C] DPX-JW062-derived residues								
		carrots		lettuce	Spring wheat			soybean		
		tops	roots	Leaves	Forage	Straw	Grain	Forage	Hay	Seed
total [^{14}C] Residues	IND	(0.04)	(0.01)	(0.01)	(0.04)	(0.12)	(0.04)	(0.03)	(0.06)	(0.02)
	TMP	(0.04)	(0.01)	(0.01)	(0.07)	(0.15)	(0.01)	(0.08)	(0.16)	(0.06)
Extracted residues	IND	91.1 (0.03)	NA[2]	NA	87.8 (0.04)	57.3 (0.07)	56.0 (0.02)	63.8 (0.02)	62.4 (0.04)	48.4 (0.01)
	TMP	68.7 (0.03)	NA	NA	78.0 (0.05)	48.2 (0.07)	65.9 (0.01)	65.5 (0.05)	68.2 (0.11)	80.6 (0.05)
Bound	IND	8.9	NA	NA	12.3	**42.7**	**44.0**	36.2	37.6	51.6

residues		(<0.01)			(0.01)	**(0.05)**	**(0.02)**	(0.01)	(0.02)	(0.01)
	TMP	31.3 (0.01)	NA	NA	22.0 (0.02)	**51.8 (0.08)**	34.1 (<0.01)	34.5 (0.03)	31.8 (0.05)	19.4 (0.01)

[1] TRR: extracted + bound residues

[2] NA: denotes samples not analyzed (TRR at day 36 <0.01 ppm)

Table B.7.6-4 Distribution of extracted and bound residues in rotational crops at day-125 plant back interval

		Day-125 rotational interval								
		Percent (ppm) total [^{14}C] DPX-JW062-derived residues								
		carrots		lettuce	Spring wheat			soybean		
		tops	roots	Leaves	Forage	Straw	Grain	Forage	Hay	Seed
total [^{14}C] Residues	IND	(0.01)	(0.01)	(0.01)	(0.02)	(0.12)	(0.03)	(0.02)	(0.17)	(0.02)
	TMP	(0.01)	(0.01)	(0.01)	(0.05)	(0.15)	(0.01)	(0.05)	(0.08)	(0.04)
Extracted residues	IND	NA[2]	NA	NA	82.9 (0.02)	72.1 (0.09)	62.6 (0.02)	59.1 (0.01)	79.8 (0.06)	56.0 (0.01)
	TMP	NA	NA	NA	63.5 (0.03)	69.2 (0.11)	74.4 (0.01)	59.9 (0.03)	80.9 (0.14)	77.1 (0.03)
Bound residues	IND	NA	NA	NA	17.1 (<0.01)	27.9 (0.03)	37.4 (0.01)	40.9 (0.01)	20.2 (0.02)	44.0 (0.01)
	TMP	NA	NA	NA	36.5 (0.02)	30.8 (0.05)	25.6 (<0.01)	40.1 (0.02)	19.1 (0.03)	**22.9 (0.02)**

[1] TRR: extracted + bound residues.

[2] NA: denotes samples not analyzed (TRR at day 36 <0.01 ppm)

Residues present in lettuce, carrots, soybean and wheat samples from the rotational crop study were further characterized and identified. For all crops and crop parts, between approximately 48 and 91% of the total residue was extractable and 9-52% remained un-extractable. Extraction efficiency was relatively low for some crop samples. Indeed, remaining unextracted radioactivity was high in wheat straw (up to 0.17 mg/kg at day-36), in wheat grain (0.02 mg/kg at day-90) and in soybean seed (0.02 mg/kg at day-125). **RMS is of the opinion that further investigation on the nature of the bound residues could be requiered.**

No single metabolite could be identified in any plant sample, despite the considerable analytical efforts made. Fractions consisted of one or more components, with no single component greater than 0.01 mg eq/kg, observed in lettuce, carrot tops and roots, wheat forage, and soybean seeds and straw. The components were all more polar than the parent compound.
A single polar component was observed in the extractable fraction of wheat grain. However, following analysis by LC/MS, a unique structure could not be assigned and no ions were detected which were consistent with the intact parent molecule.

Also a single polar component was observed in the extractable fraction of wheat straw. Upon further characterisation with- glucosidase, this was resolved into multiple polar components with no single component >0.050 mg eq/kg. These results are consistent with glucose conjugation of numerous polar components. Differences were observed in the chromatographic profiles of the indanone- and the trifluoromethoxyphenyl labelled moieties, indicating fragmentation of the DPX-KN128/IN-KN127 skeleton. The un-extracted residue in wheat straw (0.15-0.17 mg eq/kg, at 36 days rotational interval) was further characterised by cellulase, alkaline

and acid treatment. Because the concentration of residue in each of the obtained aqueous extracts was low (<0.05 mg/kg), the residues were not further analyzed. The pellets recovered from acid treatment were combusted to determine the concentration of matrix-bound residues that amounted to 0.05-0.07 mg eq/kg. In the samples of the 90-day and 125-day rotational interval, no single component was detected at a level >0.01 mg eq/kg.
No detectable DPX-KN128/IN-KN127 or IN-JT333 levels were present in the extracts of any crop fraction.
The longest interval between crop sampling and initial extraction was 111 days.

Conclusions
The average concentrations of total residues in the soil were 0.56, 0.25-0.34, 0.25-0.33, and 0.24-0.46 mg eq/kg, after rotational intervals of 0, 36, 90, and 125 days, respectively.
At 36, 90, and 125 days after soil treatment with ^{14}C-labeled DPX-JW062, no single main metabolite component was observed exceeding 0.050 mg/kg. Instead, multiple components, including glucose- and matrix-bound residues, were found in small quantities. Parent compound and the insecticidally active metabolite IN-JT333 were not detected in the crop samples. **However, due to low extraction efficiency in some samples, the RMS believes that further investigations are required on the nature of the bound residues.**

B.7.6.2. - Magnitude of residues in rotational crops

As presented in the section above, according to the available data, significant residues of indoxacarb and it metabolite IN-JT333 in rotational crops are not expected. Therefore, no magnitude of residue study in rotational crop is required.

B.7.7 - OTHER STUDIES

B.7.7.1 - Effect on the residue level in pollen and bee products

INDOXACARB 150 g/L EC (EC formulation containing 150 g/kg DPX-KN128)

The data requirement objective of these studies is to determine the residue in pollen and bee products for human consumption resulting from residues taken up by honeybees from crops at blossom.
As no final guidance document related to setting MRLs in honey is available, the effect of indoxacarb on bee products was not tested by the notifier.
However, among crops under consideration, lettuce is not attractive for the bees. Besides, residue trials showed a no residues situation in cereals grain (see section B.7.3). Therefore, no significant residue levels are expected in the blossoms and in the pollen. As maize does not produce nectar, bees are only exposed to pollen residues. Thus, exposure of indoxacarb residues to foraging bees and, consequently, possible residues of indoxacarb in honey or other bee products are considered unlikely to occur.

B.7.8 - REVIEW OF OPEN SCIENTIFIC LITTERATURE

A literature review report on indoxacarb (DPX-MP062, DPX-KN128, IN-KN127), has been submitted by the applicant in the framework of this renewal assessment.

Four databases have been searched (AGRICOLA, BIOSIS, CABA, CAplus). The time window considered for the search was from 2005 to 2013. The initial search is a single concept search capturing all data points using search terms and synonyms for the active substance. If a large number of search results are returned from the single concept search making assessment for relevance impractical, a separate, focussed search is conducted for grouped data points. A separate single concept search is also conducted for each relevant metabolite.

Table B.7.8-1 Relevance criteria

Data requirement(s) (indicated by the correspondent data point number(s) as identified in Commission Regulation (EU) 283/2013)	Criteria for relevance
All Data Points	1. The dose levels or application rates reflect the proposed GAP.
	2. The test system, target crop, or species are prescribed by Regulation (EC) No 1107/2009 or the relevance is explained if not standard.
	3. Well identified test material, including its purity and impurity profile, is described.
	4. Study design and/or execution are consistent with relevant study guidelines.
	5. The endpoint is relevant to an EU data point as prescribed by Regulations (EU) No 283/2013 and 284/2013
Toxicological and toxicokinetic studies	6. Description of the observations, examinations, analysis performed, or necropsy are well described.
	7. The conditions of exposure should be from a legally registered use of the product.
Residues in or on treated products, food and feed (metabolism and residues data)	8. The application method(s) complies with Good Agriculture Practice (GAP)
	9. Appropriate in-life/processing conditions are used and/or are well described
Fate and behaviour in the environment	10. The model is appropriate for European regulatory requirements.
	11. The input parameter selection is appropriate based on European regulatory requirements.
	12. The pedoclimatic conditions are appropriate.
Ecotoxicological studies	13. A relevant route of exposure is presented.

For indoxacarb (DPX-MP062, DPX-KN128, IN-KN127), and concerning metabolism and residues, a total of 452 summary record were found, and all of them were excluded after a rapid assessment for the relevance. Therefore, no study was identified as relevant for the residues section within the time window considered.

The area of metabolism and residues, ecotoxicology and mammalian toxicology were most represented in the search results. However, only 8 studies were retained as relevant (7 in the mammalian toxicology area and one in the ecotoxicology area).

In the table hereafter, a review of the search method step by step for indoxacarb and metabolites is detailed:

Table B.7.8-2 Details of literature search for indoxacarb

Indoxacarb/DPX-KN128 173584-44-6 / Initial search	
	Databases Searched in STN: AGRICOLA, BIOSIS, CABA, CAplus, Metabolism, Residue
Justification for using these sources:	AGRICOLA – A bibliographic database containing selective worldwide coverage of agriculture and related fields. (4.2+ million records) BIOSIS - Contains information on life sciences, including biological and biomedical areas. (18.7+ million records) CABA – Covers worldwide literature from all areas of agriculture and related applied and life sciences. (5.3+ million records) CAplus – Covers worldwide literature from all areas of chemistry, biochemistry, chemical engineering, and related sciences. (28.6+ million records)
Date of the search:	March 1, 2013
Date range of the search:	2005-2013
Search strategies used:	1. 83120 s 173584-44-6 2. 39751 s L1 and 2005-2013/py 3. 38957 s L2 not p/dt 4. 2063 s L3 and (pesticide? Or herbicid? Or fungicid? Or insecticid?) 5. 1432 dup rem L4 (631 duplicates removed) 6. 333 s L5 and (METABOL? OR RESIDU? OR BIOTRANSFORM? OR DIET?(W)RISK?)
Total number of original records retrieved:	**333**
Indoxacarb/DPX-KN128 173584-44-6 / Final search	
Date of the final search:	18 November 2014
Date range for final search	2012-2014
Search strategies used:	FILE 'CAPLUS, CABA, BIOSIS, AGRICOLA' ENTERED AT 15:43:50 ON 18 NOV 2014 L1 3481 S INDOXACARB OR KN128 OR 173584-44-6 L2 793 S L1 AND 2013-2014/PY L3 427 S L2 NOT P/DT L4 401 S L3 AND (PESTICID? OR HERBICID? OR INSECTICID? OR FUNGICID?) L5 280 DUP REM L4 (121 DUPLICATES REMOVED) L6 93 SL5 AND (METABOL? OR RESIDU? OR BIOTRANSFORM? OR DIET?(W)RISK?)
Total number of original records retrieved:	**93**
DPX-JW062 144171-61-9 / Initial search (Following the same methodology) IN-KN127 185608-75-7 (First search)	
Total number of original records retrieved:	**301**
DPX-JW062 144171-61-9 and IN-KN127 185608-75-7 (Final search)	
Total number of records retrieved:	**4**

Grand Total (both searches, DPX-KN128, IN-JW062 and IN-KN1127	739 after removing duplicates **452**

B.7.9 - REFERENCES RELIED ON

Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
CA, 6.1	Desmond, P.J.	1997	A study of the recovery of residues of DPX-KN128/ DPX-KN127[1] (formulated as either DPX-JW062 or DPX-MP062) after frozen storage on: Grapes, grape wet pomace, wine, apples, lettuce, tomatoes, apple juice, and soil; and incurred residue studies on tomatoes, DuPont Experimental Station AMR 3778-96 Study previously reviewed for EU approval in the 2000 DAR. Published: No [1] DPX-KN127 should be IN-KN127	N	N		DuPont	Y
CA, 6.3.1/03	Guinivan, R., Kennedy, C.M., Enriquez, M.A.	2003a	Combined decline and magnitude of residues of DPX-KN128 (indoxacarb) together with IN-KN127 in maize (green plant and grain) following applications of DPX-MP062 30WG – Europe, season 2001 Battelle Europe-Centre de Recherche de Geneve DuPont-6006 GLP: Yes	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not	DuPont	

			Published: No			expired at the time of submission of this dossier		
CA, 6.3.1/04	Guinivan, R.A, Kennedy, C.M., Enriquez, M.A.	2003b	Combined decline and magnitude of residues of DPX‑KN128 (indoxacarb) together with IN-KN127 in maize (green plant and grain) following applications of DPX-MP062 30WG and DPX-MP062 150SC – Europe, season 2002 Battelle Europe-Centre de Recherche de Geneve DuPont-9777 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier	DuPont	
CA, 6.1/01	Guinivan, R.A., Daussin, S.	2008	Recovery of DPX-MP062 and five metabolites from hen-derived matrices (whole eggs, muscle, fat and liver) after frozen storage Dupont Stine-Haskell Research Center DuPont-19901 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier.	DuPont	

CA, 6.2.1	Gaddamidi, V., Hashinger, B.M.,	1997b	Metabolism of [^{14}C]DPX-JW062, a racemic mixture of DPX-KN128 and IN-KN127, in grapes DuPont Experimental Station AMR 2729-93 Study previously reviewed for EU approval in the 2000 DAR. Published: No	N	N		DuPont	Y
CA, 6.2.1	Scott, M.T., Guseman, J.C.	1997	Metabolism of ^{14}C-DPX-JW062, a racemic mixture of DPX-KN128 and IN-KN127, in cotton DuPont Experimental Station AMR 2691-93 Study previously reviewed for EU approval in the 2000 DAR. Published: No	N	N		DuPont	Y
CA, 6.2.1	Brown, A.M., Young, G.A.	1997	Metabolism of [TMP(U)-^{14}C]DPX-JW062, a racemic mixture of DPX-KN128 and IN-KN127, insecticide in tomatoes DuPont Experimental Station AMR 3561-95 Study previously reviewed for EU approval in the 2000 DAR. Published: No	N	N		DuPont	Y
CA, 6.2.2	[redacted]	1997	Metabolism of ^{14}C-DPX-JW062 (racemic mixture of DPX-KN128 and IN-KN127) in laying hens [redacted] AMR 3187-94 Study previously reviewed for EU approval in the 2000 DAR. Published: No	Y	N		DuPont	Y
CA, 6.2.3	[redacted]	1997b	Metabolism of ^{14}C-DPX-JW062, a racemic mixture of DPX-KN128 and IN-KN127, in the lactating cow [redacted] AMR 2979-94, Supplement No. 1	N	N		DuPont	Y

			Study submitted in the EU Dossier in 2001 and included in the first EU approval review. Published: No					
CA, 6.3.1/01	Aitken, A.	2014a	Determination of the Decline of Residues of DPX-KN128 (Indoxacarb) along with IN-KN127 in Maize Forage Following Applications of DPX-MP062 30WG - Southern Europe – 2012 Charles River Laboratories (UK) DuPont-35172 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier	DuPont	

CA, 6.3.2/01	Giammarrusti, L., De Paoli, M.	2003	Decline of residues of DPX-KN128 (indoxacarb) together with IN-KN127 in sweet corn following application of DPX-MP062 30WG - Italy, season 2003 ERSA DuPont-13320 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier	DuPont	
CA, 6.3.3	Kennedy, C.M., Enriquez, M.A., Gasser, F., Larcinese, J.P., Belgaid, R.	2000	Combined decline and magnitude of residues of DPX-KN128 (indoxacarb) together with IN-KN127 in leaf vegetables (field lettuce) following applications of DPX-MP062 30WG - southern Europe, season 1999 Battelle Europe-Centre de Recherche de Geneve DuPont-2577 Study previously reviewed for EU approval in the 2005 DAR. Published: No	N	N		DuPont	Y
CA, 6.3.3	Kennedy, C.M., Enriquez, M.A., Larcinese, J.P., Mattou, H.	1999	Combined decline and magnitude of residues of DPX-KN128 (indoxacarb) together with IN-KN127 in leaf vegetables (lettuce) following applications of DPX-MP062 30WG southern Europe - season 1998 Battelle Europe-Centre de Recherche de Geneve AMR 5006-98 Does not supporta crop not in the representative GAP Published: No	N	N		DuPont	
CA, 6.3.3/01, Bridging	Lakaschus, S., Amann, S.	2012	Determination of magnitude of residues of DPX-KN128 (indoxacarb) together with	N	Y	The study is necessary for the regulatory decision,	DuPont	

			IN-KN127 in lettuce following applications of DPX-MP062 30WG and DPX-KN128 30WG - Europe, 2011 Eurofins Agroscience Services Chem GmbH DuPont-33518 GLP: Yes Published: No			conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier		
CA, 6.3.3/02, Bridging	Old, J., Hansford, R.J., Ward, L.	2007	Determination of magnitude of residues of DPX-KN128 (indoxacarb) together with IN-KN127 in lettuce and broccoli/cauliflower following applications of DPX-MP062-30WG and DPX-KN128-15EC - Europe 2006 Charles River Laboratories (UK) DuPont-19688 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier	DuPont	
CA, 6.3.3/03	Spence, C.	2014	Determination of magnitude and decline of residues of DPX-KN128 (indoxacarb) along with IN-KN127 in lettuce following applications of DPX-KN128 30WG - Europe - initiated 2012 Charles River Laboratories (UK) DuPont-35819 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier	DuPont	
CA, 6.4.1/01	[redacted]	2003	Magnitude of residues of indoxacarb (as DPX-MP062) in laying hen tissue and eggs: a feeding study conducted to EPA guidelines [redacted]	Y	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not	DuPont	

			[redacted] DuPont-8305 GLP: Yes Published: No			previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier.		
CA, 6.4.2	[redacted]	1997	Magnitude of residues of DPX-KN128/IN-KN127 and IN-JT333 in edible tissues and milk of lactating dairy cows following dosing with DPX-MP062 experimental insecticide [redacted] AMR 3820-96 Study previously reviewed for EU approval in the 2000 DAR. Published: No	Y	N		DuPont	Y
CA, 6.6.1	Freeman, C.J., Terranova, A.J.	1997	Accumulation of residues in confined rotational crops (carrots, lettuce, wheat, and soybeans) using field aged soil after treatment with [^{14}C]DPX-JW062, a racemic mixture of DPX-KN128 and IN-KN127 DuPont Experimental Station AMR 4029-96 Study previously reviewed for EU approval in the 2000 DAR. Published: No	N	N		DuPont	Y