NOVALURON (217)

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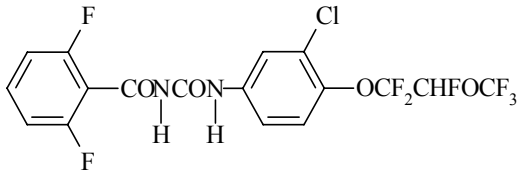
EXPLANATION

Novaluron was listed as a candidate for New Compounds at the 36th Session of the CCPR for evaluation by the 2005 JMPR. Novaluron, a benzoylphenyl urea compound, is an insect growth regulator. Novaluron inhibits chitin synthesis, affecting the moulting stages of insect development. It acts by ingestion and contact and causes abnormal endocuticular deposition and abortive moulting.

The manufacturer has submitted studies on physical and chemical properties, animal metabolism, plant metabolism (apple, cabbage, potato and cotton), environmental fate, rotational crops, analytical methods, storage stability, GAP, supervised field trials, processing studies, and livestock feeding. Additionally, the Netherlands submitted GAP information.

IDENTITY

ISO common name:	Novaluron (provisionally approved E-ISO) (applied to the racemate)
IUPAC Name	(±)-1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxy ethoxy) phenyl]-3-(2,6-difluorobenzoyl)urea
Chemical Abstract name	(±)-N-[[[3-chloro-4-[1,1,2-trifluoro-2-(trifluoromethoxy)ethoxy] phenyl] amino]carbonyl]-2,6-difluorobenzamide
CAS No.	116714-46-6
Synonyms	Novaluron (BSI)
Structural formula	
Molecular Formula	$C_{17}H_9ClF_8N_2O_4$
Molecular Weight	492.7

Physical and Chemical Properties

Pure Active Ingredient

Novaluron was evaluated by the JMPS in 2003 and the WHO specifications for the pure substance are presented in Table 1.

Table 1. Physical and chemical properties of pure novaluron.

Parameter	Value(s) and conditions	Purity %	Reference[1]
Appearance	Pale pink to white solid		Evaluation Report 672/2003, R-16922, WHO specifications
Vapour pressure:	1.6×10^{-5} Pa at 25°C	99.5	Evaluation Report 672/2003, R-16922, WHO specifications (method ref: OECD 104 equivalent to EEC A4)
Melting point and temperature of decomposition:	Melting point: 176.5 to 178.0°C Decomposition temperature: not determined	99.5	Evaluation Report 672/2003, R-16922, WHO specifications (method ref:OECD 102 equivalent to EEC A1)
Solubility in water:	3 µg/L at 20 °C at neutral pH	99.5	Evaluation Report 672/2003, R-16922, WHO specifications (method ref:OECD 105 equivalent to EEC A6)
Solubility in organic solvents	At 20°C: n-heptane 0.00839 g/L xylene 1.88 g/L 1,2-dichloroethane 2.85 g/L methanol 14.5 g/L acetone 198 g/L ethyl acetate 113 g/L	99.3	Evaluation Report 672/2003, R-16922, WHO specifications
Octanol / water partition coefficient:	log P_{OW} = 4.3 at 20-25 °C, pH 7.1	99.5	Evaluation Report 672/2003, R-16922, WHO specifications (OECD 117 equivalent to EEC A8)
Hydrolysis characteristics:	Stable at pH 5 and pH 7 at 25°C. At pH 9: half-life at 25°C: 101 days (rate constant: 0.006846 $days^{-1}$) half-life at 50°C: 1.2 days (rate constant: 0.58614 $days^{-1}$) half-life at 70°C: 0.09 days (2.2 hours) (rate constant: 7.4355 $days^{-1}$) Half-life at 20°C at pH 9 estimated (Arrhenius equation) as 217 days (rate constant: 0.00320 $days^{-1}$).	> 97	Evaluation Report 672/2003, R-16922, WHO specifications (method ref: Makhteshim method)
Photolysis characteristics:	DT_{50}= 139 days of natural summer sunlight at latitude 40°N, assuming 12 hours of daylight, pH 5	> 97	Evaluation Report 672/2003, R-16922, WHO specifications
Dissociation characteristics:	Does not dissociate.	-	-

[1] www.who.int/entity/whopes/quality/en/Novaluron_evaluation_Dec_2004.pdf

Technical Material

Table 2 presents a summary of the properties of Novaluron technical material as evaluated by the JMPS in 2003 for the establishment of the WHO specifications for the compound.

Formulations

Novaluron is available in two formulations: emulsifiable concentrate (EC) formulation containing 100 g/L active ingredient; water dispersible granule (WG) formulation containing 75 g/kg active ingredient.

Table 2. Chemical composition and properties of novaluron technical material

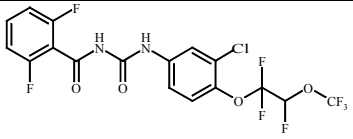
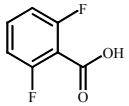
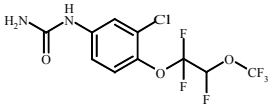
Parameters	Limits
Manufacturing process, maximum limits for	Confidential information supplied and held on file by WHO. Mass

impurities ≥ 1 g/kg, 5 batch analysis data.	balances in an early 3-batch analysis study were 99.52 to 100.11 % and percentages of unknowns were < 0.1 %. Mass balances in a subsequent 5-batch study of full production batches were 99.5 to 99.7%.
Declared minimum [ai.] content:	985 g/kg
Relevant impurities ≥ 1 g/kg and maximum limits for them:	None
Relevant impurities < 1 g/kg and maximum limits for them:	None relevant
Stabilisers or other additives and maximum limits for them:	None
Melting or boiling temperature range	Melting point: 176 to 179°C

METABOLISM AND ENVIRONMENTAL FATE

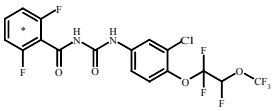
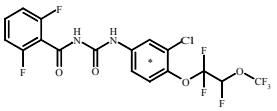
The following table summarizes metabolites identified in the various metabolism and environmental fate studies.

Table 3. Summary of Metabolites and Degradates.

Common name/code	Chemical name	Chemical structure	Found In
Novaluron	N-[[[3-chloro-4-[1,1,2-trifluoro-2-(trifluoromethoxy)ethoxy]phenyl]amino]carbonyl]-2,6-difluorobenzamide		Goat Hen Rat
275-158I	2,6-difluorobenzoic acid		Goat Rat Hydrolysis
275-352I	1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]urea		Goat Rat Hydrolysis Soil
275-309I	3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)aniline		Goat (faeces) Rat Soil
275-157I	2,6-difluorobenzamide		Rat Hydrolysis

The following indicates the location of the radiolabel (^{14}C) for the novaluron metabolism studies.

Location of the Radiolabel for Metabolism Studies

Chemical structure		
Radiolabel position	Uniformly in the difluorophenyl ring	Uniformly in the chlorophenyl ring

Animal metabolism

The Meeting received a report on the metabolism of radiolabeled novaluron in rats (O'Connor, 2000, Report No R-10004). Sprague-Dawley CD rats were orally administered [chlorophenyl-^{14}C(U)] novaluron as a single 2 mg/kg bw dose, a single 1000 mg/kg bw dose, or a repeated dose of 2 mg/kg bw daily for 14 days. Additional rats were orally administered [difluorophenyl-^{14}C(U)] novaluron as a single dose of 2 mg/kg. The distribution of TRR (total radioactive residue) was determined, and the radioactivity was characterised in major matrices. The majority of the administered radiolabel, about 96%, was recovered in the cage wash, urine, and faeces.

Novaluron (< 0.1–0.3% of administered dose) and 3-chloro-4-(1,1,2-trifluro-2-trifluoromethoxyethoxy)aniline (< 0.1 – 1.1% administered dose) were tentatively identified in urine 7 days after the final administration of chlorophenyl-^{14}C novaluron. 2,6-Difluorobenzoic acid (11% administered dose) was characterized in urine after the administration of difluorophenyl-^{14}C novaluron. For the [chlorophenyl-^{14}C(U)] novaluron 72 – 88% of the administered dose was found in faeces and was identified as novaluron. For the [difluorophenyl-^{14}C(U)] novaluron 77 – 80% of the administered dose was found in faeces and was identified as novaluron. Several metabolites were tentatively identified (co-chromatography) in tissues 7 days after the final administration of a single 2 mg/kg dose of chlorophenyl-^{14}C or difluorophenyl-^{14}C novaluron, as a percentage of TRR in the tissue: 2,6-difluorobenzamide, 7% kidney; 2,6-difluorobenzoic acid, 3% kidney; 1-[3-Chloro-4-(1,1,2-trifluro-2-trifluoromethoxyethoxy) phenyl]urea, 1–26% kidney, 3% liver; 3-Chloro-4-(1,1,2-trifluro-2-trifluoromethoxyethoxy)aniline, 4.3% kidney, 16% liver; novaluron, 39 – 54% kidney, 11 – 76% liver, 64 – 88% fat.

The Meeting received a report on the metabolism of radiolabeled novaluron that was orally administered to lactating goats (Corden, 1999; Report No. MAK 461/984693).

Goat 1 (59 kg) was dosed (orally with capsules) with 24.5 mg of [difluorophenyl-^{14}C(U)-]-novaluron for five consecutive days, the equivalent of 12.3 ppm in the diet. The radiochemical purity was > 98%, and specific activity was 134000 dpm/ug. Goat 2 (48 kg) was dosed with 20.1 mg of [chlorophenyl-^{14}C(U)]-novaluron for five consecutive days, the equivalent of 10.6 ppm in the diet. The radiochemical purity was > 99%, and specific activity was 139000 dpm/ug.

Excreta were collected (continually, 24 hr fractions). The animals were milked twice daily in the morning and afternoon, at a minimum of 6 hour intervals. The animals were slaughtered 23 hours after administration of the final dose. The following were sampled, homogenized, divided into subsamples, and stored frozen: liver, subcutaneous fat, peritoneal fat, muscle from foreleg, muscle from rump, kidney, bile, rumen (reticulum and contents), omasum and abomasum and contents, and intestines with contents.

Overall recovery of the [difluorophenyl-^{14}C(U)]-novaluron was 83%, based on the total administered dose. Of that, 4.1% was recovered in the urine, < 0.1% in cage wash, 52% in faeces, 11% in the intestine contents, 3.8% in fat (assuming 15% of the body weight is fat), 0.4% in liver, and < 0.1% in kidney. Total recovery of the [chlorophenyl-^{14}C(U)]-novaluron was 89%, based on the total administered dose. Of that, 0.9% was recovered in urine, < 0.1% in cage wash, 72% in faeces, 0.8% in intestine contents, 5% in fat (assuming 15% of the body weight is fat), 0.4% in liver, and < 0.1% in kidney.

The total radioactive residues (TRR) determined in tissues and milk (daily pooled samples) is summarized in Table 4. Liquid scintillation counting or combustion followed by liquid scintillation counting was utilized.

Table 4. Distribution of TRR in goat tissue and milk (daily pooled sample) following 5 daily administrations of chlorophenyl-14C or difluorophenyl-14C novaluron at 11 – 12 ppm in the feed (MAK 461/984693)

Substrate	TRR (mg/kg parent equivalent)	
	difluorophenyl-^{14}C	chlorophenyl-^{14}C
Peritoneal fat	1.4	1.9
Subcutaneous fat	1.1	1.3
Kidney	0.14	0.16
Liver	0.43	0.34
Foreleg muscle	0.09	0.16
Rump muscle	0.09	0.08
Milk (hrs after 1st dose)		
24	0.08	0.06
48	0.16	0.13
72	0.16	0.17
96	0.18	0.22
120	0.24	0.23

Residues did not plateau in milk over the 5 days of the study.

The extractability of the TRR from tissues by methanol was assessed by repeated extraction (4×). The results are summarised in Table 5. Greater than 90% of the TRR was extracted by methanol in all cases. Milk samples (pooled, 24–120 hrs after initial dose) were extracted with methanol/hexane. About 71 – 75% of TRR in milk was associated with the fat fraction (hexane extract) and 24 – 29 % TRR with the aqueous fraction.

Table 5. Extraction of TRR from tissues by repeated methanol extractions following 5 daily administrations of chlorophenyl-14C or difluorophenyl-14C novaluron at 11 – 12 ppm in the feed (MAK 461/984693).

Methanol	difluorophenyl-^{14}C (% TRR)				chlorophenyl-^{14}C (% TRR)			
Extract	Liver	Kidney	Muscle[2]	Fat[3]	Liver	Kidney	Muscle[2]	Fat[3]
Extract 1	44	56	54	69	48	53	60	65
Extract 2	22	25	26	25	31	29	26	26
Extract 3	12	11	10	5	10	10	9	6
Extract 4	5.8	4	4	1	4	4	3	2
Extract 5[1]	1.5	-	-	-				
Total extract	85	96	98	100	94	94	98	100
Unextracted	6.9	4	2	<1	6	6	2	<1
Total	92	100[4]	100[4]	100[4]	100[4]	100[4]	100[4]	100[4]

[1] Methanol: water, not included in characterization
[2] Muscle is foreleg muscle
[3] Fat is peritoneal fat
[4] Normalized

Some characterization of extracts was undertaken by HPLC with radiodetection and by normal and reverse phase TLC. For HPLC work, identifications were made by retention time comparisons of the radiolabeled compound in the extract and the retention time (UV detector) of the unlabeled standard from co-injections. For TLC work, chromatographic correspondence of reference standards with the radioactive components on the TLC plate was established by applying both the reference standard (unlabeled) and the extract as 2 cm wide bands on the plate. After development, the radiochromatogram was compared with the visualization under UV light. Reference materials included 2,6-difluorobenzamide, 2,6-difluorobenzoc acid, 3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy) aniline, and parent. Results are summarized in Tables 6 and 7. LOQ was 0.001 μg parent equivalent/g.

Residues amounting to 73-100% TRR were identified in goat milk and tissues using HPLC and TLC analyses. Parent novaluron was the only residue identified in milk at 93-95% TRR, in peritoneal fat at 96 -100% TRR, and in foreleg muscle at 98% TRR. Novaluron was the major residue identified in kidney and liver at 73-83% TRR and 80 - 84% TRR, respectively. Minor residues of 2,6-

difluorobenzoic acid were also identified in difluorophenyl-labelled kidney and liver at 5.1% TRR (0.007 mg/kg each), and 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]urea was identified in chlorophenyl-labelled liver, at 7.3% TRR (0.025 mg/kg). In addition, up to six unknowns were characterized in milk, kidney, and liver, each accounting for < 8% TRR (0.011 mg/kg). Two unknowns detected by HPLC, one in difluorophenyl-labelled liver at 8.5% TRR (0.036 mg/kg) and one in chlorophenyl-labelled kidney at 13.% TRR (0.021 mg/kg), were re-analyzed by TLC. TLC analysis determined that the difluorophenyl liver unknown consisted of numerous smaller polar components each accounting for < 4% TRR. TLC analysis of the chlorophenyl kidney unknown determined smaller components present at < 10% TRR; further partitioning of the isolated unknown characterized 6.4% TRR as organosoluble and 4.4% TRR as aqueous soluble.

Table 6. Proportion of components of TRR (as % of TRR) following 5 daily administrations of chlorophenyl-14C (c-14C) or difluorophenyl-14C (d-14C) novaluron at 11 – 12 ppm in the feed of goats (MAK 461/984693).

		Faeces		Urine		Liver (0.43 mg/kg)		Kidney (0.14 mg/kg)		Muscle (foreleg) (0.081 mg/kg)		Fat (peritoneal) (1.4 mg/kg)	
RT[1]	ID	d-^{14}C	c-^{14}C	d-^{14}C	c-^{14}C	d-^{14}C	c-^{14}C	d-^{14}C	c-^{14}C	d-^{14}C	c-^{14}C	d-^{14}C	c-^{14}C
4–6		< 0.02	< 0.01	< 0.8	< 0.4	8.5[6]	2.5	<1.7	**13**[2]	<2.4	<2.5	<1.2	< 0.3
16-18		< 0.02	< 0.01	< 0.8	< 0.4	0.5	<1.1	<1.7	<1.5	<2.4	<2.5	<1.2	< 0.3
20-21		< 0.02	< 0.01	< 0.8	< 0.4	0.6	<1.1	<1.7	<1.5	<2.4	<2.5	<1.2	< 0.3
22-24		< 0.02	< 0.01	53	< 0.4	< 0.4	<1.1	7.8	<1.5	<2.4	<2.5	<1.2	< 0.3
26-30		< 0.02	< 0.01	**47**[3]	24	**1.4**[5]	<1.1	**5.2**[5]	4.3	<2.4	<2.5	<1.2	< 0.3
34-37		< 0.02	1.8[7]	< 0.8	37	< 0.4	**7.3**[4]	<1.7	3.9	<2.4	<2.5	<1.2	< 0.3
38-40		< 0.02	< 0.01	< 0.8	3.1	0.4	<1.1	<1.7	<1.5	<2.4	<2.5	<1.2	< 0.3
41-45	Parent	96	87	< 0.8	2.7	80	84	83	73	98	98	99	99
	Other	< 0.02	< 0.01	< 0.8	16	< 0.4	<1.1	-	0.1	<2.4	<2.5	<1.2	< 0.3
Total extracts (approximate)		96	89			91	94	96	100	98	98	100	100
Total not analysed						1.6	-						
Total unextracted		4	11			7	6	4.2	0.5	2.1	1.7	0.2	0.5
Total		100	100			100	100	100	100	100	100	100	100

[1] Retention time in minutes, based on HPLC.
[2] A number of small components, each <10%, from TLC
[3] Primarily 2,6-diflurobenzoic acid (275-158I)
[4] Primarily 1-[3-Chloro-4-(1,1,2-trifluro-2-trifluoromethoxyethoxy)phenyl]urea (275-352I), about 5.7% TRR.
[5] 2,6-difluorobenzoic acid (275-158I). Confirmed by TLC.
[6] Normal phase TLC showed a number of polar components, none >4% TRR (0.017 mg/kg).
[7] Characterized by TLC as two components which chromatographed with 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl urea (275-352I) and 3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)aniline (275-309I), about 1.2% and 0.4%, respectively.

Table 7. Proportion of components of TRR (as % of TRR) in milk (0.22 mg/kg TRR) following 5 daily administrations of chlorophenyl-14C (c-14C) or difluorophenyl-14C (d-14C) novaluron at 11 – 12 ppm in the feed (MAK 461/984693).

		Fat soluble component (hexane soluble, 0.16 mg/kg)		Aqueous component (0.064 mg/kg)	
RT (min)	Identification	d-^{14}C	c-^{14}C	d-^{14}C	c-^{14}C
4–6		< 0.6	1.8	0.4	13[1]
16-18		< 0.6	< 0.4	< 0.3	0.8
20-21		< 0.6	< 0.4	< 0.3	< 0.6
22-24		< 0.6	< 0.4	1.3	< 0.6
26-30		0.7	< 0.4	< 0.3	< 0.6
34-37		< 0.6	< 0.4	< 0.3	< 0.6
38-40		2.6	< 0.4	< 0.3	< 0.6

RT (min)	Identification	Fat soluble component (hexane soluble, 0.16 mg/kg)		Aqueous component (0.064 mg/kg)	
		d-^{14}C	c-^{14}C	d-^{14}C	c-^{14}C
41-45	Parent[2]	**68**	**73**	**28**	**10**
	Other	0	0.5	0.1	< 0.6
Total extracts		71	75	29	24

[1]Not retained on HPLC column. TLC indicated that fraction was ~ 20% parent.

[2]96% TRR from difluorophenyl label and 83% from the chlorophenyl label identified as parent novaluron.

The metabolic pathway shown in Figure 1 is consistent with the above findings.

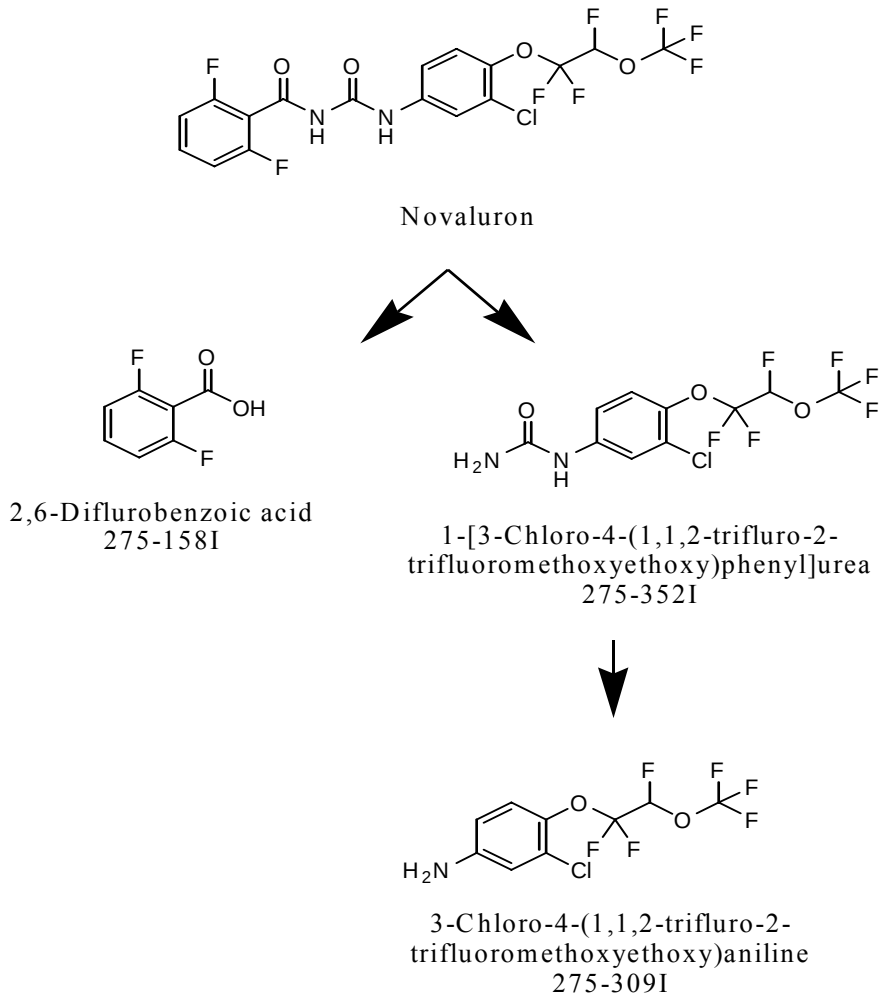


Figure 1. Proposed Biotransformation Pathway for Metabolism of Novaluron in Ruminants (MAK 461/984693).

The Meeting received a report on the metabolism of radiolabeled novaluron in *poultry* (Kane, T J, 2004. Report No. MAK 810/ 033178). [Difluorophenyl]-^{14}C-Novaluron (61.1mCi/mmol specific activity, > 97% radiochemical purity) was administered orally to 5 laying hens (Lohmann Brown strain, aged approximately 43 weeks and weighing 1.6 to 2 kg on arrival) for fourteen consecutive days at a nominal rate of 10 ppm in the diet. The actual dose rate ranged from 10 to 15 ppm or an average of 12 ppm in the diet. Excreta were collected once a day and eggs were collected at least twice daily. The hens were sacrificed 23 hours after the last dose and tissue samples were taken for analyses.

The concentrations of radioactivity (TRR) in the pooled samples of liver, kidney, thigh, breast muscle, and eggs were determined by combustion with LSC. Concentrations of radioactivity in the fat (mesenteric and abdominal), skin, and subcutaneous fat were determined directly by extraction and combustion with LSC. Concentrations of radioactivity were found to be highest in the fat with levels of 3.6 μg/g in mesenteric and abdominal fat and 1.9 μg/g in skin and subcutaneous fat. The total radioactive residues in pooled samples of tissues and eggs are summarized in Table 8.

Table 8.Total radioactive residues in tissues and eggs following administration of 14C-Novaluton to laying hens for 14 consecutive days (MAK 810/ 033178)

Tissue	Total radioactive residues (mg/kg)
Liver	0.39
Kidney	0.39
Thigh muscle	0.30
Breast muscle	0.061
Fat (mesenteric/abdominal)	3.6
Skin and subcutaneous fat	1.9
Eggs (final day sample)[1]	0.50

[1] Data were provided for the final day only, although samples were collected daily for the entire study period.

The samples of tissues and eggs were extracted with methanol, followed by liquid/Liquid clean up using hexane and then further cleaned up using a NH_2-SPE (solid-phase extraction) column. Quantification for parent was by gas chromatography/electron-capture detection (GC/ECD). In addition, solvent extracts, non-extracted residues and extract concentrates obtained from the application of the residue method to further samples of liver, thigh muscle, fat (mesenteric/abdominal), and eggs (final day sample only) were also analyzed using radiodetection methodology. Aliquots of the hexane extract prior to application to the SPE extraction system and aliquots of the post SPE concentrate were analyzed by liquid-scintillation counting (LSC). Solid tissue residues remaining after completion of the extraction procedure were weighed and replicate aliquots were taken for combustion and LSC. Samples of the post-SPE concentrate were also analyzed by thin-layer chromatography (TLC) with radiodetection.

Normal-phase TLC was carried out on pre-layered, glass-backed Kieselgel 60 F254 plates, of layer thickness 0.25 mm. Reversed-phase TLC was carried out on pre-layered, glass-backed octadecylsilane (ODS) plates, of layer thickness 0.2 mm with pre-absorbent strip. Two-dimensional chromatograms of the developed plates were obtained using a linear analyzer.

Table 9. Distribution of the Parent and the Metabolites in Poultry Matrices Following Dosing with [Difluorophenyl -^{14}C(U)]Novaluron at About 12. ppm in the Diet.

Metabolite Fraction	Eggs		Fat		Skin		Thigh Muscle		Breast Muscle		Kidney		Liver	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Novaluron	90.	0.45	96	3.5	97	1.8	103	0.31	90.	0.055	95	0.37	105	0.41
Total bound residues	-	NR[1]	-	NR	-	NR	-	NR	-	NR	-	NR	-	NR

[1] NR = Not reported.

Plant Metabolism

Studies examining the metabolism of difluorophenyl-^{14}C- or chlorophenyl-^{14}C-novaluron in apples, cabbages, potatoes, and cotton following foliar application were provided to the Meeting.

The nature of residues in mature *apple* trees (Var. Golden Delicious) was investigated in a UK study in 1997 (M. T. Corden, 1998. Report No. MAK429/983248; R-9768). Novaluron, radiolabelled in either the [chlorophenyl-^{14}C(U)] or [difluorophenyl-^{14}C(U)] ring (both radiochemical purities > 98%) was formulated as a 10% EC and sprayed onto trees growing in outdoor pots in a netted tunnel. Either two (4 trees per radiolabeled form) or three applications (2 trees per radiolabeled form) were made to trees at a rate of 2.5–2.7 mg/tree/application (equivalent to 50-80 g ai/ha based on an application volume of 1000 – 1600 L/ha of a 0.005% ai in a formulated commercial spray). The applications were made 110 days, 90 days, and 60 days (3 applications only) before harvest. A single branch on each tree was also protected during application, to assess the extent of translocation. Samples of fruit (minimum of 6) and leaves were taken after each application and at 30 day intervals thereafter until harvest. Samples of protected fruit and leaves were only taken at harvest. Typically three batches were collected for each sample type, and each batch was stored, prepared, and analyzed separately. Except for one example, only average values for the batches were reported.

Leaves and fruit samples were surface washed using acetonitrile and then homogenized and extracted with acetonitrile and acetonitrile: water (1:1). Total radioactive residues were determined from a summation of radioactivity in surface washes, extracts and unextracted residue. Unextracted residues in fruit and leaf samples were measured by combustion LSC. Total radioactive residues are given in Table 10.

Table 10. Average TRR in Apple Fruits and Leaves Following Application of [Difluorophenyl-^{14}C(U)]Novaluron or [Chlorophenyl-14C(U)]Novaluron to Apple Trees (Report No. MAK429/983248).

Sample		TRR (mg/kg, expressed as Novaluron Equivalents) [1]				
		After Application 1 (110 days before harvest)	After Application 2 (90 days before harvest)	Intermediate Sample 1 or After Application 3 (60 days before harvest)	Intermediate Sample 2 (30 days before harvest)	Final Harvest
Difluorophenyl label						
2 appl	Fruit	0.21	0.21	0.072 [2]	0.027	0.016
	Leaf	5.0	3.6	1.4	1.2	0.57
3 appl	Fruit	Same as for 2 application apples		0.079	0.043	0.034
	Leaf			6.7	3.4	2.9
Protected	Fruit	not sampled (ns)	ns	ns	ns	< 0.01
	Leaf	ns	ns	ns	ns	0.051
Chlorophenyl label						
2 appl	Fruit	0.17	0.12	0.057	0.012	0.024
	Leaf	1.9	5.2 [2]	3.0	1.4	1.0
3 appl	Fruit	Same as for 2 application apples		0.094	0.096	0.040
	Leaf			9.1	2.0	0.88
Protected	Fruit	ns	ns	ns	ns	< 0.01
	Leaf	ns	ns	ns	ns	0.035

[1] TRR was calculated by summation of radioactivity in surface washes, extracts, and non-extractable residues.
[2] Results are based on only one sample batch.

Aliquots of the surface washes and extracts were analyzed using HPLC systems equipped with a Spherisorb S5ODS2 column, and ultraviolet (UV) (232 nm) and radioactivity flow detectors. A gradient mobile phase of water and acetonitrile, or water:acetonitrile:trifluoroacetic acetic acid (98:2:0.1, v:v:v) and acetonitrile:trifluoroacetic acid (100:0.1, v:v) was used. Characterization of residues was achieved by co-chromatography of extracts or rinses with non-radiolabeled reference standards of the test substance and potential metabolites.

Normal phase TLC was carried out using Kieselgel 60 F_{254} plates developed with dichloromethane:diethy ether (3:1, v:v; Solvent System A); hexane:ethyl acetate:glacial acetic acid (50:50:1, v:v:v; Solvent System B); or hexane:ethyl acetate:glacial acetic acid (60:40:1, v:v:v; Solvent System C). Reversed-phase TLC was carried out on ODS plates developed with: methanol:water (8:2, v:v; Solvent System C) or acetonitrile:water (9:1; v:v, Solvent System C'). Radioactive areas were quantified using a radiographic imaging system and identified by comparison to reference standards which had been co-chromatographed with the surface rinses and extracts. Non-radiolabeled reference standards were visualized under UV light.

There was no significant difference in the distribution pattern for the different labelling sites. See Tables 11 - 14. Novaluron was the only identified component of the TRRs.

Table 11. Distribution of the Parent and the Metabolites in **Apple Fruit** Following Two Applications of **[Difluorophenyl-^{14}C(U)]Novaluron** to Mature Apple Trees at a Spray Concentration of 0.005% ai per Application. [1] (Report No. MAK429/983248).

Metabolite Fraction[2]	Test Substance Applied Twice									
	After Application 1		After Application 2		Intermediate Harvest 1		Intermediate Harvest 2		Final Harvest	
	(Fruit TRR = 0.208 mg/kg)		(Fruit TRR = 0.212 mg/kg)		(Fruit TRR = 0.072 mg/kg)		(Fruit TRR = 0.027 mg/kg)		(Fruit TRR = 0.016 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Surface washes	98.	0.21	70	0.15	71	0.051	53	0.014	47	0.007
Novaluron	98	0.20	70	0.15	69	0.049	52	0.014	47	0.007
Metabolite A (34-35)	< 0.1	< 0.001	< 0.1	< 0.001	0.6	< 0.001	0.7	< 0.001	<1.6	< 0.001
Metabolite B (30-31)	< 0.1	< 0.001	< 0.1	< 0.001	0.4	< 0.001	< 0.6	< 0.001	<1.6	< 0.001
Metabolite C (16-17)	< 0.1	< 0.001	< 0.1	< 0.001	0.4	< 0.001	< 0.6	< 0.001	<1.6	< 0.001
Metabolite D (13-15)	< 0.1	< 0.001	< 0.1	< 0.001	0.9	0.001	< 0.6	< 0.001	<1.6	< 0.001
Metabolite E (8-9)	< 0.1	< 0.001	< 0.1	< 0.001	0.4	< 0.001	< 0.6	< 0.001	<1.6	< 0.001
Polar	< 0.1	< 0.001	< 0.1	< 0.001	< 0.4	< 0.001	< 0.6	< 0.001	<1.6	< 0.001
Other	0.3	0.001	< 0.1	< 0.001	0.1	< 0.001	< 0.6	< 0.001	<1.6	< 0.001
Organosoluble extracts - flesh	1.5	0.003	29	0.062	2.4	0.002	5.1	0.001	6.6	0.001
- peel					22.	0.016	40	0.011	43	0.007
Novaluron			29	0.062	22	0.016	40.	0.011	42	0.007
Metabolite A (34-35)			<1.0	< 0.002	< 0.3	< 0.001	< 0.8	< 0.001	< 0.9	< 0.001
Metabolite B (30-31)			<1.0	< 0.002	< 0.3	< 0.001	< 0.8	< 0.001	< 0.9	< 0.001
Metabolite C (16-17)			<1.0	< 0.002	< 0.3	< 0.001	< 0.8	< 0.001	< 0.9	< 0.001
Metabolite D (13-15)			<1.0	< 0.002	< 0.3	< 0.001	< 0.8	< 0.001	< 0.9	< 0.001

Metabolite Fraction[2]	Test Substance Applied Twice									
	After Application 1		After Application 2		Intermediate Harvest 1		Intermediate Harvest 2		Final Harvest	
	(Fruit TRR = 0.208 mg/kg)		(Fruit TRR = 0.212 mg/kg)		(Fruit TRR = 0.072 mg/kg)		(Fruit TRR = 0.027 mg/kg)		(Fruit TRR = 0.016 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Metabolite E (8-9)			<1.0	< 0.002	< 0.3	< 0.001	< 0.8	< 0.001	< 0.9	< 0.001
Polar			<1.0	< 0.002	< 0.3	< 0.001	< 0.8	< 0.001	1.1	< 0.001
Other			<1.0	< 0.002	< 0.3	< 0.001	< 0.8	< 0.001	< 0.9	< 0.001
Total extractable (wash+extracts)	100	0.21	100	0.21	96	0.070	98	0.026	97	0.015
Total identified	98	0.20	100	0.21	91	0.066	93	0.025	89	0.014
Total unidentified	1.8	0.004	0.0	0.0	5.2	< 0.004	5.8	< 0.002	7.7	< 0.002
Nonextractable residue - peel	< 0.1	< 0.001	0.2	< 0.001	3.6	0.003	1.4	< 0.001	3.0	< 0.001
% Accountability	100		100		100		100		100	

[1] Residues following Applications 1 and 2 are the same for trees receiving two or three applications.
[2] From HPLC radiochromatograms, retention times in minutes.

Table 12. Distribution of the Parent and the Metabolites in **Apple Fruit** Following Three Applications of **[Difluorophenyl-^{14}C(U)]Novaluron** to Mature Apple Trees at a Spray Concentration of 0.005% ai per Application. (Report No. MAK429/983248)

Metabolite Fraction[2]	**Test Substance Applied Thrice [1]**					
	After Application 3		Intermediate Harvest		Final Harvest	
	(**Fruit** TRR = 0.079 mg/kg)		(**Fruit** TRR = 0.043 mg/kg)		(**Fruit** TRR = 0.034 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Surface washes	85	0.067	56	0.024	57	0.019
Novaluron	**84**	**0.067**	**56**	**0.024**	**57**	**0.019**
Metabolite A (34-35)	0.2	< 0.001	< 0.2	< 0.001	< 0.7	< 0.001
Metabolite B (30-31)	< 0.2	< 0.001	< 0.2	< 0.001	< 0.7	< 0.001
Metabolite C (16-17)	< 0.2	< 0.001	< 0.2	< 0.001	< 0.7	< 0.001
Metabolite D (13-15)	< 0.2	< 0.001	< 0.2	< 0.001	< 0.7	< 0.001
Metabolite E (8-9)	< 0.2	< 0.001	< 0.2	< 0.001	< 0.7	< 0.001
Polar	< 0.2	< 0.001	< 0.2	< 0.001	< 0.7	< 0.001
Other	0.2	< 0.001	< 0.2	< 0.001	< 0.7	< 0.001
Organosoluble extracts - flesh	2.2	0.002	5.9	0.003	3.7	0.001
- peel	13	0.010	37	0.016	37	0.013
Novaluron	**12**	**0.009**	**36**	**0.015**	**35**	**0.012**
Metabolite A (34-35)	0.9	0.001	< 0.6	< 0.001	0.8	< 0.001
Metabolite B (30-31)	< 0.3	< 0.001	< 0.6	< 0.001	< 0.4	< 0.001
Metabolite C (16-17)	< 0.3	< 0.001	< 0.6	< 0.001	< 0.4	< 0.001
Metabolite D (13-15)	< 0.3	< 0.001	< 0.6	< 0.001	< 0.4	< 0.001
Metabolite E (8-9)	< 0.3	< 0.001	< 0.6	< 0.001	< 0.4	< 0.001

Metabolite Fraction[2]	**Test Substance Applied Thrice** [1]					
	After Application 3		Intermediate Harvest		Final Harvest	
	(**Fruit** TRR = 0.079 mg/kg)		(**Fruit** TRR = 0.043 mg/kg)		(**Fruit** TRR = 0.034 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Polar	< 0.3	< 0.001	1.3	0.001	0.5	< 0.001
Other	< 0.3	< 0.001	< 0.6	< 0.001	< 0.4	< 0.001
Total extractable (wash+extracts)	100	0.079	99	0.043	97	0.033
Total identified	96	0.076	92	0.039	92	0.031
Total unidentified	3.5	0.003	7.2	0.004	5.0	< 0.002
Nonextractable residue - peel	0.4	< 0.001	0.9	< 0.001	2.6	0.001
Nonextractable residue - flesh	0.1	< 0.001	0.3	< 0.001	0.2	< 0.001
% Accountability	100		100		100	

[1] Residues following Applications 1 and 2 are the same for trees receiving two or three applications.
[2] From HPLC radiochromatograms, retention times in minutes.

Table 13.Distribution of the Parent and the Metabolites in **Apple Fruit** Following Two Applications of **[Chlorophenyl-^{14}C(U)]Novaluron** to Mature Apple Trees at a Spray Concentration of 0.005% ai per Application. [1] (Report No. MAK429/983248).

Metabolite Fraction[2]	**Test Substance Applied Twice**									
	After Application 1		After Application 2		Intermediate Harvest 1		Intermediate Harvest 2		Final Harvest	
	(**Fruit** TRR = 0.174 mg/kg)		(**Fruit** TRR = 0.115 mg/kg)		(**Fruit** TRR = 0.057 mg/kg)		(**Fruit** TRR = 0.012 mg/kg)		(**Fruit** TRR = 0.024 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Surface washes	98	0.17	94	0.11	73	0.041	45	0.005	54	0.013
Novaluron	**98**	**0.17**	**94**	**0.11**	**72**	**0.041**	**44**	**0.005**	**54**	**0.013**
Metabolite A (34-35)	< 0.4	< 0.001	< 0.4	< 0.001	0.3	< 0.001	0.6	< 0.001	< 0.5	< 0.001
Metabolite B (30-31)	< 0.4	< 0.001	< 0.4	< 0.001	< 0.2	< 0.001	< 0.5	< 0.001	< 0.5	< 0.001
Metabolite C (16-17)	< 0.4	< 0.001	< 0.4	< 0.001	< 0.2	< 0.001	< 0.5	< 0.001	< 0.5	< 0.001
Metabolite D (13-15)	< 0.4	< 0.001	< 0.4	< 0.001	< 0.2	< 0.001	< 0.5	< 0.001	< 0.5	< 0.001
Metabolite E (8-9)	< 0.4	< 0.001	< 0.4	< 0.001	< 0.2	< 0.001	< 0.5	< 0.001	< 0.5	< 0.001
Polar	< 0.4	< 0.001	< 0.4	< 0.001	< 0.2	< 0.001	< 0.5	< 0.001	< 0.5	< 0.001
Other	0.8	0.001	0.5	0.001	0.8	< 0.001	< 0.5	< 0.001	< 0.5	< 0.001
Organosoluble extracts - flesh	1.7	0.003	5.0	0.006	3.3	0.002	6.0	0.001	3.9	0.001
- peel					23	0.013	46	0.005	37	0.009
Novaluron			**5.0**	**0.006**	**22**	**0.013**	**46**	**0.005**	**37**	**0.009**
Metabolite A (34-35)			< 0.1	< 0.001	0.1	< 0.001	<1.2	< 0.001	< 0.3	< 0.001

Metabolite B (30-31)			< 0.1	< 0.001	< 0.1	< 0.001	<1.2	< 0.001	< 0.3	< 0.001
Metabolite C (16-17)			< 0.1	< 0.001	< 0.1	< 0.001	<1.2	< 0.001	< 0.3	< 0.001
Metabolite D (13-15)			< 0.1	< 0.001	< 0.1	< 0.001	<1.2	< 0.001	< 0.3	< 0.001
Metabolite E (8-9)			< 0.1	< 0.001	< 0.1	< 0.001	<1.2	< 0.001	< 0.3	< 0.001
Polar			< 0.1	< 0.001	< 0.1	< 0.001	<1.2	< 0.001	< 0.3	< 0.001
Other			< 0.1	< 0.001	0.3	< 0.001	<1.2	< 0.001	< 0.3	< 0.001
Total extractable (wash+extracts)	100	0.17	100	0.12	98	0.056	96	0.011	95	0.023
Total identified	98	0.17	99	0.11	94	0.053	90	0.011	91	0.022
Total unidentified	2.5	0.004	0.5	0.001	4.7	0.003	6.6	0.001	3.9	0.001
Nonextractable residue - peel	< 0.1	< 0.001	0.5	0.001	1.3	0.001	3.0	< 0.001	4.9	0.001
Nonextractable residue - flesh					0.3	< 0.001	0.8	< 0.001	0.3	< 0.001
% Accountability	100		100		100		100		100	

[1] Residues following Applications 1 and 2 are the same for trees receiving two or three applications.
[2] From HPLC radiochromatograms, retention times in minutes.

Table 14. Distribution of the Parent and the Metabolites in **Apple Fruit** Following Two or Three Applications of **[Chlorophenyl-^{14}C(U)]Novaluron** to Mature Apple Trees at a Spray Concentration of 0.005% ai per Application (Report No. MAK429/983248).

Metabolite Fraction[2]	**Test Substance Applied Thrice** [1]					
	After Application 3		Intermediate Harvest		Final Harvest	
	(**Fruit** TRR = 0.094 mg/kg)		(**Fruit** TRR = 0.096 mg/kg)		(**Fruit** TRR = 0.040 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Surface washes	85	0.080	69	0.066	54	0.022
Novaluron	**82**	**0.077**	**68**	**0.066**	**54**	**0.022**
Metabolite A (34-35)	0.3	< 0.001	< 0.1	< 0.001	< 0.4	< 0.001
Metabolite B (30-31)	0.7	0.001	< 0.1	< 0.001	< 0.4	< 0.001
Metabolite C (16-17)	< 0.1	< 0.001	< 0.1	< 0.001	< 0.4	< 0.001
Metabolite D (13-15)	< 0.1	< 0.001	< 0.1	< 0.001	< 0.4	< 0.001
Metabolite E (8-9)	< 0.1	< 0.001	< 0.1	< 0.001	< 0.4	< 0.001
Polar	0.2	< 0.001	< 0.1	< 0.001	< 0.4	< 0.001
Other	1.8	0.002	0.6	0.001	< 0.4	< 0.001
Organosoluble extracts - flesh	1.4	0.001	2.8	0.003	3.6	0.001
- peel	13	0.012	26	0.025	38	0.015
Novaluron	**13**	**0.012**	**26**	**0.025**	**38**	**0.015**
Metabolite A (34-35)	0.3	< 0.001	< 0.3	< 0.001	< 0.5	< 0.001
Metabolite B (30-31)	< 0.2	< 0.001	< 0.3	< 0.001	< 0.5	< 0.001
Metabolite C (16-17)	< 0.2	< 0.001	< 0.3	< 0.001	< 0.5	< 0.001
Metabolite D (13-15)	< 0.2	< 0.001	< 0.3	< 0.001	< 0.5	< 0.001

Metabolite Fraction[2]	**Test Substance Applied Thrice** [1]					
	After Application 3		Intermediate Harvest		Final Harvest	
	(**Fruit** TRR = 0.094 mg/kg)		(**Fruit** TRR = 0.096 mg/kg)		(**Fruit** TRR = 0.040 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Metabolite E (8-9)	< 0.2	< 0.001	< 0.3	< 0.001	< 0.5	< 0.001
Polar	< 0.2	< 0.001	< 0.3	< 0.001	< 0.5	< 0.001
Other	< 0.2	< 0.001	< 0.3	< 0.001	< 0.5	< 0.001
Total extractable (wash+extracts)	99	0.093	98	0.095	96	0.038
Total identified	94	0.089	95	0.091	92	0.037
Total unidentified	4.7	0.005	3.4	0.004	3.6	0.001
Nonextractable residue - peel	0.7	0.001	1.7	0.002	3.9	0.002
Nonextractable residue - flesh	0.2	< 0.001	0.2	< 0.001	0.4	< 0.001
% Accountability	100		100		100	

[1] Residues following Applications 1 and 2 are the same for trees receiving two or three applications.
[2] From HPLC radiochromatograms, retention times in minutes.

Parent novaluron was the only significant compound detected in any leaf or fruit samples and in any fraction analyzed, for both application regimes and for both radiolabeled compounds. Novaluron accounted for 90 – 100% of the TRR in/on fruits and leaves at all sampling intervals (ranging from 0 days to 110 days after application).

The Meeting was provided a UK study on the metabolism of radiolabled novaluron on *cabbage* (Var. Stonehead) (A. Crowe, 1998. Report No. MAK437/982595; R-9802). Novaluron, radiolabelled in either the [chlorophenyl-^{14}C(U)] or [difluorophenyl-^{14}C(U)] ring (radiochemical purities > 97% and > 99%, respectively) was prepared as a 10% EC formulation and sprayed onto two groups of plants growing in outdoor pots. Two applications (either 8 and 6 weeks before harvest or 5 and 2 weeks before harvest) were made to replicate a rate of 30–45 g ai/ha. Prior to and after applications of the test substances, the cabbage plants were maintained outdoors in a netted tunnel and subjected to typical environment conditions. Whole plant samples were taken after each application for both groups. For the 6 week PHI group, additional samples were taken 4, 2 and 0 weeks before harvest and for the 2 week PHI group, additional samples were taken 1 and 0 weeks before harvest.

Processing started within 24 hours of sampling. Roots were removed and discarded and whole plants were washed with acetonitrile. The washed cabbages were then separated into outer and inner leaves by cutting through the stem below the leaves that formed the heart of the cabbage head.

Residues in/on outer and inner cabbage leaves were separately and sequentially extracted (2x) with ACN and ACN:water (8:50, v:v) by homogenizing in a blender. The homogenized sample was filtered through a filter following each extraction. The ACN and the ACN/water extracts were combined and diluted to volume with ACN. An aliquot of the combined extract was partitioned (2x) with dichloromethane. The organosoluble extracts were dried over anhydrous sodium sulfate, combined, and diluted with dichloromethane. The nonextractable residues were air dried. At each stage of the procedures described above, subsamples were taken and measured for radioactivity. Total radioactive residues were determined from a summation of radioactivity in surface washes, extracts, and unextracted residue.

The washes and organosoluble extracts were initially analyzed using high-performance liquid chromatography (HPLC) on a Spherisorb ODS2 column equipped with an ultraviolet detector (232 nm) and a radiodetector. A gradient mobile phase of water:acetonitrile:trifluoroacetic acid (TFA) (98:2:0.1, v:v:v) and acetonitrile:TFA (100:0.1, v:v) was used. Characterization of residues was

achieved by co-chromatography of washes and extracts with the following non-radiolabeled standards: novaluron; 2,6-difluorobenzamide; 2,6-difluorobenzoic acid; and 4-amino-2-chlorophenol.

To confirm residue identification, certain washes and extracts were analyzed by liquid chromatography/mass spectroscopy (LC/MS). The LC conditions included a Spherisorb ODS2 column and gradient mobile phase of 0.01 M ammonium acetate with 0.1% acetic acid in water:acetonitrile (95:5, v:v) and 0.01 M ammonium acetate with 0.1% acetic acid in water:acetonitrile (20:80, v:v). The MS detection utilized electrospray ionization with scan parameters from m/z 100 to m/z 600. Total radioactive residues are given in Table 15.

Table 15. Total radioactive residue (TRR, mg/kg) in cabbage following application of [14C]-novaluron at 30 – 45 g ai/ha per application (Report No. MAK437/982595)

6 week PHI					
Applications	**1**	**2**			
Sampling time (weeks before harvest)	**8**	**6**	**4**	**2**	**0**
[difluorophenyl-^{14}C(U)]	0.84	1.0	0.63	0.45	0.23
[chlorophenyl-^{14}C(U)]	0.62	1.1	0.54	0.44	0.35
2 week PHI					
Applications	**1**	**2**			
Sampling time (weeks before harvest)	**5**	**2**	**1**	**0**	
[difluorophenyl-^{14}C(U)]	0.53	0.64	0.60	0.45	
[chlorophenyl-^{14}C(U)]	0.50	0.54	0.48	0.32	

The characterization/identification of the various extracts is given in Tables 16 – 23.

Table 16. Distribution of the Parent and Metabolites in Cabbage Following Applications of [Difluorophenyl-^{14}C(U)]Novaluron (6-week PHI group). [1] (Report No. MAK437/982595)

Metabolite Fraction	Sampling Time									
	After 1st Application		After 2nd Application		1st Intermediate Harvest		2nd Intermediate Harvest		Final Harvest	
	(TRR = 0.840 mg/kg)		(TRR = 1.029 mg/kg)		(TRR = 0.634 mg/kg)		(TRR = 0.446 mg/kg)		(TRR = 0.234 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
ACN wash	95	0.80	88	0.90	87	0.55	86	0.38	82	0.19
Novaluron	**94**	**0.79**	**88**	**0.90**	**87**	**0.55**	**85**	**0.38**	**81**	**0.19**
ACN extract: Outer leaves	3.9	0.033	9.3	0.096	11	0.067	11	0.048	13	0.030
ACN extract: Inner leaves	0.7	0.006	0.5	0.005	0.5	0.003	0.5	0.002	0.6	0.001
ACN/water extract: Outer leaves	0.4	0.004	1.8	0.018	1.0	0.006	1.7	0.008	2.1	0.005
ACN/water extract: Inner leaves	0.1	0.001	0.1	0.001	0.1	< 0.0005	ND [2]	ND	ND	ND
Organosoluble: Outer leaves	4.8	0.040	11	0.11	10	0.063	14	0.061	15	0.034
Novaluron	**4.6**	**0.039**	**11**	**0.11**	**9.6**	**0.061**	**13**	**0.058**	**14**	**0.033**
Unknown (Rt-32'00)	0.1	0.001	0.2	0.002	0.3	0.002	0.3	0.001	0.2	0.001
Organosoluble: Inner leaves	0.7	0.006	0.6	0.006	0.5	0.003	0.6	0.003	0.5	0.001
Novaluron	**0.6**	**0.005**	**0.6**	**0.006**	**0.5**	**0.003**	**0.6**	**0.003**	**0.5**	**0.001**
Unknown (Rt-32'00)	0.1	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000
Aqueous soluble: Outer leaves	0.1	0.001	0.2	0.002	0.2	0.001	0.6	0.003	0.3	0.001

Aqueous soluble: Inner leaves	0.0	0.000	0.0	0.000	0.0	0.000	ND	ND	ND	ND
Total extractable	100	0.84	99.	1.0	99	0.63	99	0.46	97	0.23
Total identified	99	0.83	99	1.0	97	0.61	99	0.44	96	0.22
Total unidentified	0.3	0.002	0.4	0.004	0.5	0.003	0.9	0.004	0.5	0.002
Nonextractable residues: Outer leaves	0.1	0.001	0.5	0.005	0.8	0.005	1.1	0.005	2.5	0.006
Nonextractable residues: Inner leaves	0.0	0.000	0.0	0.000	0.1	0.001	0.1	< 0.0005	0.2	< 0.0005
% Accountability	100		100		100		100		100	

[1] Residue values entered as "0.0" in the %TRR column are < 0.05% TRR, and those entered as "0.00" in the mg/kg column are < 0.0005 mg/kg.
[2] ND = Not detected.

Table 17. Distribution of the Parent and Metabolites in Cabbage Following Applications of [Difluorophenyl-^{14}C(U)]Novaluron (2-week PHI group). [1] (Report No. MAK437/982595)

Metabolite Fraction	Sampling Time							
	After 1st Application (TRR = 0.530 mg/kg)		After 2nd Application (TRR = 0.637 mg/kg)		1st Intermediate Harvest (TRR = 0.601 mg/kg)		Final Harvest (TRR = 0.448 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
ACN wash	97	0.51	96	0.61	93	0.56	88	0.40
Novaluron	**96**	**0.51**	**96**	**0.61**	**92**	**0.55**	**88**	**0.40**
ACN extract: Outer leaves	1.2	0.006	2.3	0.014	3.6	0.021	5.7	0.025
ACN extract: Inner leaves	1.7	0.009	0.6	0.004	2.2	0.013	4.0	0.018
ACN/water extract: Outer leaves	0.2	0.001	0.4	0.002	0.7	0.004	0.7	0.003
ACN/water extract: Inner leaves	0.2	0.001	0.1	0.001	0.4	0.003	0.7	0.003
Organosoluble: Outer leaves	1.3	0.007	2.1	0.013	6.2	0.037	7.1	0.032
Novaluron	**1.2**	**0.007**	**2.0**	**0.012**	**6.0**	**0.036**	**6.9**	**0.031**
Unknown (Rt-32'00)	0.0	0.00	0.0	0.000	0.1	0.001	0.1	< 0.0005
Organosoluble: Inner leaves	1.9	0.010	0.6	0.004	2.2	0.013	4.8	0.021
Novaluron	**1.9**	**0.010**	**0.6**	**0.004**	**2.1**	**0.013**	**4.7**	**0.021**
Unknown (Rt-32'00)	ND [2]	ND	0.0	0.000	0.0	0.000	0.0	0.000
Aqueous soluble: Outer leaves	0.1	< 0.0005	0.2	0.001	0.2	0.001	ND	ND
Aqueous soluble: Inner leaves	ND	ND	0.0	0.000	ND	ND	0.1	0.001
Total extractable	100	0.53	100	0.64	100	0.60	99	0.44
Total identified	99	0.52	08	0.63	100	0.60	100	0.45
Total unidentified	0.1	< 0.0005	0.2	0.001	0.3	0.002	0.2	0.001
Nonextractable residues: Outer leaves	0.1	0.000	0.2	0.002	0.3	0.002	0.3	0.001
Nonextractable residues: Inner leaves	0.0	0.000	0.1	0.000	0.2	0.001	0.3	0.001
% Accountability	100		100		100		100	

[1] Residue values entered as "0.0" in the %TRR column are < 0.05% TRR, and those entered as "0.00" in the mg/kg column are < 0.0005 mg/kg.
[2] ND = Not detected

Table 18. Distribution of the Parent and Metabolites in Cabbage Following Applications of [Chlorophenyl-^{14}C(U)]Novaluron (6-week PHI group). [1] (Report No. MAK437/982595)

Metabolite Fraction	Sampling Time									
	After 1st Application		After 2nd Application		1st Intermediate Harvest		2nd Intermediate Harvest		Final Harvest	
	(TRR = 0.620 mg/kg)		(TRR = 1.085 mg/kg)		(TRR = 0.544 mg/kg)		(TRR = 0.435 mg/kg)		(TRR = 0.345 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
ACN wash	97	0.60	94	1.0	91	0.50	91	0.40	89	0.31
Novaluron	95	0.59	93	1.0	90	0.49	89	0.39	88	0.30
Unknown (Rt-36'00)	1.8	0.011	0.9	0.010	1.2	0.006	1.4	0.006	1.1	0.004
ACN extract: Outer leaves	1.7	0.011	4.2	0.045	6.3	0.034	6.5	0.028	6.6	0.023
ACN extract: Inner leaves	0.8	0.005	0.4	0.004	1.0	0.005	0.7	0.003	1.1	0.004
ACN/water extract: Outer leaves	0.3	0.002	0.5	0.006	0.6	0.003	0.8	0.004	0.3	0.001
ACN/water extract: Inner leaves	0.1	0.001	0.1	0.001	0.1	0.001	0.1	0.001	ND [2]	ND
Organosoluble: Outer leaves	1.6	0.010	4.4	0.048	6.4	0.035	7.5	0.033	7.5	0.026
Novaluron	1.6	0.010	4.2	0.046	6.1	0.033	7.1	0.031	7.2	0.025
Unknown (Rt-31'00)	0.0	0.000	0.0	0.000	0.0	0.000	0.1	< 0.0005	0.0	0.000
Unknown (Rt-36'00)	0.0	0.000	0.1	0.001	0.2	0.001	0.2	0.001	0.2	0.001
Organosoluble: Inner leaves	0.8	0.005	0.4	0.005	1.1	0.006	0.8	0.003	0.9	0.003
Novaluron	0.8	0.005	0.4	0.005	1.0	0.006	0.8	0.003	0.9	0.003
Unknown (Rt-31'00)	0.0	0.000	ND	ND	ND	ND	ND	ND	ND	ND
Unknown (Rt-36'00)	0.0	0.000	0.0	0.000	0.0	0.000	ND	ND	0.0	0.000
Aqueous soluble: Outer leaves	0.1	< 0.0005	0.1	0.001	0.2	0.001	0.2	0.001	0.2	0.001
Aqueous soluble: Inner leaves	0.0	0.000	ND	ND	0.0	0.000	ND	ND	ND	ND
Total extractable	100	0.62	100	1.1	99	0.54	99	0.43	97	0.34
Total identified	97	0.60	98	1.1	97	0.53	97	0.42	96	0.33
Total unidentified	1.9	0.011	1.1	0.012	1.6	0.008	1.9	0.008	1.5	0.006
Nonextractable residues: Outer leaves	0.1	0.001	0.3	0.004	0.6	0.003	0.8	0.003	2.5	0.009
Nonextractable residues: Inner leaves	0.1	0.000	0.0	0.000	0.1	0.001	0.1	0.001	0.2	0.001
% Accountability	100		100		100		100		100	

Residue values entered as "0.0" in the %TRR column are < 0.05% TRR, and those entered as "0.00" in the mg/kg column are < 0.0005 mg/kg.
[2] ND = Not detected.

Table 19. Distribution of the Parent and Metabolites in Cabbage Following Applications of [Chlorophenyl-^{14}C(U)]Novaluron (2-week PHI group).[1] (Report No. MAK437/982595)

Metabolite Fraction	Sampling Time							
	After 1st Application		After 2nd Application		1st Intermediate Harvest		Final Harvest	
	(TRR = 0.496 mg/kg)		(TRR = 0.535 mg/kg)		(TRR = 0.479 mg/kg)		(TRR = 0.323 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg

Metabolite Fraction	Sampling Time							
	After 1st Application		After 2nd Application		1st Intermediate Harvest		Final Harvest	
	(TRR = 0.496 mg/kg)		(TRR = 0.535 mg/kg)		(TRR = 0.479 mg/kg)		(TRR = 0.323 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
ACN wash	98	0.48	94	0.50	92	0.44	90	0.29
Novaluron	95	0.47	92	0.49	89	0.43	88	0.28
Unknown (Rt-36'00)	1.3	0.006	1.2	0.007	1.4	0.006	1.5	0.005
ACN extract: Outer leaves	1.3	0.007	3.5	0.019	4.3	0.021	5.1	0.016
ACN extract: Inner leaves	0.6	0.003	1.6	0.009	2.8	0.014	3.2	0.010
ACN/water extract: Outer leaves	0.2	0.001	0.4	0.002	0.5	0.003	0.7	0.002
ACN/water extract: Inner leaves	0.1	< 0.0005	0.1	0.001	0.4	0.002	0.6	0.002
Organosoluble: Outer leaves	1.4	0.007	3.6	0.019	4.7	0.023	5.8	0.019
Novaluron	1.4	0.007	3.4	0.018	4.6	0.022	5.6	0.018
Unknown (Rt-36'00)	0.0	0.000	0.1	0.001	0.1	0.001	0.1	< 0.0005
Organosoluble: Inner leaves	0.7	0.003	1.6	0.008	1.8	0.009	3.3	0.011
Novaluron	0.7	0.003	1.5	0.008	1.8	0.009	3.2	0.010
Unknown (Rt-36'00)	0.0	0.000	0.00	0.000	0.0	0.000	0.1	< 0.0005
Aqueous soluble: Outer leaves	ND [2]	ND	0.1	< 0.0005	ND	ND	ND	ND
Aqueous soluble: Inner leaves	ND	ND	0.0	0.000	1.0	0.005	0.3	0.001
Total extractable	100	0.50	100	0.53	100	0.48	100	0.32
Total identified	98	0.48	97	0.52	96	0.46	96	0.31
Total unidentified	1.3	0.006	1.4	0.008	2.5	0.012	2.0	0.006
Nonextractable residues: Outer leaves	0.1	0.000	0.3	0.002	0.2	0.001	0.3	0.001
Nonextractable residues: Inner leaves	0.0	0.000	0.1	0.000	0.2	0.001	0.1	0.000
% Accountability	100		100		100		100	

[1] Residue values entered as "0.0" in the %TRR column are < 0.05% TRR, and those entered as "0.00" in the mg/kg column are < 0.0005 mg/kg.
[2]ND=Not detected

Table 20. Summary of Characterization and Identification of Radioactive Residues in Cabbage Following Applications of [Difluorophenyl-^{14}C(U)]Novaluron (6-week PHI group) (Report No. MAK437/982595)

Compound	Sampling Time									
	After 1st Application		After 2nd Application		1st Intermediate Harvest		2nd Intermediate Harvest		Final Harvest	
	(TRR = 0.84 mg/kg)		(TRR = 1.0 mg/kg)		(TRR = 0.63 mg/kg)		(TRR = 0.45 mg/kg)		(TRR = 0.23 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Identified										
Novaluron	99	0.83	99.	1.0	97	0.61	99	0.44	96	0.22
Characterized										
Unknown (Rt-32'00)	0.2	0.001	0.2	0.002	0.3	0.002	0.3	0.001	0.2	0.001
Aqueous residue	0.1	0.001	0.2	0.002	0.2	0.001	0.6	0.003	0.3	0.001
Total identified	99	0.83	99	1.0	97	0.61	99	0.44	96	0.22
Total characterized	0.3	0.002	0.4	0.004	0.5	0.003	0.9	0.004	0.5	0.002
Total extractable	100	0.84	99	1.0	99	0.63	99	0.44	97	0.23

Compound	Sampling Time									
	After 1st Application		After 2nd Application		1st Intermediate Harvest		2nd Intermediate Harvest		Final Harvest	
	(TRR = 0.84 mg/kg)		(TRR = 1.0 mg/kg)		(TRR = 0.63 mg/kg)		(TRR = 0.45 mg/kg)		(TRR = 0.23 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Nonextractable residues	0.1	0.001	0.5	0.005	0.9	0.006	1.1	0.005	2.7	0.006

Table 21. Summary of Characterization and Identification of Radioactive Residues in Cabbage Following Applications of [Difluorophenyl-^{14}C(U)]Novaluron (2-week PHI group). (Report No. MAK437/982595)

Compound	Sampling Time							
	After 1st Application		After 2nd Application		1st Intermediate Harvest		Final Harvest	
	(TRR = 0.53 mg/kg)		(TRR = 0.64 mg/kg)		(TRR = 0.60 mg/kg)		(TRR = 0.45 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Identified								
Novaluron	99.	0.52	98	0.63	100	0.60	100	0.45
Characterized								
Unknown (Rt-32'00)	0.0	0.000	0.0	0.000	0.1	0.001	0.1	< 0.0005
Aqueous residue	0.1	< 0.0005	0.2	0.001	0.2	0.001	0.1	0.001
Total identified	99	0.52	98	0.63	100	0.60	100	0.45
Total characterized	0.1	< 0.0005	0.2	0.001	0.3	0.002	0.2	0.001
Total extractable	100	0.53	100	0.64	100	0.60	99	0.44
Nonextractable residues	0.1	< 0.0005	0.3	0.002	0.5	0.003	0.6	0.002

Table 22. Summary of Characterization and Identification of Radioactive Residues in Cabbage Following Applications of [Chlorophenyl-14C(U)]Novaluron (6-week PHI group). (Report No. MAK437/982595)

Compound	Sampling Time									
	After 1st Application		After 2nd Application		1st Intermediate Harvest		2nd Intermediate Harvest		Final Harvest	
	(TRR = 0.62 mg/kg)		(TRR = 1.1 mg/kg)		(TRR = 0.54 mg/kg)		(TRR = 0.44 mg/kg)		(TRR = 0.34 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Identified										
Novaluron	97	0.60	98	1.1	97	0.53	97	0.42	96	0.33
Characterized										
Unknown (Rt-36'00)	1.8	0.011	1.0	0.011	1.4	0.007	1.6	0.007	1.3	0.005
Unknown (Rt-31'00)	0.0	0.000	0.0	0.000	0.0	0.000	0.1	0.000	0.0	0.000
Aqueous residue	0.1	< 0.0005	0.1	0.001	0.2	0.001	0.2	0.001	0.2	0.001
Total identified	97	0.60	98	1.1	97	0.53	97	0.42	96	0.33
Total characterized	1.9	0.011	1.1	0.012	1.6	0.008	1.9	0.008	1.5	0.006
Total extractable	100	0.62	100	1.1	99	0.54	99	0.43	97	0.33
Nonextractable residues	0.2	0.001	0.3	0.004	0.7	0.004	0.9	0.004	2.7	0.010

Table 23. Summary of Characterization and Identification of Radioactive Residues in Cabbage Following Applications of [Chlorophenyl-^{14}C(U)]Novaluron (2-week PHI group). (Report No. MAK437/982595)

Compound	Sampling Time							
	After 1st Application		After 2nd Application		1st Intermediate Harvest		Final Harvest	
	(TRR = 0.50 mg/kg)		(TRR = 0.54 mg/kg)		(TRR = 0.48 mg/kg)		(TRR = 0.32 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Identified								
Novaluron	98	0.48	97	0.52	96	0.46	96	0.31
Characterized								
Unknown (Rt-36'00)	1.3	0.006	1.3	0.008	1.5	0.007	1.7	0.005
Aqueous residue	ND	ND	0.1	< 0.0005	1.0	0.005	0.3	0.001
Total identified	98	0.48	97	0.52	96	0.46	96	0.31
Total characterized	1.3	0.006	1.4	0.008	2.5	0.012	2.0	0.006
Total extractable	100	0.50	100	0.53	100	0.48	100	0.32
Nonextractable residues	0.1	< 0.0005	0.4	0.002	0.4	0.002	0.4	0.001

The nature of residues in potatoes (Var. Maris Peer) in a UK study in 1997 was reported to the Meeting (Crowe, 1998. Report No. MAK438/983684, R-9803). Novaluron, radiolabelled in either the [chlorophenyl-^{14}C(U)] or [difluorophenyl-^{14}C(U)] ring (radiochemical purities > 97% and > 99%, respectively) was prepared as a 10% EC formulation and sprayed onto plants growing in outdoor field plots. Two applications (43 and 29 days before harvest) were made to replicate plants at a rate of 91-100 g ai/ha. Whole plant samples were taken after each application and also at 22, 10 and 0 days before harvest.

Samples were separated into foliage and tuber. Foliage was surface washed using acetonitrile (ACN) and then homogenized and extracted with acetonitrile and acetonitrile:water (1:1), before partitioning with dichloromethane. Surface washes and extracts containing significant levels of radioactivity were analyzed by HPLC with UV detection. LC-MS was used to confirm the identity of compounds, for representative samples. Unextracted radioactivity was measured by combustion LSC. Total radioactive residues were determined from a summation of radioactivity in surface washes, extracts and unextracted residue. Tuber samples were simply homogenized in CO_2 and total radioactive residue was measured by combustion LSC. Total radioactive residues for both foliage and tuber samples are given in Table 24.

Table 24. Total radioactive residue (mg/kg) in potato following application of [14C)] novaluron (Report R-9803)

Applications	1	2			
Sampling time (days before harvest)	43	29	22	10	0
Foliage					
[difluorophenyl-^{14}C(U)]	2.2 mg/kg	4.8	4.4	0.78	9.9
[chlorophenyl-^{14}C(U)]	1.6	7.0	4.3	2.2	5.9
Tuber[1]					
[difluorophenyl-^{14}C(U)]	< 0.001	< 0.001	< 0.001	0.001	< 0.001
[chlorophenyl-^{14}C(U)]	< 0.001	< 0.001	< 0.001	0.001	0.001

[1] No further characterization/identification work was conducted on tubers.

There was no significant difference in the distribution pattern for the different labelling sites and hence, results for foliage samples are reported as means. The distribution of radioactivity is given in 25.

Table 25. Percent TRR Distribution of radioactive residue in potato foliage (mean of both label sites) (Report No. MAK438/983684)

Applications	1	2			
Sampling time (days before harvest)	43	29	22	10	0
Acetonitrile wash	95	91	88	87	82
Acetonitrile extracts	5.0	8.5	11	12	17
Unextractable residue	0.2	0.9	0.5	0.9	1.0

Parent novaluron was the only compound identified in any foliage samples and in any fraction analyzed and accounted for greater than 96% TRR in all samples. See Tables 26 and 27.

Table 26. Summary of Characterization and Identification of Radioactive Residues in Potato Foliage Following Applications of [Difluorophenyl-^{14}C(U)]Novaluron. (Report No. MAK438/983684).

Metabolite Fraction	Sampling Time									
	After 1st Application		After 2nd Application		1st Intermediate Harvest		2nd Intermediate Harvest		Mature Harvest	
	(TRR = 2.172 mg/kg)		(TRR = 4.814 mg/kg)		(TRR = 4.370 mg/kg)		(TRR = 0.785 mg/kg)		(TRR = 9.874 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Identified										
Novaluron	99	2.2	98	4.7	100	4.4	98	0.77	97	9.6
Characterized										
Unknown (Rt-31'30")	0.1	0.001	0.1	0.004	0.2	0.007	0.4	0.003	0.2	0.023
Aqueous soluble	0.2	0.004	0.2	0.010	0.3	0.013	0.6	0.005	0.5	0.049
Total identified	99	2.2	98	4.7	100	4.4	98	0.77	97	9.6
Total characterized	0.3	0.005	0.3	0.014	0.5	0.020	1.0	0.008	0.7	0.072
Total extractable	100	2.2	99	4.8	100	4.4	99	0.78	99	9.8
Nonextractable residues	0.2	0.004	0.7	0.033	0.4	0.015	1.1	0.008	1.2	0.12

Table 27. Summary of Characterization and Identification of Residues in Potato Foliage Following Applications of [Chlorophenyl-^{14}C(U)]Novaluron. (Report No. MAK438/983684)

Metabolite Fraction	Sampling Time									
	After 1st Application		After 2nd Application		1st Intermediate Harvest		2nd Intermediate Harvest		Mature Harvest	
	(TRR = 1.6 mg/kg)		(TRR = 7.0 mg/kg)		(TRR = 4.3 mg/kg)		(TRR = 2.2 mg/kg)		(TRR = 5.9 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Identified										
Novaluron	98	1.5	96	6.7	98	4.2	96	2.1	97	5.7
Characterized										
Unknown (Rt-33'00)	1.2	0.019	1.5	0.106	1.4	0.061	1.9	0.042	1.3	0.074
Aqueous soluble	0.1	0.001	0.1	0.010	0.4	0.019	0.3	0.006	0.2	0.009
Total identified	98	1.5	96	6.7	98	4.2	96	2.1	97	5.7
Total characterized	1.3	0.020	1.6	0.12	1.8	0.080	2.2	0.048	1.5	0.083

Metabolite Fraction	Sampling Time									
	After 1st Application		After 2nd Application		1st Intermediate Harvest		2nd Intermediate Harvest		Mature Harvest	
	(TRR = 1.6 mg/kg)		(TRR = 7.0 mg/kg)		(TRR = 4.3 mg/kg)		(TRR = 2.2 mg/kg)		(TRR = 5.9 mg/kg)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Total extractable	100	1.6	99	6.9	100	4.3	99	2.2	99	5.8
Nonextractable residues	0.2	0.002	1.1	0.078	0.5	0.023	0.7	0.014	0.8	0.048

The Meeting received a *cotton* metabolism study report. Cotton plants grown outdoors were treated with ^{14}C Novaluron at an application rate equivalent to 50 g ai/ha/treatment (Aikens, P J, 2000. Report No. MAK549/002671, R-11087). Two treatment regimes were used; regime 1 consisted of two applications, 14 days apart with a 90 day PHI and regime 2 consisted of two applications 14 days apart with a 30 day PHI. Samples from plants treated according to regime 1 were taken for analysis after each application and at 60 and 30 days before the normal harvest. Samples of gin trash and delinted seed were taken for analysis of the total radioactive residue (TRR) and, where appropriate, the nature of the radioactive residue was investigated by chromatography. Two radiolabels were used, [chlorophenyl-^{14}C] Novaluron or [difluorophenyl-^{14}C] Novaluron.

In addition to the treatment regimes described above, the potential for translocation of residues was investigated. At each application, bolls (or immature bolls) on a single plant for each radiolabel and application regime, were protected from direct application using polythene bags. Protected bolls were collected for analysis at final harvest to determine whether translocation of residues occurred from the treated foliage to the protected lint and seed.

The TRRs in gin trash sampled from cotton treated under regime 1 immediately after the second application of ^{14}C Novaluron were 0.8 - 1.2 mg/kg. The TRR decreased to 0.1 - 0.2 ppm at 30 days PHI. At final harvest the TRR concentrations were 0.2 - 0.3 mg/kg. The apparent increase from 30 days PHI to 0 days PHI may be a result of desiccation of plant material prior to harvest. Residues in undelinted seed remained constant with time, 0.002 - 0.003 mg/kg.

The radioactive residues in gin trash sampled from cotton treated under regime 2 were 0.4 - 0.6 mg/kg, following the second spray application of ^{14}C-Novaluron, and 0.002 - 0.003 mg/kg in the undelinted seed. TRR in samples taken at harvest were 0.7 - 0.9 mg/kg in gin trash and 0.002 - 0.005 mg/kg in delinted seed. Total radioactive residues in mature bolls protected from direct application of test formulation were low (0.001 - 0.002 mg/kg), showing that little translocation of residue derived from ^{14}C Novaluron had taken place.

Following acetonitrile (ACN) extraction (> 90% extracted in most cases) and analysis by HPLC and TLC, the only discreet radioactive component detected was ^{14}C Novaluron. The extracts were initially analyzed using high-performance liquid chromatography (HPLC) on a Spherisorb S5ODS2 column equipped with an ultraviolet detector (232 nm) and a radiodetector. The gradient mobile phases were water:ACN:trifluoroacetic acid (TFA) (98:2:0.1, v:v:v; Mobile Phase A) and ACN:TFA (100:0.1, v:v; Mobile Phase B). Characterization of residues was achieved by co-chromatography of extracts with reference substances.

To confirm residue identification, certain extracts were analyzed by normal phase TLC and reversed phase TLC. In all cases Novaluron represented greater than 90% of the TRR in gin trash samples.

Table 28. TRR (mg/kg novaluron equivalents) in gin trash and undelinted seed following application of [chlorophenyl-14C] Novaluron or [difluorophenyl-14C] Novaluron to cotton plants. (Report No. MAK549/002671)

	Regime1 (2X50 g ai/ha, 90 d PHI)					Regime2 (2X50 g ai/ha, 30 d PHI)		
	Appl. 1 (109 PHI)	Appl. 2 (90 PHI)	Inter. 1 (60 PHI)	Inter. 2 (30 PHI)	Final Harvest	Appl. 1 (44 PHI)	Appl. 2 (30 PHI)	Final Harvest
Chlorophenyl-^{14}C Novaluron								
---Gin trash	0.60 mg/kg	0.88	0.36	0.15	0.29	0.26	0.47	0.77
--- Undelinted seed	ns	ns	0.001	0.02	0.003	0.002	0.002	0.002
Protected								
--- Gin trash	ns	ns	ns	ns	0.047	ns	ns	0.65
--- Bolls	ns	ns	ns	ns	0.002	ns	ns	0.002
Difluorophenyl-^{14}C Novaluron								
---Gin trash	0.63 mg/kg	1.1	0.45	0.20	0.27	0.37	0.56	0.85
--- Undelinted seed	ns	ns	0.002	0.003	0.003	0.003	0.003	0.005
Protected								
--- Gin trash	ns	ns	ns	ns	0.241	ns	ns	0.81
--- Bolls	ns	ns	ns	ns	0.002	ns	ns	0.001

ns - No Sample

Table 29. Distribution of the Parent and Metabolites in Cotton Matrices Following Applications of [Difluorophenyl-14C(U)]Novaluron and [Chlorophenyl-14C(U)]Novaluron. (Report No. MAK549/002671)

TREATMENT REGIME [1]										
Labelled form, matrix, and fraction	After 1st Application		After 2nd Application		Intermediate Sample 1		Intermediate Sample 2		Final Harvest	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Difluorophenyl										
RAC: Gin byproducts	TRR = 0.63 mg/kg		TRR = 1.1 mg/kg		TRR = 0.45 mg/kg		TRR = 0.20 mg/kg		TRR = 0.27 mg/kg	
Acetonitrile (ACN) extract	97	0.61	96	1.1	97	0.44	90	0.18	91	0.24
Novaluron	**96**	**0.60**	**91**	**1.0**	**94**	**0.42**	**86**	**0.18**	**88**	**0.23**
Others	1.8	0.011	4.8	0.054	3.1	0.014	3.4	0.007	3.6	0.010
Total extractable	97	0.61	96	1.1	97	0.44	90	0.18	91	0.24
Total identified	96	0.60	91	1.0	94	0.42	86	0.18	88	0.23
Total unidentified	1.8	0.011	4.8	0.054	3.1	0.014	3.4	0.007	3.6	0.010
Nonextractable residues	2.7	0.02	3.8	0.04	2.9	0.01	10.5	0.02	8.8	0.02
% Accountability	100		100		100		100		100	
RAC: Undelinted seed	TRR= no sample (ns)		TRR = ns		TRR = 0.002 mg/kg; not analyzed (na)		TRR = 0.003 mg/kg; na		TRR = 0.003 mg/kg; na	
Chlorophenyl										
RAC: Gin byproducts	TRR = 0.60 mg/kg		TRR = 0.888 mg/kg		TRR = 0.36 mg/kg		TRR = 0.15 mg/kg		TRR = 0.29 mg/kg	
ACN extract	98	0.59	96	0.84	97	0.35	94	0.14	94	0.27
Novaluron	**95**	**0.57**	**94**	**0.82**	**94**	**0.34**	**91**	**0.14**	**90**	**0.26**
Others	2.8	0.017	2.0	0.018	3.0	0.011	3.1	0.005	3.8	0.011
Total extractable	98	0.59	96	0.84	97	0.35	94	0.14	94	0.27
Total identified	95	0.57	94	0.82	94	0.34	91.	0.14	90	0.26
Total unidentified	2.8	0.017	2.0	0.018	3.0	0.011	3.1	0.005	3.8	0.011
Nonextractable residues	2.4	0.01	3.9	0.03	3.5	0.01	5.6	0.01	6.2	0.02

% Accountability	100		100		100	100	100	
RAC: Undelinted seed	TRR= ns		TRR = ns		TRR = 0.001 mg/kg; na	TRR = 0.002 mg/kg; na	TRR = 0.003 mg/kg; na	
TREATMENT REGIME 2								
Labelled form, matrix, and fraction	After 1st Application		After 2nd Application				Final Harvest	
	% TRR	mg/kg	% TRR	mg/kg			% TRR	mg/kg
Difluorophenyl								
RAC: Gin byproducts	TRR = 0.37		TRR = 0.56				TRR = 0.85	
ACN extract	98	0.36	96	0.53			94	0.80
Novaluron	**98**	**0.36**	**93**	**0.52**			**93**	**0.79**
Others	0.9	0.003	3.1	0.017			1.0	0.009
Total extractable	98	0.36	96	0.53			94	0.80
Total identified	98	0.36	93	0.52			93	0.79
Total unidentified	0.9	0.003	3.1	0.017			1.0	0.009
Nonextractable residues	1.7	0.01	4.2	0.02			6.4	0.05
% Accountability	100		100				100	
RAC: Undelinted seed	TRR= 0.003; na		TRR = 0.003; na				TRR = 0.005; na	
Chlorophenyl								
RAC: Gin byproducts	TRR = 0.26		TRR = 0.47				TRR = 0.77	
ACN extract	98	0.26	98	0.46			97	0.74
Novaluron	**97**	**0.26**	**96**	**0.46**			**95**	**0.73**
Others	1.7	0.004	1.9	0.009			1.5	0.012
Total extractable	98	0.26	98	0.46			97	0.74
Total identified	97	0.26	96	0.46			95	0.73
Total unidentified	1.7	0.004	1.9	0.009			1.5	0.012
Nonextractable residues	1.5	< 0.01	1.6	0.01			3.4	0.03
% Accountability	100		100				100	
RAC: Undelinted seed	TRR= 0.002; na		TRR = 0.002; na				TRR = 0.002; na	

Environmental fate

The Meeting received a study report on the *hydrolytic stability* of novaluron in water media at pHs 5, 7, and 9 (Shaw, D, 1998. Report No. MAK 445/973392, R-9703). Sterile aqueous buffer solutions were prepared containing [14C-chlorophenyl] novaluron (ca 1.5 µg ai/L) or [^{14}C-difluorophenyl] novaluron (ca 1.5 µg ai/L). Samples were incubated under sterile conditions in the dark at 25°C (all pHs), 50°C (pH 9) or 70°C (pH 9) for up to 30 days. Single samples (one for each label) were taken at up to six time points between 0 - 30 days after application, extracted with either diethyl ether or ethyl acetate and the radioactivity in the extracts quantified by LSC. Adjustment of pH in the remaining aqueous phase to 2 and further extraction with ethyl acetate was performed on selected pH 9 samples and samples incubated at 50°C, pH adjustment took place before any extraction of the 70°C samples. Analyte identity was addressed by co-chromatography using normal and reverse phase radio-TLC and RP HPLC-UV (232 nm) and confirmed by MS-MS. Sample extracts were stored at -15°C for up to 2 months before analysis.

At 25°C, results for total solvent-extracted radioactivity were 95-103 % (pH 5), 98-106 % (pH 7) and 89-118 % (pH 9), with the majority of results between 95-105%. Total recoveries of radioactivity were not recorded. Of the extracted radioactivity, novaluron comprised 97-98 % at day 0, decreasing to 77-81% after 25-30 days (pH 9 only).

There was no significant hydrolysis of novaluron at pH 5 and pH 7. At pH 9 (25°C), novaluron degraded with a first-order DT50 of about 100 days. At 50 and 70 °C, first order DT50s were 1.2 and 0.09 days, respectively (pH 9). Major metabolites exceeding 10% of applied radioactivity were identified as the chlorophenyl ring urea (275-352-I) and 2,6-difluorobenzoic acid (275-158-I). See Table 30.

All identified metabolites resulted from cleavage of the urea linkage at different positions. Minor metabolites (< 10% applied radioactivity) included 2,6-difluorobenzamide (H3, 275-157-I), H4, H5 and a number of other unidentified metabolites (non-discrete radioactivity).

Table 30. Identification and mass balance of radioactivity in buffer solutions during hydrolysis at 25 °C, pH 9 (% in organic solvent fraction). (Shaw, D, 1998. Report No. MAK 445/973392, R-9703)

Days Incubation	0	3	6	10	15	20	25	30
Chlorophenyl label								
Parent	98	97	94	87	90	85	79	77
H1 (275-352-I)		2.3	2.7	2.7	6.9	8.1	11	10
H4						1.0	0.9	0.8
H5						1.0	2.3	3.9
H6 (275-309-I)								
H7				3.3				
H8							0.8	2.1
Polar							0.7	0.5
Others	2.3	0.9	2.9	6.6	3.5	4.9	5.2	6.1
Difluorophenyl label								
Parent	99	99	91	91	77	97	76	85
H2 (275-158-I)			6.0	8.3	7.9	2.1	22	13
H3 (275-157-I)			1.0	0.4	1.1	1.0	0.9	0.9
H5								
Others	1.2	1.4	1.9	0.4	14.1	0.3	0.8	0.5

The Meeting was provided with a study report on residues in succeeding or *confined rotational crops*. (Shaw, D, 2000. Report No. MAK559/002865; R-11236). Twelve plastic pots (50 cm X 70 cm X 30 cm deep) filled with sandy loam soil were aged in a controlled environment. Six containers were treated with chlorophenyl-^{14}C(U)]-novaluron (radiochemical purity > 97%; EC formulation) at a rate of 100 g ai/ha (approximately 3.5 mg ai/container). The radiolabeled material (110 mL) was applied to the soil surface with a pipette. The soils were cultivated to a depth of 20 cm with a metal trowel 30 and 120 days after treatment (immediately before planting seeds). Rotational crops of spinach, turnips, and spring wheat were planted into separate containers (one container per crop at each plantback interval of 30 and 120 days). The plants were watered and weeded as required and received fertilizer once during the study. The containers were maintained at a nominal temperature of 15^{o}C (temperatures ranging 14.5-21.3^{o}C and a 13 hour light/11 hour dark cycle for 96 days after sowing of seeds and 16 hour light/8 hour dark cycle thereafter). Control containers of untreated soil were sown with the same crops.

Crop and soil samples were taken at times after sowing that were representative of immature harvest, early harvest, and final harvest. Crop information is summarized in Table 31. The total radioactive residues (TRR) were determined in all samples by combustion LSC. Results for TRR in treated crops are given in Table 32. All control samples of both crops and soil showed residues below the detection limit of 0.0003-0.0006 mg/kg.

Table 31. Rotational Crop Information (Report No. MAK559/002865)

Crop; crop group	Variety	Plantback intervals (days) [1]	Growth stage at harvest [2]	Harvested RAC	Harvesting procedure
Spinach; Vegetable, leafy (except Brassica vegetables), group 4	Space F1	30	35 (immature), and 68 and 102 (mature) DAP	Leaves	Cut just above the soil surface.
Turnip; Vegetable, root and tuber, group 1	Snowball	30	35 (immature) and 69 and 97 (mature) DAP	Tops (foliage)	Removed from the soil, washed to remove adhering soil, and the tops separated from the root.
				Tubers	
Spring wheat; Grain, cereal, group 15, and Grain, cereal, forage, fodder, and straw, group 16	Axona	30	Immature, 55 DAP	Forage	Cut approximately 2.5 cm above the soil surface.
			Immature, 133 DAP	Hay	
			Mature, 165 DAP	Straw and grain	Grain was separated from the straw (including chaff).

[1] Separate containers were also planted at the 120-day plantback interval; however, no information was provided concerning these samples because only the 30-day plantback interval samples were analyzed.
[2] DAP = Days after planting. First sampling point was conducted as soon as sufficient material was available; the second sampling point represents the earliest harvest possible and the last sampling interval represents final harvest.

Table 32. Total Radioactive Residues (TRR) in Rotated Crop Matrices. (Report No. MAK559/002865).

Matrix	Plantback interval (days)	Chlorophenyl-label (ppm)
Spinach, Immature	30	not analyzed
Spinach, Earliest mature harvest		0.001
Spinach, Final harvest, mature		0.001
Turnip, foliage: Immature	30	not analyzed
Turnip, Earliest mature harvest		0.001
Turnip, Final harvest, mature		0.001
Turnip, root: Immature	30	not analyzed
Turnip root, Earliest mature harvest		0.004
Turnip root, Final harvest, mature		0.001
Wheat, forage: Immature	30	0.001
Wheat, hay: Earliest mature harvest		0.002
Wheat, grain: Final harvest, mature		0.001
Wheat, straw: Final harvest, mature		0.003

The total radioactive residues in the soils at treatment and various post-treatment intervals are summarized in Table 33.

Table 33. TRR in soil at different harvest intervals. (Report No. MAK559/002865)

Sample	Sampling stage	Days after application	Days after planting	TRR (mg/kg equiv)
SOIL (Core samples, 2.5 cm diameter X 20 cm depth)				
Sown with wheat	Application	0	-	0.040
	Sowing of seeds	30	-	0.034

Sample	Sampling stage	Days after application	Days after planting	TRR (mg/kg equiv)
SOIL (Core samples, 2.5 cm diameter X 20 cm depth)				
	Immature harvest	85	55	0.030
	Earliest possible harvest	163	133	nd
	Final harvest	195	165	0.064
Sown with spinach	Application	0	-	0.12
	Sowing of seeds	30	-	0.064
	Immature harvest	65	35	0.076
	Earliest possible harvest	98	68	nd
	Final harvest	132	102	0.024
Sown with turnip	Application	0	-	0.066
	Sowing of seeds	30	-	0.052
	Immature harvest	65	35	0.032
	Earliest possible harvest	99	69	nd
	Final harvest	127	97	0.061

nd = not determined.

As all crop samples had a TRR of less than 0.01 mg/kg equivalents, only soil samples were further characterized. Samples were extracted with acetonitrile, acetonitrile/water and acetonitrile/hydrochloric acid reflux. Extracts were analyzed by reversed phase HPLC and TLC. Extracted soil was analyzed by combustion LSC. Characterization of soil radioactivity is given in Table 34.

Table 34. Characterization of soil radioactivity at different intervals. (Report No. MAK559/002865).

Component	Time after application					
	0 days		30 days		Final harvest (127-195 days)	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Soil sown with wheat						
Total extract	100	0.040	96	0.033	86	0.055
novaluron	98	0.039	74	0.026	32	0.020
275-352 I	nd	nd	12	0.004	14	0.009
275-309 I	nd	nd	7.5	0.003	30	0.019
Unidentified	2.4	0.001	1.5	0.001	10	0.006
Unextractable	0	< 0.0003	4.4	0.002	14	0.009
TRR	100	0.040	100	0.034	100	0.064
Soil sown with spinach						
Total extract	100	0.12	99	0.063	89	0.021
novaluron	99	0.12	92	0.059	46	0.011
275-352-I	nd	nd	3.0	0.002	10	0.002
275-309-I	nd	nd	2.1	0.001	21	0.005
Unidentified	1.2	0.001	1.5	0.001	11	0.003
Unextractable	0	< 0.0003	1.1	0.001	11	0.003
TRR	100	0.12	100	0.064	100	0.024
Soil sown with turnip						
Total extract	100	0.066	98	0.051	90	0.055
novaluron	98	0.065	90	0.046	49	0.030
275-352-I	nd	nd	4.0	0.002	10	0.006
275-309-I	nd	nd	2.3	0.001	25	0.015
Unidentified	1.7	0.001	2.5	0.001	5.3	0.003
Unextractable	0	< 0.0003	1.6	0.001	9.9	0.006
TRR	100	0.066	100	0.052	100	0.061

nd = not determined.
275-309-I = 3-chloro-4-(1,1,2-trifluoro-2- trifluoromethoxyethoxy)aniline
275-352-I = 1-[3-chloro-4-(1,1,2-trifluoro-2- trifluoromethoxyethoxy)phenyl]urea

RESIDUE ANALYSIS

Analytical methods

The Meeting was presented with reports of two methods for the determination of novaluron only in plant and plant processed commodities, along with variations of these methods. Additionally, methods based on the plant commodity methods were provided for the determination of novaluron in animal products.

A gas chromatography method was presented for the determination of novaluron only in apples, cabbages, and potatoes (Todd, M A, 1998. Report No. MAK 453/972510, R-9345). The method (MAK453) consisted of extraction of homogenized samples into aqueous methanol, followed by liquid/Liquid partition into hexane. The hexane extract was passed through a NH_2 SPE (solid phase extraction) cartridge and analyzed by gas chromatography with electron capture detection (GC/ECD). This method was found to give acceptable recoveries over the ranges of 0.05 to 1.0 mg/kg for apples and cabbages and 0.01 to 0.5 mg/kg for potatoes, respectively. See Table 35.

Table 35. Recoveries from method MAK453 validation of novaluron in apples, cabbages and potatoes. (Report MAK 453/972510)

Crop matrix	Spiking level (mg/kg)	Recoveries (%)	Range (%)	Average % Recovery (CV)
Apples	0.05	87, 78, 85, 90, 79	78-90	84% ± 6.2%
	0.25	96, 100, 101, 93, 99	93-101	98% ± 3.3%
	1.0	97, 99, 93, 101, 101	93-101	98% ± 3.3%
		Total =15		Overall Mean Recovery = 93% CV = 8.4%
Cabbages	0.05	80, 90, 86, 81, 84	80-90	84% ± 4.8%
	0.25	90, 96, 96, 104, 107	90-107	99% ± 6.9%
	1.0	98, 102, 96, 98, 100	96-102	98% ± 2.3%
		Total = 15		Overall Mean Recovery = 93% CV = 8.9%
Potatoes	0.01	107, 100, 102, 110, 104	100-110	105% ± 3.8%
	0.1	98, 97, 91, 97, 98	91-98	96% ± 3.1%
	0.5	87, 89, 93, 90, 91	87-93	90% ± 2.5%
		Total = 15		Overall Mean Recovery = 97% CV = 7.1%

The method described above underwent independent laboratory validation for residues of novaluron in apple samples **(**Rose, J E, 2001. Report No. PTRL 993W; R-12608). Untreated samples of apples obtained from a local grocery were fortified with novaluron at 0.05 ppm (LOQ), 0.10 ppm (2 x LOQ), and 1.0 ppm (20 x the LOQ). Fortified samples were analyzed using the method for pome fruits, except calibration standards were diluted with acetone instead of hexane. Acceptable recoveries were obtained with the first method trial.

In addition, confirmation of the novaluron chromatographic peak was conducted by GC/MS. The GC/MS of the fortified apple extract confirmed the presence of novaluron at the retention time determined for novaluron reference standard. Acceptable recoveries were found, as indicated in Table 36.

Table 36. Recovery Results Obtained by an Independent Laboratory Validation of the GC/ECD Method MAK453 for the Determination of Novaluron in Apples. (Report No. PTRL 993W)

Matrix	Spiking Level (mg/kg)	% Recoveries Obtained	Mean % Recovery ± SD [CV]
Apple	0.05	74, 81, 86	80 ± 6 [8]
	0.10	70, 75, 79	75 ± 5 [6]
	1.0	75, 79, 80	78 ± 3 [3]

The method was validated for the determination of novaluron in apple puree, juice, and dry pomace (Munro, S, 2000. MAK 593/002216, Report R-11447). The recovery data are summarized in Table 37. The results validated the method with an LOQ of 0.01 mg/kg for all matrices.

Table 37. Recoveries from EC/GC method MAK453 for determination of novaluron in apple processed fractions. (Report R-11447)

Matrix	Fortification Level (mg/kg)	Recovery (%)	Mean recovery[1] (%)	% RSD
Apple puree	0.01	74,85,91,86,79	83	7.9, n=5
	0.1	85,81,84,86,87	85	2.7, n=5
	1.0	88,87,91,95,93	91	3.7, n=5
	Overall	74 – 95	86	6.3, n=15
Apple juice	0.01	78,80,72,76,85	78	6.2, n=5
	0.1	85,85,83,87,84	85	1.7, n=5
	1.0	90,85,82,83,78	84	5.3, n=5
	Overall	72 – 90	82	5.7, n = 15
Apple dry pomace	0.01	97,79,91,104,88	92	10.3, n=5
	0.1	71,74,73,74,73	73	1.7, n=5
	1.0	78,87,88,79,80	82	5.7, n=5
	Overall	71 – 104	82	11.8, n=15

[1] All recoveries corrected for an apparent control amount of 0.0005 mg/kg for apple puree, 0.001 mg/kg for apple juice, and 0.0003 for dry pomace.

A modified method based on the Method MAK 453 (above) was developed and validated for the determination of novaluron in broccoli, tomatoes, and orange processed fractions (Todd, M A, 1999; MAK 499/984521; R-10233). The sample was extracted with methanol: water, followed by liquid/Liquid partition using hexane. Orange peel was extracted with acetonitrile, followed by liquid/Liquid partition with hexane. For all matrices, final clean up was done using NH_2 Bond Elute (SPE) cartridge prior to quantitation by GC using electron capture detection.

The method was validated over the range of 0.01 – 1.0 mg/kg for all matrices. The recovery data are summarized in Table 38.

Table 38. Summary of recovery data for validation of method for various matrices (MAK 499/984521)

Matrix	Fortification (mg/kg)	Recovery (%)	Mean recovery, Standard Deviation (%)
Broccoli[1]	0.01	81,73,70,71,70	73 ± 6.4
	0.1	77,80,79,81,77	79 ± 2.3
	1.0	77,80,79,81,77	79 ± 2.3
Tomato[2]	0.01	87,75,82,83,81	82 ± 5.3
	0.1	83,81,78,87,86	83 ± 4.4
	1.0	81,86,82,91,86	85 ± 4.7
Orange pulp[3]	0.01	78,83,71,73,89	79 ± 9.3
	0.1	82,84,72,70,86	79±9.3

Matrix	Fortification (mg/kg)	Recovery (%)	Mean recovery, Standard Deviation (%)
	1.0	83,96,82,96,96	91 ± 8.2
Orange peel[4]	0.01	79,74,78,73,83	77 ± 5.2
	0.1	71,95,81,81,76	81±11
	1.0	95,98,98,90,75	91 ± 11
Orange juice[5]	0.01	71,71,76,76,71	73 ± 3.8
	0.1	91,94,96,93,99	95 ± 3.2
	1.0	86,97,96,96,96	94 ± 4.9
Marmalade[6]	0.01	76,85,79,87,82	82 ± 5.4
	0.1	87,98,94,93,93	93 ± 4.2
	1.0	96,96,96,96,98	96 ± 0.9
Orange pomace (dry)[7]	0.01	102,98,97,83,89	94 ± 8.2
	0.1	70,72,78,70,74	73 ± 4.6
	1.0	82,89,83,88,83	85 ± 3.8

[1] Control samples had apparent novaluron concentrations of 0.0010 – 0.0024 mg/kg.
[2] Control samples had apparent novaluron concentrations of 0.0008 – 0.0010 mg/kg.
[3] Control samples had apparent novaluron concentrations of 0.00006 – 0.00075 mg/kg.
[4] Control samples had apparent novaluron concentrations of < 0.004 mg/kg
[5] Control samples had apparent novaluron concentrations of 0.00008 – 0.00031 mg/kg
[6] Control samples had apparent novaluron concentrations of 0.0009 – 0.0021 mg/kg
[7] Control samples had apparent novaluron concentrations of < 0.004 mg/kg

In a variation of the GC method, a mass selective detector (MSD) was substituted for the electron capture detector (Tornisielo, V L, 2004, Report No RF-0002.034.115.04, R-17892)**.** Residues of novaluron were extracted from tomato fruit with methanol. After filtration and concentration, the concentrated filtrate was partitioned between 5% sodium chloride solution and dichloromethane. The dichloromethane fraction was evaporated to dryness. The residue was dissolved in toluene and analyzed by gas chromatography with mass selective detection. Monitored ions were m/z 337 and m/z 335. The method was validated by fortifying control samples at levels of 0.02 and 0.5 mg/kg novaluron. Recovery data are summarized in Table 39.

Table 39. Recovery data for validation of a GC/MSD method for determination of novaluron residues in tomato fruit (Report No. RF-0002.034.115.04)

Fortification level (mg/kg)	Recovery (%)	Average ± standard deviation (%)
0.02	106	
0.02	104	
0.02	96	100 ± 5.3
0.5	94	
0.5	99	
0.5	106	100 ± 6.1
	Overall recovery	101 ± 5.3

A second method used HPLC with UV detection to determine residues of novaluron in plant matrices after extraction with acetone, extraction with methylene chloride, exchange to acetonitrile, extraction of the acetonitrile with hexane (discard), purification on a Florisil column, and column chromatography with mixed silica and Rumsil (ISAGRO S.p.A., 1989. Report R-8750). The method was validated at two fortification levels, 0.01 mg/kg and 0.1 mg/kg, for apple, pear, peach, and maize forage. The HPLC column was reverse phase Supelcosil LC18, and the UV detector was operated at 252 nm. Calibration was with external standards, with a novaluron retention time of 9.1 – 9.2 minutes. Recovery results are summarized in Table 40.

Table 40. Recoveries from an HPLC method for determination of novaluron in plant matrices (Report R-8750)

Crop	Fortification Level (mg/kg)	Recovery (%)	Mean recovery (%)	% RSD
Apple	0.01	105 97 100	100	3.8
	0.1	100 98 100	100	3.0
Pear	0.01	100 103 85	97	11.
	0.1	96 96 100	97	2.3
Peach	0.01	88 110 96	97	10
	0.1	97 99 91	96	4.4
Maize forage	0.01	100 89 96	96	7.7
	0.1	92 86		
		95	91	5.0

The HPLC method was validated for soybean seeds and soybean plants by fortifying control samples at levels of 0.01 – 0.02 mg/kg novaluron (Tornisielo, V L, 1999 and 2000; Reports R-11389; R-11787; R-11788). Recoveries are summarized in Table 41. The limit of quantitation for the method was validated at 0.01 mg/kg novaluron.

Table 41. Recovery data from determination of novaluron in soybeans. (Reports R-11389; R-11787; R-11788)

Matrix	Fortification Level (mg/kg)	Recovery (%)	Mean recovery (%)	% RSD
Soybean seeds (R-11787)	0.011	73 74 74	74	1.3
	0.021	70 71 71	71	0.7
	0.11	84 85 84	84	0.8
Soybean plants (R-11788)	0.01	80 75 88	81	8.6
	0.02	82 96 95	91	8.4
	0.11	97 98 100	99	1.2

A variation of the HPLC/UV method was reported to the Meeting (Mai L, 1998, Report STM CR 60, R-10587). The sample matrix was extracted with acetonitrile and diluted in dichloromethane to separate water. The organic phase was then evaporated to dryness and repeatedly partitioned between hexane and acetonitrile. The hexane fraction was discarded. Lipid was removed from high fat matrices by gel permeation chromatography. Final cleanup was by silica gel chromatography and

residues were quantitated by HPLC (Maxsil C18; mobile phase 60/5/35/v/v/v acetonitrile/methanol/1% triethanolamine at pH 5.1) with UV detection at 264 nm. At a flow rate of 1 ml/minute, the novaluron retention time was 11 minutes. The LOQ was reported as 0.05 mg/kg for cotton seed, apples, and tomatoes, and 0.2 mg/kg for cottonseed oil. Method recoveries are reported in Table 42.

Table 42. Recoveries from HPLC method for determination of novaluron in plant matrices (Report STM CR 60)

Fortification level (mg/kg)	Recovery (%)				
	Undelinted cotton seed	Cotton foliage	Cotton seed oil	Apples	Tomatoes
0.05	138,74,66,71,94,98 (90 ± 27)			80,88,80,88,86 (84±4.1)	88,86,91,79 (86±5.1)
0.2	90,66		71,111		
0.5		90,111,90,79 (92±12)	74,97	80,92,82,82,78 (83±5.4)	93,97,99,67 (89±15)
1.9		102, 105			
20		83,74,102,100,82 (88±12)			

The HPLC/UV was further validated for cottonseed matrices (Rose, J E, 2001. Report No. AASI AI990801, R-11255). The sample matrix was extracted two times with acetonitrile (ACN) and repeatedly partitioned with hexane. The extract was then concentrated and purified by gel permeation chromatography, and further purified by silica gel chromatography. Quantitation was via HPLC with detection at 264 nm, using external standards. Analytical recovery from fortified matrices is summarized in Table 43.

Table 43. Recoveries from method validation of novaluron in cotton matrices (Report No. AASI AI990801)

Fortification level (mg/kg)	Recovery (%)				
	Undelinted seed	Gin trash	Seed meal	Seed hulls	Refined oil
0.05	94, 96	110, 110	80, 86	90, 104	80, 112
0.10	97, 98	102, 110	76, 84	91, 97	92, 117
10.0	80, 90	81, 87	73, 86	82, 90	82, 93
Mean	93	100	81	92	96
SD	7	13	5	7	15
%RSD	8	13	6	8	15

An independent laboratory validation of the HPLC/UV method for cottonseed was reported to the Meeting (Class, T, 2001; Report B 463 G, R-13888)**.** Cottonseed samples were extracted with acetonitrile and the extract partitioned with hexane. The acetonitrile phase was evaporated to dryness, the residue was dissolved in ethyl acetate: cyclohexane (1:1 v/v) and then fractionated by Gel Permeation Chromatography (GPC) followed by column chromatography on 10 g activated silica gel. The fraction from the silica gel column that contained Novaluron was concentrated to dryness, redissolved in acetonitrile/methanol/1% triethylamine in water (60/5/35 v/v/v) and analyzed by RP-C_{18}-HPLC using an acetonitrile/water gradient and UV detection at 264 nm. The method limit of quantitation (LOQ) for novaluron was demonstrated at 0.05 mg/kg.

Table 44. Recovery results from an independent laboratory validation (ILV) for the determination of novaluron in cotton matrices (Report B 463 G)

Plant matrix	Spiking Level (mg/kg)	Recoveries obtained	Range (%)	Average Percent Recovery% ± RSD%
Undelinted Cotton Seed	0.05 0.5	100, 100, 96 90, 80, 84	96 – 100 80 - 90	99% ± 2% 85% ± 6%
	Overall	n = 6	80 - 100	92% ± 9%

Another variation of the HPLC method for plant commodities involved the use of MS/MS as the detector (Munro, S, 2000; Report No. MAK 668/01R, R-12364). Novaluron was extracted from samples of apples and potatoes using methanol: water (70:30, v:v), followed by a liquid: liquid clean-up using hexane. Final cleanup was by NH_2 solid phase extraction (SPE) cartridge. Quantification was performed using liquid chromatography with tandem mass spectrometric detection (LC-MS/MS) in the negative electrospray ionization mode. A gradient elution was utilized from 0.01 M ammonium acetate/0.1% acetic acid in water/acetone (80/20, v/v) to 0.01 M ammonium acetate/0.1% acetic acid in water/acetone (20/80, v/v). Novaluron m/z 491>471 at 20 eV was monitored. Control samples were fortified with Novaluron at levels of 0.05 and 0.5 mg/g for apples and 0.01 and 0.10 mg/kg for potatoes. A summary of the recovery data is presented in Table 45.

Table 45. Recovery of Novaluron from Apples and Potatoes using an LC/MS/MS Method (Report No. MAK 668/01R0.

Fortification (mg/kg)	Recovery (%)[1]	Mean ± sd (%)
Apples		
0.05	90,83,94,98,86	90 ± 6.0
0.50	91,91,84,78,71	83 ± 8.6
Overall Range	71-98	
Potatoes		
0.01	107,107,92,102,87	99 ± 9.1
0.10	89,77,96,83,71	83 ± 9.8
Overall Range	71 – 107	

[1] Control samples had no detectable residues (< 0.005 mg/kg for apples, < 0.002 mg/kg for potatoes)

A report on the independent laboratory validation (ILV) of the above method (MAK 668) was provided to the Meeting (Lindsell, S R, 2001; Report No. MAK 669/012109; R-12365). Fortified apples or potatoes were macerated and extracted with methanol:water. The extract was partitioned into hexane. Further cleanup was performed using NH_2 SPE cartridges. Residues were quantified using HPLC with tandem mass spectrometric detection (LC-MS/MS). The method was validated over a range of 0.05 to 0.5 mg/kg for apples and 0.01 to 0.11 mg/kg for potatoes (see Table 46).

Table 46. Independent Laboratory Validation of Method MAK668 (MAK 669/012109)

Fortification (mg/kg)	Recovery (%)[1]	Mean ± sd (%)
Apples		
0.05	91,94,98,96,95	95±2.6
0.50	94,92,106,105,103	100±6.5
Overall Range	91-106	
Potatoes		
0.01	78,104,114,104,96	99±13
0.10	95,59,71,87,94	81±16
Overall Range	59-114	

[1] Control samples had no detectable residues (< 0.005 mg/kg for apples, < 0.002 mg/kg for potatoes)

A report on a gas chromatography/electron-capture detection (GC/ECD) method for the analysis of novaluron residues in *eggs, milk, and ruminant tissues* was provided to the Meeting (Todd M A, 1998 Report No. MAK 454/972535, R-9346). The subject method is similar in principle to the GC/ECD method previously described for plant commodities and is for data collection purposes. Briefly, homogenized bovine tissue samples (fat, muscle, kidney, and liver) were extracted with methanol and centrifuged to separate the phases. Milk and egg samples were extracted with methanol by ultrasonication and then centrifuged to separate the phases. The extracts were concentrated to the aqueous phase and repeatedly partitioned with hexane. The resulting hexane fractions were cleaned up by chromatography through NH_2-SPE (solid-phase extraction), the eluate was evaporated to dryness, and residues were redissolved in hexane for analysis by GC/ECD. Calibration was with external standards. The validated limit of quantitation (LOQ) is 0.01 ppm in fat, kidney, liver, muscle, milk, and egg. See Table 47.

Table 47. Recovery of Novaluron from Fortified Animal Commodities by a GC/ECD Data Collection Method (Report No. MAK 454/972535)

Matrix	Spiking Level (mg/kg)	Recoveries (%)[1]	Mean Recovery ± SD [1]
Fat	0.01	81, 86, 89, 91, 94	88 ± 5.0
	0.1	95, 96, 98, 98, 101	98 ± 2.3
	0.5	102, 104, 105, 109, 111	106 ± 3.8
Kidney	0.01	90, 96, 96, 97, 105	97 ± 5.4
	0.1	79, 81, 82, 86, 87	83 ± 3.4
	0.5	84, 87, 92, 92, 94	90 ± 4.2
Liver	0.01	91, 102, 104, 107, 116	104 ± 9.0
	0.1	72, 72, 84, 87, 98	83 ± 10.9
	0.5	72, 80, 82, 100, 102	87 ± 13.3
Muscle	0.01	75, 77, 81, 82, 99	83 ± 9.5
	0.1	100, 100, 101, 103, 106	102 ± 2.5
	0.5	94, 103, 103, 105, 109	103 ± 5.5
Milk	0.01	100,102, 103, 106, 107	104 ± 2.9
	0.1	83, 87, 107, 107, 109	99 ± 12.4
	0.5	93, 96, 102, 108, 108	101 ± 6.7
Egg	0.01	77, 77, 84, 86, 87	82 ± 4.9
	0.1	78, 83, 91, 94, 100	89 ± 8.6
	0.5	81, 90, 93, 94, 95	91 ± 5.5

[1]The report contained recoveries corrected for apparent mean control residues. Uncorrected recoveries are reported herein which were calculated from the residue levels (mg/kg). This had a significant effect (> 2%) only on the recovery of the 0.01 mg/kg fortification for liver and kidney, raising the recoveries from 84% and 79% to the table values.

This method was *radiovalidated* by the use of samples from the poultry nature of the residue study (Kane, T J, 2004. Report No. MAK 810/033178). Samples of liver, fat (mesenteric/abdominal), and thigh muscle and eggs (final day sample only) were extracted and analyzed according to method MAK 454/972535. To radiovalidate this method, samples of extracts were radioassayed by LSC and the final post-SPE samples were analyzed by TLC with radiodetection. Recovery of radioactivity through the application of the validated analytical method is shown in Table 48. Both methods of analysis gave similar results.

Table 48. Comparison of residues of Novaluron detected using GC/EC analytical method MAK454 and with radiodetection in selected pooled tissues and eggs from laying hens dosed with [difluorophenyl- 14C(U)]Novaluron (Report No. MAK 810/ 033178).

Matrix type	Residues Novaluron detected (method MAK454)	Residues Novaluron detected (method radiodetection)
Liver	0.42	0.35
Thigh muscle	0.36	0.30
Fat (mesenteric/abdominal)	4.2	3.8
Eggs (final day sample)	0.48	0.41

A similar method was validated for cream and reported in a ruminant feeding study (Redgrave, VA, 2001. Report No. MAK 605/003999; R-10993). Novaluron was extracted from a fortified cream sample by using acetonitrile. Clean up was by liquid: liquid partition using hexane, followed by NH_2 solid phase extraction (SPE) cartridge. Quantitation was performed by using gas chromatography with electron capture detection. The method was validated over the range of 0.01 to 0.50 mg/kg in cream. The results are presented in Table 49.

Table 49. Recovery data from determination of novaluron in cream (Report No. MAK 605/003999)

Fortification Level (mg/kg)	Recovery[1] (%)	Mean recovery (%)	RSD (%)
0.01	71 73 76	73	3.4
0.10	77 79 82	79	3.2
0.50	88 79 86	84	5.6
	Overall	79	7.1, n=9

[1] Control samples had no detectable residues.

A variation of the LC/MS/MS method MAK668 used for plant commodities was developed for the determination of novaluron in tissues (fat, kidney, liver, muscle) and milk (Munro, S, 2001; Report No. MAK 670/012154; R-12366). Fat, liver, kidney, and muscle samples were extracted with methanol followed by a liquid:liquid clean-up using hexane. The method for milk comprised extraction with methanol and acetonitrile followed by liquid: liquid clean-up using hexane. Final clean up for all matrices was by NH_2 solid phase extraction (SPE) cartridge. Quantification was performed using liquid chromatography with tandem mass spectrophotometric detection (LC-MS/MS). The system was operated in the negative electrospray mode and the novaluron m/z 491>471 at 20 eV was monitored. Calibration was with external standards. The method was validated over a range of 0.1 mg/kg to 1.0 mg/kg for fat, 0.05 mg/kg to 0.5 mg/kg for kidney and liver, and 0.02 mg/kg to 0.2 mg/kg for muscle and milk. The recovery data are summarized in Table 50.

Table 50. Recovery data on animal matrices determined by LC/MS/MS (Report No. MAK 670/012154)

Matrix	Fortification level[1] (mg/kg)	Recovery (%)	Mean recovery $\pm$ sd (%)
Fat	0.1	82,76,71,78,79	77$\pm$4.1
	1	77,95,82,90,85	86$\pm$7.0
Kidney	0.05	86,71,94,87,76	83$\pm$9.2

Matrix	Fortification level[1] (mg/kg)	Recovery (%)	Mean recovery ± sd (%)
	0.5	87,105,107,99,93	98±8.3
Liver	0.05	74,85,82,86,86	83±5.1
	0.5	83,81,84,78,78	81±2.8
Muscle	0.02	99,111,100,96,101	101±5.7
	0.2	84,71,94,92,89	86±9.2
Milk	0.02	80,80,90,77,78	81±5.2
	0.2	70,75,76,80,77	76±3.6

[1] Novaluron was found to be below the limit of detection in all control samples, with limits of detection of 0.002 mg/kg for milk, kidney, and muscle and 0.004 mg/kg for liver and fat.

An Independent Laboratory Validation (ILV) was reported for the LC/MS/MS method for animal commodities MAK670 (Lindsell, S R, 2001; Report No. MAK 671/012110; R-12367). Adequate recoveries were obtained from milk, muscle, and liver with the first method trial. No major modifications to the method were required; however, the laboratory did cite that emulsions occurred with each hexane partitioning; therefore these solutions were centrifuged to allow transfer of the hexane fraction. In addition, the laboratory cited different instrumentation and sources of the solvents which were used in the ILV study. Recoveries of novaluron from the ILV study are reported in Table 51.

Table 51. Recovery Results Obtained by an Independent Laboratory Validation of the HPLC/MS/MS Method for the Determination of Novaluron in Milk, Muscle, and Liver (Report No. MAK 671/012110)

Matrix	Spiking Level (mg/kg)	Recoveries Obtained [1]	Mean Recovery ± SD
Milk	0.02	89, 93, 94, 94, 102	94 ± 4.7
	0.20	80, 81, 82, 86, 98	85 ± 7.4
Muscle	0.02	87, 93, 98, 101, 120	100 ± 12
	0.20	75, 91, 99, 106, 108	96 ± 13
Liver	0.05	74, 75, 80, 86, 96	82 ± 9.1
	0.50	87, 89, 94, 97, 99	93 ± 5.1

[1] The recoveries were reported corrected for apparent mean control residues. Uncorrected recoveries are reported herein which were calculated from the residue levels (mg/kg). This had no significant effect (> 2%) except for the 0.02 mg/kg fortification of milk, where the recovery was increased from 78% to the table value

The Meeting received a report on the testing of Novaluron in the US FDA Multiresidue Method Test (MRM) guidelines in Pesticide Analytical Manual (PAM) Vol. I, Appendix II (1/94) (Koch, D A, 2002. Study No, 2002-022, Report R-15546). The results indicate that novaluron is not adequately recovered by any of the multiresidue methods

Novaluron did not exhibit natural fluorescence at an excitation wavelength of 253 nm; therefore, Protocol A testing was terminated. Testing using Protocol B was not required because novaluron is not an acid or phenol.

Testing using Protocol C Level II yielded adequate responses using a DB-1 column and electron capture (ECD) and electrolytic conductivity (ELCD) detectors; however, significant peak tailing was observed for both detectors.

Novaluron could not be accurately quantitated using the usual Protocol D procedures (peak heights) due to varying peak shapes and relative intensity from injection to injection. Corrected recoveries for fortified apples, obtained by summing the peak areas for standards and samples were 140% and 140% at the 0.1 mg/kg level, and 81% and 72% at the 2.0 mg/kg level.

Protocols E and F require the evaluation of Florisil cleanup. Novaluron was recoverable from the 303/304 C1 cleanup in the 15% and 50% diethyl ether/hexane fractions but was not recoverable (< 30%) from the 303/304 C2 cleanup in eluent 3. Novaluron was partially recovered with Protocol E testing using extraction 303 E4/C1 with apples at 0.5 mg/kg (56% and 80%), but high bias recoveries were obtained at 2.0 mg/kg (118% and 139%). Variable results and inconsistent recoveries were obtained with Protocol F testing using extraction 304 E1/C1 with ground beef; recoveries were 6% and 30% at 0.05mg/kg, and 33% and 84% at 2.0 mg/kg.

Stability of pesticide residues in stored analytical samples

Frozen storage stability studies were reported to the Meeting for a variety of substrates that include apple, pear, apple processed fractions, cottonseed, tomato, broccoli, cabbage, orange, and potatoes. In general, control samples were fortified with known concentrations of novaluron and then placed in frozen storage at approximately -18 C or less. The fortified samples were analyzed periodically for residues of novaluron using the same analytical method as that used for the residue field trial or processing samples. Sample extracts were not stored prior to analysis; therefore, storage stability data for residues in sample extracts are not required.

Frozen storage stability studies were not conducted for animal products.

Untreated samples of homogenized apples were fortified with unlabelled novaluron (chemical purity 99.5%) at concentrations of 0.05, 0.25 and 1.00 mg/kg (Todd, M A, 1999; Report No. MAK 470/992503; R-10014). Sub-samples from each concentration and unfortified control samples were analyzed immediately, while the remaining fortified samples were stored frozen at -18°C. Stored sub-samples were analyzed after 1, 3, 6 and 12 months, using GC/ECD following the method described in Report No. MAK 453/972510.

Table 52. Frozen storage stability data for novaluron in apple (Report No. MAK 470/992503)

Matrix	Storage Period Months	Fortification mg/kg	Apparent Remainder[1]/%	Procedural Recovery[2] %
Apple fruit	0 day	0.05	85	88
	1		73	84
	3		69	94
	6		78	100
	12		67	84
Apple fruit	0 day	0.25	93	88
	1		87	90
	3		88	93
	6		80	99
	12		60	82
Apple fruit	0 day	1.0	95	94
	1		90	100
	3		95	106
	6		87	89
	12		76	70

[1] Average of 2 analyses, not corrected for procedural recovery
[2] Procedural recovery from samples spiked on day of analysis

In a trial conducted in conjunction with residue trials on pome fruit and processed fractions, the stability of frozen samples of pear fruit over a period of 5 months and apple juice over a period of 3 months was determined (Willard, T R, 2002; Report No. AA010703; R-13886). Samples of pear fruit and apple juice were fortified at levels of 0.1 and 0.5 mg/kg, respectively. Samples were immediately analyzed by GC with electron capture detection and at various time intervals after frozen storage. Results are shown in Table 53.

Table 53. Frozen storage stability data for novaluron in pear and apple juice (Report No. AA010703)

Matrix	Storage Period days	Fortification mg/kg	Apparent Reminder[1] %	Procedural Recovery[2] %
Pear fruit	0	0.1	73	73
	26		64	81
	90		65	81
	158		62	71
Apple juice	0	0.5	114	114
	29		100	98
	99		108	109

[1] Average of 2 analyses, not corrected for procedural recovery
[2] Procedural recovery from samples spiked on day of analysis

Samples of homogenized potatoes were fortified with novaluron at concentrations of 0.01, 0.1 and 0.5 mg/kg (Todd, M A, 1999; Report No. MAK 470/992503; R-10014). Sub-samples from each concentration and unfortified control samples were analyzed immediately, while the remaining fortified samples were stored frozen at -18°C. Stored sub-samples were analyzed after 1, 3, 6 and 12 months, using GC/ECD following the method described in Report No. MAK 453/972510. See Table 54.

Table 54. Frozen storage stability data for novaluron in potato (Report No. MAK 470/992503)

Matrix	Storage Period Months	Fortification mg/kg	Apparent Remainder[1/] %	Procedural Recovery[2/] %
Potato	0 day	0.01	93	102
	1		105	98
	3		96	109
	6		100	108
	12		66	109
Potato	0 day	0.10	97	105
	1		79	96
	3		94	97
	6		89	98
	12		74	79
Potato	0 day	0.50	107	105
	1		94	87
	3		101	92
	6		93	99
	12		86	87

[1] Average of 2 analyses, not corrected for procedural recovery
[2] Procedural recovery from samples spiked on day of analysis

A storage stability test was reported to the Meeting for delinted cottonseed and cotton gin trash samples (Willard, T R, 2001; Report No. AA990801; R-11255). Samples of delinted cottonseed and gin trash were fortified at 0.1 mg/kg and frozen for up to 5 months (151 days) at -20°C. The method is very similar to that described above under Study STM CR 60. The method involved extraction of the sample substrate with acetonitrile, which was repeatedly partitioned with hexane, clean up by silica gel chromatography, and determination of novaluron by HPLC. The demonstrated LOQ for the method was 0.05 mg/kg novaluron.

The results, not corrected for procedural recoveries, are summarized in Table 55.

Table 55. Residues of novaluron in delinted cottonseed and gin trash samples following periods of frozen storage (Report No. AA990801),

Matrix	Storage Period Days	Fortification mg/kg	Apparent Remainder[1/] %	Procedural Recovery[2/] %
Undelinted cotton seed	0	0.1	-	98
	30		75	75
	164		79	89
Cotton gin trash	0	0.1	-	106
	30		93	97
	151		77	73

[1] Average of 2 analyses, not corrected for procedural recovery.
[2] Procedural recovery from samples spiked on day of analysis

Previously treated samples of broccoli, cabbage, tomato, orange pomace (wet and dry), orange peel and marmalade were taken from field trials, or after processing (where relevant) (Munro, S, 1999; Report No. MAK557/994033, R-11205). Incurred residues were determined before and after storage at -18°C. Prior to analysis, sub-samples were extracted with methanol/water, methanol or acetonitrile, for cabbage, broccoli and tomato, orange pomace and marmalade or orange peel respectively. All extracts were then partitioned with hexane. Extracts were analyzed for novaluron by GC/ECD, with a validated LOQ of 0.05 mg/kg for cabbage and 0.01 mg/kg for all other matrices.

Mean recovery results, which were not corrected for procedural recoveries, are summarized in Table 56.

Table 56. Mean percentage recoveries of residues of novaluron in frozen (-18oC) samples of various matrices (Report No. MAK557/994033).

Matrix	Incurred residue before storage[1] (mg/kg)	Storage period (months)	% Remaining after storage[2]
Broccoli	0.80	6	86
Broccoli	0.05	6	100
Cabbage	0.39	7	90
Cabbage	0.02	7	75
Tomato	0.13	12	92
Tomato	0.06	12	108
Orange: wet pomace	0.11	8	155
Orange: wet pomace	0.32	8	133
Orange: dry pomace	0.61	8	106
Orange: dry pomace	1.8	8	89
Orange: marmalade	0.02	8	150
Orange: marmalade	0.07	8	143
Orange: peel	1.2	8	71
Orange: peel	0.40	8	121

[1] Details of this determination were not provided
[2] *Not* corrected for concurrent (procedural) recoveries. Concurrent recoveries at six months were broccoli 72% at 0.5 mg/kg; cabbage 70% at 0.2 mg/kg; tomatoes 78% at 0.1 mg/kg; orange pomace wet 71% at 0.2 mg/kg; orange pomace dry 70% at 1 mg/kg; orange peel 71% at 0.8 mg/kg; and orange marmalade 81% at 0.05 mg/kg

USE PATTERN

Novaluron is registered in many countries for use on several crops for the control of a variety of foliage feeding insects. Novaluron is an insect growth regulator (IGR) that acts primarily by disrupting cuticle formation and deposition occurring when insect moult, resulting in their death. It affects developing immature stages of the target insects. Consequently, fully developed adult stages of pests and beneficial species are not affected.

The product is mixed with water and applied as foliar spray or broadcast treatment using aerial or ground equipment equipped for conventional insecticide spraying on crops. Novaluron must

be ingested by insect larvae to be fully effective. Consequently, the timing of application is largely dependent on the feeding behaviour of the target pest.

The manufacturer supplied GAP information (labels) for numerous countries, and the NL indicated that there are no approved uses in that country.

GAPs related to the supervised field trial studies submitted are summarized in Table 57.

Table 57. Registered Uses of novaluron[1].

Crop	Country	Formulation	Application				PHI days
			Method	Rate, kg ai/ha	Spray conc. kg ai/hL	No. or max (kg ai/ha/ season)	
Apple & pear	Chile	100 g/L EC	Foliar		0.07		14
Apple & pear	USA	75 g/kg WG	Foliar	0.37	0.009-0.05 (tree over 3 m ht) 0.08 (tree under 3 m ht)	4 (1.1 max)	14
Cotton	Brazil	100 g/L EC	Foliar	0.01	0.005		93
Cotton	Mexico	100 g/L EC	Foliar	0.015		2	30
Cotton	South Africa	100 g/L EC	Foliar	0.035	0.007 ground 0.12 aerial	3	Do not Graze Treated fields
Cotton	USA	100 g/L EC	Foliar	0.1	0.53 aerial 0.21 ground	4 (0.3 max) 7 day retreatment	30
Potato	Mexico	100 g/L EC	Foliar	0.015		1	30
Potato	Switzerland	100 g/L EC	Foliar	0.02		2	21
Potato	USA	100 g/L EC	Foliar	0.087	0.19 aerial 0.093 ground	2 (0.17 max)	14
Soya beans	Brazil	100 g/L EC	Foliar	0.01			53
Tomato	Argentina	100 g/L EC	Foliar	0.1 (calculated)	0.005	4 (7 – 10 day)	1
Tomato	Brazil	100 g/L EC	Foliar	0.02	0.002	As needed	7

[1] Only GAP related to the supplied Supervised Field Trial studies are included.

The Meeting received information on novaluron supervised filed trials for the crops listed in Table 58. Note that all applications were foliar.

Table 58. Supervised Field Trials for the Foliar Application of Novaluron.

Commodity	Country	Table Number
Apples	Chile	60
	Canada	61
	USA	61
Pears	Canada	62
	USA	62
Tomato	Argentina	63
	Brazil	64
Soya	Brazil	65
Potato	EU	66
	Mexico	66
	USA	66
Cotton	Brazil	67

Commodity	Country	Table Number
	South Africa	67
	USA	67

Where multiple samples were taken from a single plot or multiple analyses conducted on a single sample, the average value is reported. Where results from separate plots with distinguishing characteristics such as different formulations, varieties or treatment schedules were reported, results are listed for each plot. Underlined values were used for the estimation of MRLs and STMRs. Results have *not* been corrected for concurrent method recoveries unless indicated.

Pome Fruit

Table 59. Supervised Field Trials for the Foliar Application of Novaluron to Apples in Chile (Gonzalez, R.H., 2001, R-14452)

Crop Location, year	Application				Interval, days	PHI, days	Residues mg/kg	Reference/Trial[1]
	Form.	kg ai/ha	kg ai/hL	No or (max)				
Apples								
GAP Chile	*100 g/L EC; at a rate of 0.07 kg ai/hL and PHI of 14 days.*							
Chile, 2001	100 g/L EC	0.1	0.0050	5	21 - 27	0 7	0.27 0.20	R-14452
						11 22	0.17 0.15	
Chile, 2001	75 g/kg WG	0.1	0.0053	5	21 - 27	0 7 11 22	0.22 0.15 0.14 0.04	R-14452

[1] Average recovery was 97% (0.05, 0.27, and 0.53 mg/kg fortifications).

Table 60. Supervised Field Trials for the Foliar Application of Novaluron to Apples in Canada and the USA (Willard, T R, 2002, Report No. AA010703; R-13886; Willard, T H, 2003, Study No. R-15425)

Crop Location, year	Application				Interval, days	PHI, days	Residues[2] mg/kg	Reference /Trial
	Form.	kg ai/ha	kg ai/hL	No[1] or (max)				
Apples								
GAP USA:	*75 g/kg WG, at a rate of 0.37 kg ai/ha or seasonal maximum rate of 1.1 kg ai/ha, 0.009 - 0.05 kg ai/hL spray concentration (tree over 3 meter height), 0.08 kg ai/hL spray concentration (trees under 3 meter height), PHI 14 days*							
California, USA	75 g/kg WG	0.38	0.075	3 (1.2)- ES	7	14	0.23	R-13886
2001				3 (1.1)- LS				Trial CA1
California, USA	75 g/kg WG	0.38	0.01	3 (1.1)- ES	7	14	0.44	R-13886
2001				3 (1.1)- LS				Trial CA1
Illinois	75 g/kg WG	0.38	0.076	3 (1.1)- ES	7	14	0.50	R-13886
USA				3 (1.1)- LS				Trial IL1
2001								
Michigan	65 g/kg WG	0.37	0.076	3 (1.1)- ES	7	14	0.54	R-13886
USA				3 (1.1)- LS				Trial MI1
2001								
Michigan	65 g/kg WG	0.38	0.011	3 (1.1)- ES	7	14	0.27	R-13886
USA				3 (1.1)- LS				Trial MI2
2001								
New York	75 g/kg WG	0.38	0.081	3 (1.1)- ES	7	14	0.68	R-13886

Crop Location, year	Application				Interval, days	PHI, days	Residues[2] mg/kg	Reference /Trial
	Form.	kg ai/ha	kg ai/hL	No[1] or (max)				
Apples								
GAP USA:	*75 g/kg WG, at a rate of 0.37 kg ai/ha or seasonal maximum rate of 1.1 kg ai/ha, 0.009 - 0.05 kg ai/hL spray concentration (tree over 3 meter height), 0.08 kg ai/hL spray concentration (trees under 3 meter height), PHI 14 days*							
USA				3 (1.1)- LS				Trial NY1
2001								
Virginia	75 g/kg WG	0.38	0.078	3 (1.1)- ES	7	14	0.35	R-13886
USA				3 (1.2)- LS				Trial VA1
2001								
Oregon	65 g/kg WG	0.37	0.075	3 (1.1)- ES	7	14	0.49	R-13886
USA				3 (1.1)- LS				Trial OR1
2001								
Pennsylvania	65 g/kg WG	0.38	0.078	3 (1.1)- ES	7	14	0.60	R-13886
USA				3 (1.1)- LS				Trial PA1
2001								
Pennsylvania	65 g/kg WG	0.38	0.078	3 (1.1)- ES	7	14	1.1	R-13886
USA				3 (1.1)- LS				Trial PA2
2001								
Pennsylvania	65 g/kg WG	0.38	0.011	3 (1.1)- ES	7	14	0.40	R-13886
USA				3 (1.13)- LS				Trial PA2
2001								
Utah	65 g/kg WG	0.38	0.075	3 (1.1)- ES	7	14	0.44	R-13886
USA				3 (1.13)- LS				Trial UT1
2001								
Washington	65 g/kg WG	0.51	0.014	3 (1.2)- ES	7	14	0.52	R-13886
USA				3 (1.13)- LS				Trial WA1
2001								
Washington	65 g/kg WG	0.38	0.081	3 (1.2)- ES	7	14	0.93	R-13886
USA				3 (1.1)- LS				Trial WA1
2001								
Washington	65 g/kg WG	0.38	0.08	3 (1.1)- ES	7	0	0.94	R-13886
USA				3 (1.1)- LS		3	0.79	Trial WA2
2001						7	0.61	
						14	0.59	
						28	0.75	
Washington	65 g/kg WG	0.38	0.08	3 (1.1)- ES	7	14	0.71	R-13886
USA				3 (1.1)- LS				Trial WA3[3]
2001								
Michigan, USA	75 g/kg WG	0.38	0.085	3 (1.1)- ES	7	14	0.81	R-15425
2002				3 (1.1)- LS				Trial MI1
Michigan, USA	75 g/kg WG	0.38	0.085	3 (1.1)	7	14	0.73	R-15425
2002								Trial MI1
New York, USA	75 g/kg WG	0.38	0.081	3 (1.1)- ES	7	14	0.55	R-15425
2002				3 (1.1)-LS				Trial NY1
New York, USA	75 g/kg WG	0.38	0.081	3 (1.1)	7	14	0.77	R-15425
2002								Trial NY1
Oregon, USA	75 g/kg WG	0.39	0.079	3 (1.2)- ES	7	14	0.37	R-15425
2002				3 (1.2)-LS				Trial OR1
Oregon, USA	75 g/kg WG	0.39	0.079	3 (1.12	7	14	0.50	R-15425

Crop Location, year	Application				Interval, days	PHI, days	Residues[2] mg/kg	Reference /Trial
	Form.	kg ai/ha	kg ai/hL	No[1] or (max)				
Apples								
GAP USA:	*75 g/kg WG, at a rate of 0.37 kg ai/ha or seasonal maximum rate of 1.1 kg ai/ha, 0.009 - 0.05 kg ai/hL spray concentration (tree over 3 meter height), 0.08 kg ai/hL spray concentration (trees under 3 meter height), PHI 14 days*							
2002								Trial OR1
Virginia, USA	75 g/kg WG	0.38	0.076	3 (1.1)- ES	7	14	0.65	R-15425
				3 (1.1)-LS				Trial VA1
Virginia, USA	75 g/kg WG	0.38	0.076	3 (1.1)	7	14	0.67	R-15425
2002								Trial VA1
Nova Scotia,	65 g/kg WG	0.38	0.079	3 (1.2)- ES	7	15	0.27	R-13886
Canada				3 (1.12)-LS				Trial NS1
2001								
Ontario,	65 g/kg WG	0.38	0.080	3 (1.13)- ES	7	14	0.86	R-13886
Canada				3 (1.1)-LS				Trial ON1
2001								
Ontario,	65 g/kg WG	0.39	0.080	3 (1.17)- ES	7	14	0.96	R-13886
Canada				3 (1.2)-LS				Trial ON2
2001								
Quebec,	65 g/kg WG	0.38	0.076	3 (1.1)- ES	7	14	0.67	R-13886
Canada				3 (1.1)-LS				Trial PQ1
2001								
Quebec,	65 g/kg WG	0.37	0.079	3 (1.1)- ES	7	14	0.49	R-13886
Canada				3 (1.2)-LS				Trial PQ2
2001								
Quebec,	65 g/kg WG	0.38	0.086	3 (1.1)- ES	7	14	0.71	R-13886
Canada				3 (1.1)-LS				Trial PQ3
2001								

[1] ES is early season, the first application at or near petal fall, then at 7-day intervals. LS is late season, from about 30 days before mature harvest. Bloom to harvest interval is 70 – 170 days in the US, depending on the variety. Exact treatment dates were not provided.
[2] Analytical method MAK 453/972510. The average fortification recovery was 92% at spiking levels of 0.05mg/kg to 1.0 mg/kg (range: 72% - 115%; s.d.: 12%; n = 28).
[3] Apples from this trial were used in a processing study (see below).

Table 61. Supervised Field Trials for the Foliar Application of Novaluron to Pears in Canada and the USA (Willard, T R, 2002, Report No. AA010703; R-13886).

Crop Location, year	Application					PHI	Residues	Reference
	Form.	kg ai/ha	kg ai/hL	No[1] or (max)	Interval, days	days	mg/kg	
Pears								
GAP USA: (same as apple)	*75 g/kg WG, at a rate of 0.37 kg ai/ha or seasonal maximum rate of 1.1 kg ai/ha,0.009 - 0.05 kg ai/hL spray concentration (tree over 3 meter height), 0.08 kg ai/hL spray concentration (trees under 3 meter height), PHI 14 days*							
CA, USA	75 g/kg WG	0.37	0.075	3 (1.1)- ES 3 (1.1)-LS	7	14	0.59	R-13886 Trial CA2
CA, USA	75 g/kg WG	0.38	0.01	3 (1.1)- ES 3 (1.2)-LS	7	14	0.79	R-13886 Trial CA2
CA, USA	75 g/kg WG	0.38	0.085	3 (1.1)- ES	7	14	0.18	R-13886
				3 (1.13)-LS				Trial CA3
OR, USA	75 g/kg WG	0.37	0.078	3 (1.1)- ES 3 (1.1)-LS	7	14	0.47	R-13886 Trial OR2
OR, USA Decline	75 g/kg WG	0.37	0.077	3 (1.1)- ES 3 (1.1)-LS	7	0 3	0.74 0.61	R-13886 Trial OR3

Crop Location, year	Application					PHI	Residues	Reference
	Form.	kg ai/ha	kg ai/hL	No[1] or (max)	Interval, days	days	mg/kg	
						7 14 28	0.51 0.42 0.28	
PA, USA	75 g/kg WG	0.37	0.079	3 (1.1)- ES 3 (1.1)-LS	7	14	0.46	R-13886 Trial PA3
WA, USA	75 g/kg WG	0.38	0.081	3 (1.1)- ES	7	14	1.3	R-13886
				3 (1.1)-LS				Trial WA4
WA, USA	75 g/kg WG	0.38	0.011	3 (1.1)- ES 3 (1.1)-LS	7	14	0.43	R-13886 Trial WA4
Nova Scotia, Canada	65 g/kg WG	0.38	0.079	3 (1.2)- ES 3 (1.1)-LS	7	14	1.0	R-13886 Trial NS2
Ontario,	65 g/kg WG	0.38	0.080	3 (1.1)- ES	7	14	1.8	R-13886
Canada				3 (1.1)-LS				Trial ON3
Ontario, Canada	65 g/kg WG	0.38	0.08	3 (1.1)- ES 3 (1.1)-LS	7	14	0.91	R-13886 Trial ON4
Ontario, Canada	65 g/kg WG	0.37	0.08	3 (1.1)- ES 3 (1.1)-LS	7	14	1.6	R-13886 Trial ON5

[1] ES is early season, the first application at or near petal fall, then at 7-day intervals. LS is late season, from about 30 days before mature harvest. Bloom to harvest interval is 100 – 170 days in the US, depending on the variety.

Fruiting vegetables (non-cucurbit)

Table 62. Supervised Field Trials for the Foliar Application of Novaluron to Tomatoes in Argentina (Carrancio, L, 1999. R-11446).

Crop Location, year	Application				Interval, days	PHI, days	Residues [1]mg/kg	Reference
	Form.	kg ai/ha	kg ai/hL	No				
Tomato								
GAP Argentina:	*100 g/L EC, 0.005 kg ai/hL,4 applications at 7 to 10 day intervals, PHI of 1 day*							
Santa Fe, Argentina, 1999	100 g/L EC	0.12 (calc)	0.01	3	11 13	0 3 7 11 15 30	0.21 0.15 0.14 0.11 0.076 0.041	R-11446
Santa Fe, Argentina, 1999	100 g/L EC	0.24 (calc)	0.02	3	11 13	0 3 7 11 15 30	0.36 0.29 0.20 0.18 0.073 0.033	R-11446

[1] Analysis by HPLC/UV (see R8750). Values, average of three samples, were reported corrected for a recovery of 85.3% from a fortification (0.01 mg/kg). Correction has been removed from the listings in the table.

Table 63. Supervised Field Trials for the Foliar Application of Novaluron to Tomatoes in Brazil (Tornisielo, V. L., 1999. Study Nos. R-11387 and R-11388; Tornisielo, V. L., 2004. Report numbers RF-0002.034.114.04 (R-17895), R-0002.034.115.04 (R-17893); RF-0002.034.116.04 (R-17894); and RF-0002.034.117.04 (R-17892)).

Crop Location, year	Application				Interval, days	PHI, days	Residues [1]mg/kg	Reference
	Form.	kg ai/ha	kg ai/hL	No				
Tomato								
GAP Brazil:	*100 g/L EC, 0.02 kg ai/ha; 0.002 kg ai/hL, PHI of 7 days*							
Paraná, Brazil, 1999	100 g/L EC		0.002	7	7	5	< 0.01	Study Ref: R-11387
Paraná, Brazil, 1999	100 g/L EC		0.004	7	7	5	< 0.01	Study Ref: R-11387
Sao Paolo, Brazil, 1999	100 g/L EC	0.004	0.002	7	7	7 14 21 28 35	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	Study Ref: R-11388
Sao Paolo, Brazil, 1999	100 g/L EC	0.008	0.004	7	7	7 14 21 28 35	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	Study Ref: R-11388
Piedade, SP Brazil, 2004	100 g/L EC		0.002	4	7	5 7	< 0.02 < 0.02	Study Ref. RF-0002.034.114.04 R-17895
	100 g/L EC		0.004	4	7	5 7	< 0.02 < 0.02	
Jaiba, MG Brazil, 2004	100 g/L EC		0.002	4	7	5 7	< 0.02 < 0.02	Study Ref. RF-0002.034.115.04 R-17892
	100 g/L EC		0.004	4	7	5 7	< 0.02 < 0.02	
Sumare, SP Brazil, 2004	100 g/L EC		0.002	4	7	5 7	< 0.02 < 0.02	Study Ref. RF-0002.034.116.04 R-17893
	100 g/L EC		0.004	4	7	5 7	< 0.02 < 0.02	
Iracemapolis Sao Paolo, Brazil, 2004	100 g/L EC		0.002	4	7	0 1 3 5 7	< 0.02 < 0.02 < 0.02 < 0.02 < 0.02	Study Ref. RF-0002.034.117.04 R-17894

Crop Location, year	Application				Interval, days	PHI, days	Residues [1]mg/kg	Reference
	Form.	kg ai/ha	kg ai/hL	No				
	100 g/L EC		0.004	4	7	5 7	< 0.02 < 0.02	

[1] GC/EC method used where the LOQ is 0.01 mg/kg. Method recoveries ranged from 77 – 85% at a fortification of 0.009 mg/kg GC/MSD (m/z 337 and m/z 335) used where the LOQ is 0.02 mg/kg, with method recoveries ranging from 96 – 107% at a fortification of 0.02 mg/kg.

Legumes

Table 64. Supervised Field Trials for the Foliar Application of Novaluron to Soya in Brazil (Tornisielo, V. L, 2000, Study Nos. 11787 and 11788; Tornisielo, V L, 1999. Study Nos. R-11389 and 11390)

Crop Location, year	Application				Sample analyzed[1]	PHI, days	Residue mg/kg	Reference
	Form.	kg ai/ha	kg ai/hL	No				
GAP Brazil:	*100 g/L EC at the rate of 0.012 kg ai/ha or 0.01 kg ai/hL, 53-day PHI*							
R-11/00 Brazil, 1999	100 g/L EC	0.010	0.005	1	Green. Plant	15	< 0.01	Study Ref: R-11788
					Green Plant	25	< 0.01	
					Green Plant	35	< 0.01	
					Bean (immature seed)	55	< 0.01	
R-11/00 Brazil, 1999	100 g/L EC	0.015	0.008	1	Green Plant	15	< 0.01	Study Ref: R-11788
					Green Plant	25	< 0.01	
					Green Plant	35	< 0.01	
					Bean	55	< 0.01	
R-11/00 Brazil, 1999	100 g/L EC	0.020	0.010	1	Green Plant	15	< 0.01	Study Ref: R-11788
					Green Plant	25	< 0.01	
					Green Plant	35	< 0.01	
					Bean	55	< 0.01	
R-11/00 Brazil, 1999	100 g/L EC	0.030	0.015	1	Green Plant	15	< 0.01	Study Ref: R-11788
					Green Plant	25	< 0.01	
					Green Plant	35	< 0.01	
					Bean	55	< 0.01	
R-10/00 Brazil, 1999	100 g/L EC	0.010	0.005	1	Green Plant	0	< 0.01	Study Ref: R-11787
					Green Plant	7	< 0.01	
					Green Plant	15	< 0.01	
					Green Plant	25	< 0.01	
					Green Plant	35	< 0.01	
					Bean	55	< 0.01	
R-10/00 Brazil, 1999	100 g/L EC	0.015	0.008	1	Green Plant	0	< 0.01	Study Ref: R-11787
					Green Plant	7	< 0.01	
					Green Plant	15	< 0.01	
					Green Plant	25	< 0.01	
					Green Plant	35	< 0.01	
					Bean	55	< 0.01	
R-10/00 Brazil, 1999	100 g/L EC	0.020	0.010	1	Green Plant	0	< 0.01	Study Ref: R-11787
					Green Plant	7	< 0.01	
					Green Plant	15	< 0.01	
					Green Plant	25	< 0.01	
					Green Plant	35	< 0.01	
					Bean	55	< 0.01	
R-10/00 Brazil, 1999	100 g/L EC	0.030	0.015	1	Green Plant	0	< 0.01	Study Ref: R-11787
					Green Plant	7	< 0.01	
					Green Plant	15	< 0.01	

Crop Location, year	Application				Sample analyzed[1]	PHI, days	Residue mg/kg	Reference
	Form.	kg ai/ha	kg ai/hL	No				
GAP Brazil:	*100 g/L EC at the rate of 0.012 kg ai/ha or 0.01 kg ai/hL, 53-day PHI*							
					Green Plant Green Plant Bean	25 35 55	< 0.01 < 0.01 < 0.01	
R-65/99 Brazil, 1999	100 g/L EC	0.008	0.004	2	Bean Bean Bean Bean Bean Bean	53 61 68 75 82	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	Study Ref: R-11390
R-65/99 Brazil, 1999	100 g/L EC	0.015	0.008	2	Bean Bean Bean Bean Bean	53 61 68 75 82	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	Study Ref: R-11390
R-64/99 Brazil, 1999	100 g/L EC	0.008	0.004	2	Bean	66	< 0.01	Study Ref: R-11389
R-64/99 Brazil, 1999	100 g/L EC	0.015	0.008	2	Bean	66	< 0.01	Study Ref: R-11389

[1] HPLC/UV(252 nm). Fortification recoveries were 72, 73, and 74% at 0.01 mg/kg for beans and 74, 79, and 88% at 0.01 mg/kg for green plants.

Root and tuber vegetables

Table 65. Supervised Field Trials for the Foliar Application of Novaluron to Potato in Europe (France, Germany, Italy, Spain) (Farrell P, 2001. Study No. R-11617), Mexico (Paden, R. 2003. Study No. R-14247), and the USA (Willard, T R, 2003. Study No. R-15426).

Crop Location, year	Application				Interval days	PHI, days	Residues mg/kg	Reference
	Form.	kg ai/ha	kg ai/hL	No or (max)				
Potato tubers								
GAP USA:100 g/L EC at rate of 0.087 kg ai/h, 2 applications per season and a seasonal maximum of 0.17 kg ai/ha and PHI of 14 days								
Madras, Oregon, USA, 2002	100 g/L EC	0.29 0.28	0.083	2 (0.58 kg ai/ha)	14	7	< 0.05	Study Ref R-15426[1] Trial OR1
Germansville, Pennsylvania, USA, 2002	100 g/L EC	0.28 0.28	0.089	2 (0.58 kg ai/ha)	14	7	< 0.05	Study Ref R-15426 Trial OR1
GAP Switzerland: 100g/L EC at rate of 0.02 kg ai/ha, 2 applications, and a PHI of 21 days								
Baiertal, Germany, 2000	100 g/L EC	0.026	0.0043	2	14	22	< 0.01 (< 0.002)	Study Ref R-11617[2] MAK/600-01
Baiertal, Germany, 2000	100 g/L EC	0.025	0.0043	2	14	22	< 0.01 (0.0026)	Study Ref R-11617
								MAK/600-02
Mackensheim, Germany, 2000	100 g/L EC	0.027	0.0045	2	14	21	< 0.01 (< 0.002)	Study Ref R-11617 MAK/600-03
Biberach, Germany, 2000	100 g/L EC	0.027	0.0043	2	15	21	< 0.01 (< 0.002)	Study Ref R-11617 MAK/600-04
Livry-Louvercy, North France,	100 g/L EC	0.026	0.0043	2	14	21	< 0.01 (< 0.002)	Study Ref R-11617

Crop Location, year	Application				Interval days	PHI, days	Residues mg/kg	Reference
	Form.	kg ai/ha	kg ai/hL	No or (max)				
Potato tubers								
2000								MAK/600-05
Dampierre-sur-Moivre, North France, 2000	100 g/L EC	0.027	0.0046	2	14	21	< 0.01 (< 0.002)	Study Ref R-11617 MAK/600-06
Faux-Vesignuel, North France, 2000	100 g/L EC	0.026	0.0044	2	14	21	< 0.01 (< 0.002)	Study Ref R-11617 MAK/600-07
Benimamet, Spain, 2000	100 g/L EC	0.026	0.0043	2	13	21	< 0.01 (< 0.002)	Study Ref R-11617 MAK/600-08
Benimamet, Spain, 2000	100 g/L EC	0.026	0.0041	2	14	21	< 0.01 (< 0.002)	Study Ref R-11617 MAK/600-09
La Aljorra, Spain, 2000	100 g/L EC	0.027	0.0041	2	14	21	< 0.01 (0.0024)	Study Ref R-11617 MAK/600-10
Brantes, South France, 2000	100 g/L EC	0.026	0.0044	2	14	21	< 0.01 (< 0.002)	Study Ref R-11617 MAK/600-11
Montbrun-les-Bains, South France, 2000	100 g/L EC	0.027	0.0045	2	14	21	< 0.01 (< 0.002)	Study Ref R-11617 MAK/600-12
Caleppio, Italy, 2000	100 g/L EC	0.026	0.0043	2	14	21	< 0.01 (< 0.002)	Study Ref R-11617 MAK/600-13
Cremona, Italy, 2000	100 g/L EC	0.026	0.0044	2	14	21	< 0.01 (< 0.002)	Study Ref R-11617 MAK/600-14
GAP Mexico: 100 g/L EC at rate of 0.015 mg/ha, 1 application, and PHI of 30 days								
Guanajato, Mexico 2002	100 g/L EC	0.028	0.01	2	14	14	< 0.01	Study No. R-14247[3] MX0017-4010R
Sinaloa, Mexico 2002	100 g/L EC	0.027	0.01	2	14	14	< 0.01	Study No. R-14247 MX0017-4010R

[1] Determination by GC/EC, with fortification recoveries at 0.05 mg/kg of 74% and 77%.
[2] Determination by GC/EC, with fortification recoveries at 0.01 mg/kg of 73, 78, 89, and 91%. Stated limit of detection, 0.002 mg/kg.
[3]Full report provided for only the field portion of the study.

Oilseeds

Table 66. Supervised Field Trials for the Foliar Application of Novaluron to Cotton in Brazil, Mexico, South Africa, and the USA (Tornisielo, V L, 1999, Study Nos. R-11391 and 11392; (Paden, R, 2000. Study No.R-11217; Viljoen, A J, 1998; Willard, T R, 2002. Study No. 13887)

Crop Location, year	Application				Interval days	PHI, days	Residues mg/kg	Ref
	Form.	kg ai/ha	kg ai/hL	No or (max)				
Cottonseed								
GAP Brazil:	*100 g/L EC at rate of 0.01 kg ai/ha or 0.005 kg ai/hL and a PHI of 93 days*							
Paraná, Brazil 1999	100 g/L EC	0.01	0.005	2	20	62	< 0.01	R-11391[1]
Paraná, Brazil 1999	100 g/L EC	0.02	0.01	2	20	62	< 0.01	R-11391
São Paulo, Brazil, 1999	100 g/L EC	0.01	0.005	2	19	93 100 107 114 121	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	R-11392[1]
São Paulo, Brazil, 1999	100 g/L EC	0.02	0.01	2	19	93 100 107 114 121	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	R-11392
GAP Mexico: 100 g/L EC at 0.01 kg ai/ha, 2 applications, and a PHI of 30 days.								
Baja California, Mexico, 1999	100 g/L EC	0.049		2	14	30	0.11	R-11217
Chihuahua, Mexico, 1999	100 g/L EC	0.05	0.055	2	14	30	0.03	R-11217
GAP South Africa: 100 g/LEC at 0.035 kg ai/ha, 0.007 kg ai/hL ground and 0.12 kg au/hl aerial, 3 applications, no PHI specified.								
Groblebsdal, South Africa, 1999	100 g/L EC	0.1		1		71	< 0.05	R-10715[3]
Groblebsdal, South Africa, 1999	100 g/L EC	0.2		1		71	< 0.05	R-10715
GAP USA: 100 g/L EC at0.1 kg ai/ha, 0.53 kg ai/hL aerial and 0.21 kg ai/hL ground, with a maximum seasonal total of 0.3kg ai/ha and a PHI of 30 days								
Shoffner, Arkansas, USA 2001	100 g/L EC	0.059 (2x) 0.10 (3x)	0.032 (2x) 0.054 (3x)	5 (0.42)	- 14 60 7 7	30	< 0.05	R-13887[4] Trial AR1
Maricopa, Arizona, USA, 2001	100 g/L EC	0.057 (2x) 0.10 (3x)	0.021 (2x) 0.036 (3x)	5 (0.42)	- 14 84 7 7 (10% open boll)	30	< 0.05	R-13887 Trial AZ1
Porterville, California, USA, 2001	100 g/L EC	0.059 (2x)	0.020 (2x)	5 (0.42)	- 14	30	< 0.05	R-13887 Trial

Crop Location, year	Application				Interval days	PHI, days	Residues mg/kg	Ref
	Form.	kg ai/ha	kg ai/hL	No or (max)				
		0.10 (3x)	0.033 (3x)		62 7 7			
Hanford, California, USA, 2001	100 g/L EC	0.058 (2x) 0.10 (3x)	0.018 (2x) 0.031 (3x)	5 (0.42)	- 14 68 7 (30%) 7 (90% open boll)	30	<u>< 0.05</u>	R-13887 Trial CA2
Chula, Georgia, USA, 2001	100 g/L EC	0.058 (2x)	0.018 (2x)	5 (0.42)	- 14	30	<u>0.19</u>	R-13887 Trial GA1
		0.10 (3x)	0.031 (3x)		68 7 (25%) 7 (50% open boll)			
Washington, Louisiana, USA, 2001	100 g/L EC	0.059 (2x) 0.10 (3x)	0.026 (2x) 0.046 (3x)	5 (0.42)	- 14 81 7 7 (10% open boll)	29	<u>< 0.05</u>	R-13887 Trial LA1[6]
	100 g/L EC	0.29 (2x) 0.50 (3x)	0.12 (2x) 0.24 (3x)	5 (2.1)	- 14 81 7 7 (10% open boll)	29	0.06	
Greenville, Mississippi, USA, 2001	100 g/L EC	0.057 (2x)	0.030 (2x)	5 (0.42)	- 14	0	0.25	R-13887 Trial MS1
		0.10 (3x)	0.047 (3x)		81 7 (75%) 7 (90% open boll)	7	0.14	
						14 30 45	0.29 <u>0.25</u> 0.094	
Colony, Oklahoma, USA, 2001	100 g/L EC	0.059 (2x) 0.10 (3x)	0.027 (2x) 0.045 (3x)	4 (0.43)	- 13 68 (30%) 7 (50%) 7(70% open boll)	30	<u>0.060</u>	R-13887 Trial OK1
Edmonson, Texas, USA, 2001	100 g/L EC	0.059 (2x)	0.030 (2x)	4 (0.42)	- 14	30	<u>0.066</u>	R-13887 Trial

Crop Location, year	Application				Interval days	PHI, days	Residues mg/kg	Ref
	Form.	kg ai/ha	kg ai/hL	No or (max)				
		0.10 (3x)	0.050 (3x)		70 (1%) 7 (10%) 7 (25% open boll)			TX1
Levelland, Texas, USA, 2001	100 g/L EC	0.059 (2x) 0.10 (3x)	0.030 (2x) 0.052 (3x)	4 (0.42)	- 14 64 (<5%) 7 (40%) 7 (50% open boll)	30	0.22	R-13887 Trial TX2
Claude, Texas, USA, 2001	100 g/L EC	0.059 (2x) 0.10 (3x)	0.029 (2x) 0.051 (3x)	4 (0.43)	- 14 43 7 7 (?% open boll)	30	0.40	R-13887 Trial TX3
Uvalde, Texas, USA, 2001	100 g/L EC	0.058 (2x) 0.10 (3x)	0.027 (2x) 0.050 (3x)	4 (0.42)	- 14 43 7 7 (few open bolls)	29	0.10	R-13887 Trial TX4
Shoffner, Arkansas, USA, 2002 (Bridging)	100 g/L EC	0.060 (2x) 0.103 (3x)	0.029 (2x) 0.050 (3x)	5 (0.42)	- 14 44 7 7 (10% open boll)	32	0.067	R-15424[5] Trial AR1
		0.059 (1x) 0.10 (2x)	0.028 (1x) 0.050 (2x)	3 (0.26 kg ai/ha)	- 36 45 (10% open boll)	32	< 0.05	
Porterville, California, USA, 2002 (Bridging)	100 g/L EC	0.060 (2x) 0.10 (3x)	0.021 (2x) 0.036 (3x)	5 (0.42)	14 44 7 7 (open bolls present)	28	0.21	R-15424 Trial CA1

Crop Location, year	Application				Interval days	PHI, days	Residues mg/kg	Ref
	Form.	kg ai/ha	kg ai/hL	No or (max)				
		0.059 (1x) 0.10 (2x)	0.021 0.036 (2x)	3 (0.26)	- 36 45 (open bolls present)	29	< 0.05	
Chula, Georgia, USA, 2002 (Bridging)	100 g/L EC	0.059 (2x) 0.10 (3x)	0.017 0.022 0.035 0.039 0.040	5 (0.43)	- 14 44 (40%) 7 (60%) 7 (80% open boll)	30	0.069	R-15424, Trial GA1
		0.058 (1x) 0.10 (2x)	0.017 0.038 0.041	3 (0.26)	- 62 45 (80% open boll)	30	< 0.05	
Dill City, Oklahoma, USA, 2002 (Bridging)	100 g/L EC	0.058 (2x) 0.10 (3x)	0.027 (2x) 0.046 (3x)	5 (0.42)	- 14 44 7 7 (?% open boll)	34	0.34	R-15424, Trial OK1
		0.059 (1x) 0.10 (2x)	0.027 (1x) 0.046 (2x)	3 (0.26)	- 36 45 (?% open boll)	34	0.21	
Cotton Gin Trash								
GAP USA: 100 g/L EC at0.1 kg ai/ha, 0.53 kg ai/hL aerial and 0.21 kg ai/hL ground, with a maximum seasonal total of 0.3kg ai/ha and a PHI of 30 days								
Shoffner, Arkansas, USA 2001	100 g/L EC	0.059 (2x) 0.10 (3x)	0.032 (2x) 0.054 (3x)	5 (0.42)	- 14 60 7 7	30	10.	R-13887[4] Trial AR1
		0.10 (3x)	0.033 (3x)		62 7 7			
Hanford, California, USA, 2001	100 g/L EC	0.058 (2x)	0.018 (2x)	% (0.42)	- 14	30	27.	R-13887 Trial

Crop Location, year	Application				Interval days	PHI, days	Residues mg/kg	Ref
	Form.	kg ai/ha	kg ai/hL	No or (max)				
		0.10 (3x)	0.031 (3x)		68 7 (30%) 7 (90% open boll)			CA2
		0.10 (3x)	0.031 (3x)		68 7 (25%) 7 (50% open boll)			
Greenville, Mississippi, USA, 2001	100 g/L EC	0.057 (2x) 0.10 (3x)	0.030 (2x) 0.047 (3x)	4 (0.42)	- 14 81 7 (75%) 7 (90% open boll)	0 7 14 30 45	9.0 8.5 (4.87, 12.2) 3.1 4.0 1.4	R-13887 Trial MS1
Edmonson, Texas, USA, 2001	100 g/L EC	0.059 (2x) 0.10 (3x)	0.030 (2x) 0.050 (3x)	4 (0.42)	- 14 70 (1%) 7 (10%) 7 (25% open boll)	30	3.7	R-13887 Trial TX1
Levelland, Texas, USA, 2001	100 g/L EC	0.059 (2x) 0.10 (3x)	0.030 (2x) 0.052 (3x)	4 (0.42)	- 14 64 (<5%) 7 (40%) 7 (50% open boll)	30	11.	R-13887 Trial TX2
Claude, Texas, USA, 2001	100 g/L EC	0.059 (2x) 0.10 (3x)	0.029 (2x) 0.051 (3x)	4 (0.43)	- 14 43 7 7 (?% open boll)	30	6.7	R-13887 Trial TX3
Uvalde, Texas, USA, 2001	100 g/L EC	0.058 (2x)	0.027 (2x)	4 (0.42)	- 14	29	20.	R-13887 Trial TX4
		0.10 (3x)	0.050 (3x)		43 7 7 (few open bolls)			

Crop Location, year	Application				Interval days	PHI, days	Residues mg/kg	Ref
	Form.	kg ai/ha	kg ai/hL	No or (max)				
-	100 g/L EC	0.060 (2x) 0.103 (3x)	0.029 (2x) 0.050 (3x)	5 (0.42)	- 14 44 7 7 (10% open boll)	32	4.5	R-15424[5] Trial AR1
		0.059 (1x) 0.10 (2x)	0.028 (1x) 0.050 (2x)	3 (0.26 kg ai/ha)	36 45 (10% open boll)	32	1.7	
Porterville, California, USA, 2002 (Bridging)	100 g/L EC	0.060 (2x) 0.10 (3x)	0.021 (2x) 0.036 (3x)	5 (0.42)	14 44 7 7 (open bolls present)	28	17	R-15424 Trial CA1
		0.059 (1x) 0.10 (2x)	0.021 0.036 (2x)	3 (0.26)	- 36 45 (open bolls present)	29	13	
Chula, Georgia, USA, 2002 (Bridging)	100 g/L EC	0.059 (2x) 0.10 (3x)	0.017 0.022 0.035 0.039 0.040	5 (0.43)	- 14 44 (40%) 7 (60%) 7 (80% open boll)	30	5.4	R-15424, Trial GA1
		0.058 (1x) 0.10 (2x)	0.017 0.038 0.041	3 (0.26)	- 62 45 (80% open boll)	30	2.8	
Dill City, Oklahoma, USA, 2002 (Bridging)	100 g/L EC	0.058 (2x) 0.10 (3x)	0.027 (2x) 0.046 (3x)	5 (0.42)	- 14 44 7 7 (?% open boll)	34	7.3	R-15424, Trial OK1
		0.059 (1x) 0.10 (2x)	0.027 (1x) 0.046 (2x)	3 (0.26)	- 36 45 (?% open boll)	34	4.3	

[1] Determination by GC/EC. Recoveries at a fortification of 0.0106 mg/kg were 91.5, 102.8, and 87.7%.

[2] Determination by GC/EC (MAK571). Stated limits of determination and detection were 0.01 m/kg and 0.004 mg/kg, respectively.
[3] Only very summary information supplied, with no detail of field portion or analytical phase.
[4] Determination by HPLC/UV. Recoveries of a fortification of cotton seed (undelinted) at 0.05 mg/kg were 92% and 92%. Recoveries of a fortification of cotton gin trash at 0.5 mg/kg were 94% and 99%, and at 0.1 mg/kg 86% and 104%.
[5] Determination by GC/EC. Recoveries of a fortification of cotton seed (undelinted) at 0.05 mg/kg were 96.8% and 74.4%. Recoveries of a fortification of cotton gin trash at 0.05 mg/kg were 66.0% and 44.2% and at 25 mg/kg, 88.8% and 92.4%.
[6] Undelinted cotton seed from this trial was used for a processing study (see below).

FATE OF RESIDUES IN STORAGE AND IN PROCESSING

In storage

No information was received on the fate of novaluron on food commodities stored under commercial conditions.

In processing

The Meeting received reports on the fate of incurred residues of novaluron during the processing of apples and cotton seed. A processing study was conducted on apples from a supervised field trial conducted in Ephrata, Washington State, USA, in 2002. (Willard T R, 2002. Study No. R-13886). The samples were collected from trees treated 6 times with a WG formulation containing 65 g/kg novaluron, at the nominal rate of 0.38 kg ai/ha, with retreatment intervals of 7, 7, 97, 7, and 7 days. Mature fruits were collected 14 days after the last application and sent to the processing laboratory on the day of sampling and kept frozen until processing.

Samples were processed according to simulated commercial procedures within 5 days of harvest into juice and wet pomace. Prior to processing, a representative unwashed sample of apple was removed and reserved as a RAC sample in frozen storage. The remaining apples were washed, crushed to apple pulp in a hammer mill, and transferred to a steam-jacket kettle. The pulp was heated (40–50ºC), treated with enzyme, transferred to a plastic tub, and allowed to sit for about 2 hours. The enzyme-treated pulp was pressed twice using a fruit press to obtain fresh juice and wet pomace. The fresh juice sample was filtered, and the wet pomace sample was analyzed for moisture content (the results of this moisture content analysis were not reported).

Residues of novaluron were determined by GC/ECD. The method was validated for apple juice (75%, 80%, and 89% recoveries from 0.05 mg/kg fortifications) and apple pomace (71%, 99%, and 97% recoveries from 0.05 mg/kg fortifications). The results are summarized in Table 67.

Table 67. Processing Factors for Apple Processed Fractions (Willard T R, 2002. Study No. R-13886).

Fraction	Residues mg/kg	Processing Factors	Reference
Apple fruit (RAC)	0.40	-	R-13886
Apple juice	< 0.05	0.1	
Apple wet pomace[1]	2.9	7.2	

[1] Percentage of water content was not reported.

A *cottonseed processing study* was conducted in the United States from samples harvested from plants treated with five applications of a 10EC formulation of novaluron at a total application of 0.42 kg ai/ha, or about 1.4× the seasonal label rate and from samples harvested from plants treated with five applications at a total application of 2.1 kg ai/ha (Willard, T R, 2002. Study No. R-13887). Cotton samples (about 70kg each treatment) were harvested 29 days after the final application and shipped to a processing facility.

Undelinted cottonseed was processed into meal, hulls, and refined oil within 13 –15 days of harvest using simulated commercial processing procedures. Burrs, sticks, and other plant parts (gin byproducts) were removed using a Mitchell stick extractor; a sample of undelinted (ginned) cottonseed was collected and frozen at this point. The remaining lint cotton was saw-ginned to

remove the majority of the lint, then mechanically cracked and screened to separate hulls from the kernel. The kernel material with some hull material was heated to 79 – 90°C for 30 minutes and then flaked. The flaked material was fed into an expander/extruder, injecting steam directly on the product. The material exiting from the expander (collets) was dried in an oven at 65 - 82°C for 30 – 40 minutes, ground in a mill, and subjected to solvent extraction. The collets were extracted with hexane several times, and the solvent removed. Warm air was passed through the extracted collets to remove residual solvent, and a sample of cotton meal was collected from the collets. The hexane extract mixture (miscella) was evaporated (vacuum evaporator, 73 – 90°C) to remove the hexane, yielding crude cotton seed oil. The crude oil was then mixed with sodium hydroxide and heated to produce refined oil and soapstock.

Residues of novaluron were determined in cottonseed and cotton processed fractions by HPLC with UV detector, following the method described in Method No. STM CR60, R-10587 (see above). Laboratory procedural recoveries were as follow: 92% for cottonseed fortified at 0.05 to 0.6 mg/kg; 73% for cotton meal; 94% for hulls; and 81% for refined oil, each fortified at 0.05 mg/kg. Results are summarized in Table 68.

Table 68. Processing Factors for Cottonseed Processed Fractions (Willard, T R, 2002. Study No. R-13887)

Processed Fraction	Residues mg/kg	Processing Factors	Reference
Undelinted seed (0.42 kg ai/ha)	0.081[1]	-	R-13887
Meal	< 0.05	0.6	
Hulls	< 0.05	0.6	
Refined oil	< 0.05	0.6	
Undelinted seed (2.1 kg ai/ha)	< 0.05[2]		R-13887
Meal	< 0.05	-	
Hull	< 0.05	-	
Refined oil	< 0.05	-	

[1] Concentrations for field samples were reported as < 0.05, < 0.05 mg/kg. The 0.081 mg/kg value is from a sub sample of the material processed.
[2] Concentrations for field samples were reported as < 0.05, 0.061 mg/kg. The < 0.05 mg/kg value is from a sub sample of the material processed.

RESIDUES IN ANIMAL COMMODITIES

Direct animal treatments

No direct animal treatment uses were reported.

Farm animal feeding studies

In feeding a study conducted in 2000, novaluron (purity > 99.5%) was administered to lactating Friesian cows (*Bos taurus*; 547-724 kg) (Redgrave, V A, 2000. Study No. R-10993). Three or six animals were assigned to groups 1 to 5, which were dosed at 0 (control), 7, 53, 159 or 530 mg ai./cow/day, respectively. Dose levels based on feed were not provided, but the recorded daily consumptions (by group) of hay and ration concentrate may be used to calculate such levels. Using the average hay consumption over 42 treatment days for the control group, 14 ± 3 kg/cow/day (16 kg/cow/day dry matter basis), and the concentrate consumption, 4 kg (total provided)/cow/day, the daily intake is estimated as 20 kg/cow/day. The dose groups thus correspond to 0, 0.35, 2.6, 8.0, and 26 ppm concentrations of novaluron in the feed. Doses were split and administered twice daily via corn oil, mixed with dry ration. Food was supplemented with untreated hay. All animals were dosed for 42, 43, or 44 consecutive days. Whole milk samples were taken from all animals daily throughout

the dosing period. Additional samples were taken after 14, 28 and 42 days and separated into cream and skimmed milk.

All cows (three per group) in groups 1, 2, and 4 and three of the six cows in each of groups 3 and 5 were sacrificed within 16 – 24 hours of the final dose. Animals in groups 3 and 5 were sacrificed after increasing withdrawal periods of up to 35 days after the final dose. Samples of subcutaneous and peritoneal fat, muscle, liver and kidneys were then taken from each animal.

Daily milk samples (a.m. and p.m.) were composited for each cow. Subsamples of Day 14, 28, and 42 milk from each dose group cow were separated into cream and skimmed milk by using a commercial cream separator. Tissue samples were washed with water, coarsely chopped, mixed, and frozen, after which they were homogenized with dry ice.

The fat content of whole milk and cream samples was determined using the Gerber (butyrometer) Method. The fat content ranged 2.0-3.4% in whole milk and 40-52% in cream, and was consistent throughout the dosing period.

A GC/EC method was used to analyze the milk and tissues. Homogenized tissue samples (fat, muscle, kidney, and liver) were extracted twice with methanol and centrifuged to separate the phases. Milk samples were extracted with methanol and then acetonitrile (ACN) with trasonication and then centrifuged to separate the phases; the methanol and ACN extracts were combined. Cream samples were extracted twice with ACN and then centrifuged to separate the phases. Milk, cream, and tissue extracts were concentrated to aqueous by rotary evaporation, and repeatedly partitioned with hexane. The resulting hexane fractions were combined and concentrated to a low volume by rotary evaporation. For tissue and cream samples, residues were cleaned up by chromatography through a NH_2-SPE cartridge; residues were eluted with acetone:hexane (50:50, v:v). The eluate was evaporated to dryness under a stream of nitrogen. For all samples, residues were redissolved in hexane and determined by GC/ECD.

The stated limits of detection are 0.002 mg/kg in cream and 0.04 mg/kg in milk and tissues. The method was validated during this study for cream fortified at 0.01 mg/kg novaluron, with recoveries of 71%, 73%, and 76%. See also Table 47, Report MAK 454/972535. Concurrent method recoveries were acceptable for all commodities at a fortification of 0.1 mg/kg.

The storage intervals from collection to analysis were not stated, and no storage stability information was provided for the various ruminant commodities. However, the Relevant Study Dates provided under GLP indicates that all experimental work was completed with 53 days of the first sacrifice.

Findings for the individual cows at the various dosing concentrations are summarized in Table 69.

Table 69. Residue Data from Ruminant Feeding Study with Novaluron (Redgrave, V A, 2000. Study No. R-10993)

Matrix/Collection Time		Novaluron Residues (mg/kg)			
		Cow 1	Cow 2	Cow 3	Average
Dosing Level: 7 mg ai/day, or about 0.35 ppm in feed					
Whole Milk	Day 3	*(0.0079)*	(*0.0082)*	*(0.0091*)	< 0.01
	Day 7	0.01	0.02	0.01	0.01
	Day 10	0.02	0.02	0.02	0.02
	Day 14	0.02	0.03	0.02	0.02
	Day 18	0.03	0.03	0.03	0.03

Matrix/Collection Time		Novaluron Residues (mg/kg)			
		Cow 1	Cow 2	Cow 3	Average
	Day 21	0.02	0.04	0.04	0.03
	Day 25	0.02	0.04	0.04	0.03
	Day 28	0.03	0.04	0.03	0.03
	Day 32	0.03	0.05	0.04	0.04
	Day 36	0.03	0.06	0.05	0.05
	Day 39	0.05	0.05	0.05	0.05
	Day 42	0.03	0.05	0.03	0.04
Cream	Day 14	0.59	0.82	0.64	0.68
	Day 28	0.63	0.87	1.00	0.83
	Day 42	0.66	1.12	1.03	0.94
Skimmed Milk	Day 14	ND	*(0.0052)*	ND	< 0.01
	Day 28	ND	ND	ND	< 0.01
	Day 42	*(0.0042)*	ND	*(0.0072)*	< 0.01
Muscle		0.03	0.04	0.05	0.04
Kidney		0.05	0.06	0.04	0.05
Liver		0.04	0.05	0.05	0.05
Subcutaneous Fat		0.27	0.43	0.21	0.30
Peritoneal Fat		0.30	0.56	0.49	0.45
Dosing Level: 53 mg ai/day, or about 2.6 ppm in feed					
Whole Milk	Day 1	ND	ND	ND	< 0.01
	Day 3	0.04	0.04	0.03	0.04
	Day 5	0.07	0.05	0.02	0.05
	Day 7	0.06	0.06	0.06	0.06
	Day 10	0.08	0.07	0.06	0.07
	Day 12	0.11	0.08	0.07	0.09
	Day 14	0.07	0.05	0.06	0.06
	Day 18	0.10	0.08	0.09	0.09
	Day 21	0.12	0.08	0.07	0.09
	Day 23	0.13	0.12	0.11	0.12
	Day 25	0.11	0.11	0.10	0.11
	Day 28	0.12	0.08	0.09	0.10
	Day 32	0.14	0.10	0.12	0.12
	Day 36	0.12	0.13	0.17	0.14
	Day 39	0.12	0.15	0.12	0.13
	Day 42	0.15	0.14	0.10	0.13
Cream	Day 14	2.03	1.91	1.72	1.89
	Day 28	2.53	2.58	2.45	2.52
	Day 42	2.72	3.06	2.62	2.80
Skimmed Milk	Day 14	0.01	*(0.0086)*	*(0.0067)*	< 0.01

Matrix/Collection Time		Novaluron Residues (mg/kg)			
		Cow 1	Cow 2	Cow 3	Average
	Day 28	*(0.0088)*	0.02	ND	< 0.01
	Day 42	*(0.0083)*	0.02	*(0.0092)*	< 0.01
Muscle		0.07	0.09	0.08	0.08
Kidney		0.13	0.11	0.14	0.13
Liver		0.14	0.12	0.13	0.13
Subcutaneous Fat		1.24	0.61	1.22	1.02
Peritoneal Fat		1.72	2.25	1.23	1.73
Dosing level : 159 mg ai/day, or about 8.0 ppm in feed					
Whole Milk	Day 3	0.08	0.08	0.08	0.08
	Day 7	0.26	0.12	0.14	0.17
	Day 10	0.34	0.16	0.14	0.21
	Day 14	0.35	0.15	0.15	0.22
	Day 18	0.33	0.33	0.22	0.29
	Day 21	0.35	0.33	0.26	0.31
	Day 25	0.39	0.39	0.26	0.35
	Day 28	0.40	0.35	0.37	0.37
	Day 32	0.41	0.34	0.32	0.36
	Day 36	0.40	0.37	0.24	0.34
	Day 39	0.43	0.42	0.34	0.40
	Day 42	0.42	0.41	0.32	0.38
Cream	Day 14	7.66	3.94	1.80	4.5
	Day 28	6.34	6.19	4.58	5.7
	Day 42	7.09	6.79	5.91	6.6
Skimmed Milk	Day 14	0.03	0.01	0.02	0.02
	Day 28	0.02	0.04	0.02	0.03
	Day 42	0.02	0.04	0.02	0.03
Muscle		0.21	0.17	0.34	0.24
Kidney		0.31	0.35	0.33	0.33
Liver/		0.17	0.41	0.36	0.31
Subcutaneous Fat		3.52	2.80	4.36	3.6
Peritoneal Fat		4.57	4.32	6.83	5.2
Dosing level : 530 mg ai/day, about 26 ppm in feed					
Whole Milk	Day 1	ND	ND	ND	< 0.01
	Day 3	0.20	0.28	0.29	0.26
	Day 5	0.48	0.57	0.53	0.53
	Day 7	0.55	0.62	0.41	0.53
	Day 10	0.63	0.71	0.47	0.60
	Day 12	0.77	0.91	0.71	0.80
	Day 14	0.85	1.29	0.75	0.96

Matrix/Collection Time		Novaluron Residues (mg/kg)			
		Cow 1	Cow 2	Cow 3	Average
Day 18		0.89	1.54	0.86	1.1
Day 21		1.14	1.44	0.84	1.1
Day 23		0.83	0.92	0.83	0.86
Day 25		1.06	1.49	0.86	1.1
Day 28		1.38	1.52	0.96	1.3
Day 32		1.53	1.85	0.96	1.4
Day 36		1.31	1.71	0.90	1.3
Day 39		1.58	1.69	1.45	1.6
Day 42		1.60	2.07	1.46	1.7
Cream	Day 14	13.31	19.73	12.56	15.
Day 28		19.49	20.90	13.02	18.
Day 42		16.61	12.64	11.41	14.
Skimmed Milk	Day 14	0.04	0.10	0.05	0.06
Day 28		0.12	0.07	0.11	0.10
Day 42		0.14	0.09	0.13	0.12
Muscle		0.52	0.53	0.56	0.54
Kidney		1.20	1.17	0.89	1.1
Liver		1.36	1.17	1.31	1.3
Subcutaneous Fat		8.21	4.07	5.45	5.9
Peritoneal Fat		10.30	11.35	12.89	12.

Table 70. Summary of Residue Data from Ruminant (Lactating Cattle) Feeding Study with Novaluron (Redgrave, V A, 2000. Study No. R-10993**).**

Matrix	Feeding Level (ppm in feed)	Residue Levels (mg/kg)					
		N	Min	Max	Highest daily average	Mean	Std. dev.
Whole milk	0.35	36	< 0.01	0.06	0.05	0.031	0.014
	3.6	48	< 0.01	0.17	0.14	0.087	0.040
	8	36	0.08	0.43	0.40	0.29	0.11
	26	48	< 0.01	2.1	1.7	0.95	0.51
Cream	0.35	9	0.59	1.1	0.94	0.82	0.20
	3.6	9	1.7	3.1	2.8	2.4	0.43
	8	9	1.8	7.7	6.6	5.6	1.8
	26	9	11.	21.	18.	16.	3.7
Skimmed milk	0.35	9	< 0.01	< 0.01	< 0.01	0.005	0.001
	3.6	9	< 0.01	0.02	< 0.01	0.011	0.006
	8	9	0.01	0.04	0.03	0.024	0.010
	26	9	0.04	0.14	0.12	0.094	0.035
Muscle	0.35	3	0.03	0.05		0.04	0.01

Matrix	Feeding Level (ppm in feed)	Residue Levels (mg/kg)					
		N	Min	Max	Highest daily average	Mean	Std. dev.
	3.6	3	0.07	0.09		0.08	0.01
	8	3	0.17	0.34		0.24	0.09
	26	3	0.52	0.56		0.54	0.02
Kidney	0.35	3	0.04	0.06		0.05	0.01
	3.6	3	0.11	0.14		0.13	0.02
	8	3	0.31	0.35		0.33	0.02
	26	3	0.89	1.20		1.09	0.17
Liver	0.35	3	0.04	0.05		0.05	0.01
	3.6	3	0.12	0.14		0.13	0.01
	8	3	0.17	0.41		0.31	0.13
	26	3	1.2	1.4		1.3	0.10
Subcutaneous Fat	0.35	3	0.21	0.43		0.30	0.11
	3.6	3	0.61	1.2		1.0	0.36
	8	3	2.8	4.4		3.6	0.78
	26	3	4.1	8.2		5.9	2.1
Peritoneal Fat	0.35	3	0.30	0.56		0.45	0.13
	3.6	3	1.2	2.2		1.7	0.51
	8	3	4.3	6.8		5.2	1.4
	26	3	10.	13.		12.	1.3

The results from the depuration study are summarized in Table 71.

Table 71. Summary of Residues of Novaluron in Milk and Tissues of Dairy Cows from the Depuration Study (Redgrave, V A, 2000. Study No. R-10993)

Matrix/Collection Time		Pre-Slaughter Interval (days)	Novaluron Residues (ppm) [1]			
			Cow 4	Cow 5	Cow 6	Average
Feeding Level : 2.6 ppm (in feed)						
Whole Milk	Day 42	0	0.15	0.15	0.14	0.15
	Day 46	4	0.11	0.01	0.09	0.07
	Day 50	8	0.08	0.07	0.06	0.07
	Day 53	11	--	0.07	0.08	0.08
	Day 57	15	--	0.05	0.06	0.06
	Day 60	18	--	--	0.04	0.04
	Day 64	22	--	--	0.04	0.04
	Day 67	25	--	--	0.03	0.03
	Day 71	29	--	--	0.07	0.07
	Day 74	32	--	--	0.04	0.04
	Day 78	36	--	--	0.04	0.04

Matrix/Collection Time		Pre-Slaughter Interval (days)	Novaluron Residues (ppm) [1]			
			Cow 4	Cow 5	Cow 6	Average
Muscle/ sacrifice	Day 50	8	0.06	--	--	0.06
	Day 57	15	--	0.02	--	0.02
	Day 78	36	--	--	0.04	0.04
Kidney/ sacrifice	Day 50	8	0.14	--	--	0.14
	Day 57	15	--	0.05	--	0.05
	Day 78	36	--	--	0.06	0.06
Liver/ sacrifice	Day 50	8	0.12	--	--	0.12
	Day 57	15	--	0.08	--	0.08
	Day 78	36	--	--	0.06	0.06
Subcutaneous Fat/ sacrifice	Day 50	8	1.08	--	--	1.08
	Day 57	15	--	0.22	--	0.22
	Day 78	36	--	--	0.72	0.72
Peritoneal Fat/ sacrifice	Day 50	8	1.5	--	--	1.46
	Day 57	15	--	0.73	--	0.73
	Day 78	36	--	--	0.83	0.83
Feeding Level: 26 ppm (in feed)						
Whole Milk	Day 42	N/A	1.7	1.4	1.6	1.6
	Day 46	4	0.65	0.76	1.03	0.81
	Day 50	8	0.40	0.71	0.86	0.66
	Day 53	11	--	0.71	0.85	0.78
	Day 57	15	--	0.37	0.61	0.49
	Day 60	18	--	--	0.57	0.57
	Day 64	22	--	--	0.43	0.43
	Day 67	25	--	--	0.36	0.36
	Day 71	29	--	--	0.31	0.31
	Day 74	32	--	--	0.25	0.25
	Day 78	36	--	--	0.21	0.21
Muscle/ sacrifice	Day 50	8	0.30	--	--	0.30
	Day 57	15	--	0.48	--	0.48
	Day 78	36	--	--	0.07	0.07
Kidney/ sacrifice	Day 50	8	0.88	--	--	0.88
	Day 57	15	--	0.41	--	0.41
	Day 78	36	--	--	0.32	0.32
Liver/ sacrifice	Day 50	8	0.75	--	--	0.75
	Day 57	15	--	0.51	--	0.51
	Day 78	36	--	--	0.24	0.24
Subcutaneous Fat/ sacrifice	Day 50	8	0.63	--	--	0.63
	Day 57	15	--	6.3	--	6.3
	Day 78	36	--	--	1.3	1.3

Matrix/Collection Time		Pre-Slaughter Interval (days)	Novaluron Residues (ppm) [1]			
			Cow 4	Cow 5	Cow 6	Average
Peritoneal Fat/ sacrifice	Day 50	8	4.0	--	--	4.0
	Day 57	15	--	8.6	--	8.6
	Day 78	36	--	--	2.0	2.0

As a sequel to the dairy cattle feeding study, a beef cattle study was undertaken to obtain a comparison of the depuration in the muscle and fat of dairy cattle and in dairy cattle (Redgrave, 2002, Report MAK 609/004000, R-10994). Calves (16 total, in groups of 4, 236 – 290 kg) were orally dosed with novaluron at a level equivalent to approximately 5 ppm in the feed for 28 days. Sacrifice occurred within 24 hours of the final dose administration and after depuration periods of 7, 14, 42, and 77 days. The calves were gaining weight at an average of 1.4 kg/day over the treatment period. Residue data are summarized in Table 72.

Table 72. Maximum concentration of novaluron residues in tissues of beef cattle following dosing at the equivalent of 5 ppm in the feed for 28 days (Redgrave, 2002.Report MAK 609/004000, R-10994)

Days after withdrawal	Days after first administration	Muscle	Kidney	Liver	Fat[1]
0	28	0.13	0.48	0.31	3.2
7	35	0.11	0.30	0.18	2.3
14	42	0.06	0.27	0.15	1.6
42	70	0.06	0.11	0.06	0.82
77	105	0.02	0.07	0.04	0.45

[1] Subcutaneous and peritoneal pooled.

Using an extended exponential curve fit, the DT50 was estimated as 23 days for muscle (9 - 37 days at 95% CI) and 16 days for fat (3 - 29 days at the 95% CI).

A poultry feeding study was not provided.

APPRAISAL

Novaluron, or (±)-1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxy ethoxy) phenyl]-3-(2,6-difluorobenzoyl)urea, is an insect growth regulator. Novaluron inhibits chitin synthesis, affecting the moulting stages of insect development. It acts by ingestion and contact and causes abnormal endocuticular deposition and abortive moulting. It is being evaluated for the first time by the 2005 JMPR.

Animal metabolism

The metabolism of novaluron uniformly radiolabeled in the difluorphenyl ring and separately in the chlorophenyl ring was studied in goats and chickens. *Lactating goats* were dosed with the radiolabled compounds at rates equivalent to 11 – 12 ppm in the feed for five consecutive days. Most of the radioactivity was eliminated in the faeces, 52% of the administered dose for the [difluorophenyl-^{14}C(U)]-novaluron and 72% for the [chlorophenyl-^{14}C(U)]- novaluron. The Total Radioactive Residue (TRR) did not reach a plateau in milk during the five days, with the final concentration being 0.23 – 0.24 mg/kg. TRR concentrations in the tissues resulting from administration of the two radiolabelled compounds were similar: peritoneal fat, 1.4 – 1.9 mg/kg; kidney, 0.14–0.16 mg/kg; liver, 0.34 – 0.43 mg/kg, muscle, 0.09 – 0.16 mg/kg. Methanol extraction released 80 100% of the TRR from the various tissues, and greater than 90% of the TRR was extracted from milk with hexane/methanol.

Novaluron was the only residue identified in milk (93-95% TRR), peritoneal fat (96- 100% TRR), and foreleg muscle (98% TRR). It was the major component in kidney (73–83% TRR) and liver (80–84% TRR). The metabolite 2,6-difluorobenzoic acid was found in kidney (5.1% TRR), and

1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoro methoxyethoxy)phenyl]urea was identified in liver, at 7.3% TRR (0.025 mg/kg). In faeces, 3-chloro-4-(1,1,2-trifluoro-2-trifluoro methoxyethoxy)aniline was tentatively identified. Very little degradation of the parent novaluron occurred, and the metabolites found are consistent with cleavage at the benzoyl – urea linkage.

Even less metabolism/degradation of novaluron was observed in poultry. [Difluorophenyl] ^{14}C-Novaluron was administered orally to five laying hens for fourteen consecutive days at a nominal rate of 10 ppm in the diet. The TRR concentrations were as follows: liver, 0.39 mg/kg; kidney, 0.39 mg/kg; muscle, 0.061 – 0.30 mg/kg; fat, 3.6 mg/kg; eggs (day 14), 0.50 mg/kg. Novaluron was the only TRR component detected and identified, accounting for 90 – 107% of the TRR.

The results of the ruminant metabolism studies compare favourably to those of a rat metabolism study. The ruminant metabolites 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl] urea and 3-chloro-4-(1,1,2-trifluoro-2-trifluoro methoxyethoxy) aniline were also found in the rat. Additionally, 2,6-difluorobenzamide was found in rat kidney (7% TRR).

The Meeting concluded that novaluron undergoes only minor metabolism in goats and hens, and that the limited metabolism is consistent with a cleavage of the benzoyl urea bond.

Plant metabolism

The metabolism of difluorophenyl-^{14}C- or chlorophenyl-^{14}C-novaluron in apples, cabbages, potatoes, and cotton following foliar application(s) was reported to the Meeting. Novaluron, radiolabelled in either the [chlorophenyl-^{14}C(U)] or [difluorophenyl-^{14}C(U)] ring was formulated as a 10% EC and sprayed onto trees growing in outdoor pots in a netted tunnel. Either 2 (4 trees per radiolabelled form) or 3 applications (2 trees per radiolabelled form) were made to trees at a rate of 2.5–2.7 mg/tree/application. The applications were made 110 days, 90 days, and 60 days (3 applications only) before harvest. Novaluron comprised > 90% TRR in all fruit samples from all applications and sampling intervals. No metabolite (HPLC) comprised more than 1% (< 0. 01 mg/kg) of the TRR.

Novaluron, radiolabelled in either the [chlorophenyl-^{14}C(U)] or difluorophenyl-^{14}C(U)] ring was prepared as a 10% EC formulation and sprayed onto two groups of cabbage plants growing in outdoor pots. Two applications (either, 8 and 6 weeks before harvest or 5 and 2 weeks before harvest) were made to replicate a rate of 30–45 g ai/ha. Residues (TRR) were 0.23 – 0.35 for the 6 week PHI application and 0.32 – 0.45 mg/kg for the 2 week PHI application. An acetonitrile wash removed 81 – 90% of the TRR at final harvest. Acetonitrile/water extraction released an additional 9 – 15% TRR, the majority of which was on the outer cabbage leaves. About 96 – 100% of the TRR on cabbage heads at final harvest (and at earlier harvest intervals) was identified as novaluron.

Novaluron, radiolabelled in either the [chlorophenyl-^{14}C(U)] or [difluorophenyl-^{14}C(U)] ring was prepared as a 10% EC formulation and sprayed onto potato plants growing in outdoor field plots. Two applications (43 and 29 days before harvest) were made to replicate plants at a rate of 91-100 g ai/ha. Whole plant samples were taken after each application and also at 22, 10 and 0 days before harvest. For both radiolabels, the TRR on tubers at all intervals was < 0.001 mg/kg. At harvest (29 days after the second application) the TRR on plants was 9.9 mg/kg for the [difluorophenyl-^{14}C(U)] and 5.9 mg/kg for the [chlorophenyl-^{14}C(U)] novaluron. An acetonitrile wash removed 82% of the TRR, and an acetonitrile/water extraction released an additional 17% TRR. Novaluron comprised 97% of the TRR for both labelled compounds. An unknown (1.3% TRR, 0.074 mg/kg) was found with the [chlorophenyl-^{14}C(U)] novaluron.

Cotton plants grown outdoors were treated with [chlorophenyl-^{14}C] novaluron or [difluorophenyl-^{14}C] novaluron at an application rate equivalent to 50 g ai/ha/treatment. Two treatment regimes were used; Regime 1 consisted of two applications, 14 days apart with a 90 day PHI and Regime 2 consisted of two applications 14 days apart with a 30 day PHI. Samples from plants treated according to Regime 1 were taken for analysis after each application and at 60 and 30

days before the normal harvest. The maximum TRR on undelinted seed (for both treatment regimes) was 0.005 mg/kg, and no isolation and characterization of the residue was attempted. The TRR on cotton gin trash at harvest ranged from 0.27 mg/kg (90 day PHI) to 0.85 mg/kg (30 day PHI). Acetonitrile extraction released 91 – 97% TRR from the various final harvest gin trashes. Novaluron constituted 88 – 95% TRR. Total unidentified components in the extracts were < 4% TRR (< 0.012 mg/kg)

The Meeting concluded that novaluron is stable when used as a foliar spray on various food crop plants. There is no appreciable metabolism or degradation under typical GAP conditions.

Environmental fate

Novaluron is stable in water at pH 5 and pH 7. At pH 9 (25°C), however, novaluron degraded with a first-order DT_{50} of about 100 days. At 50 and 70 °C, first order DT_{50}s were 1.2 and 0.09 days, respectively (pH 9). Major metabolites exceeding 10% of applied radioactivity were identified as the chlorophenyl ring urea (1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]urea) and 2,6-difluorobenzoic acid. These degradates are also the metabolites observed in livestock metabolism.

In a confined rotational crop study, six containers of soil were treated with chlorophenyl-^{14}C(U)]-novaluron at a rate of 100 g ai/ha (approximately 3.5 mg ai/container). Rotational crops of spinach, turnips, and spring wheat were planted into separate containers (one container per crop at each plantback interval of 30 and 120 days). Crop and soil samples were taken at times after sowing that was representative of immature harvest, early harvest, and final harvest. At the 30 day plantback interval, all crops contained only very low levels of TRR, 0.001 – 0.004 mg/kg. Soil samples were extracted and analysed. Novaluron declined from 98 – 99% of the TRR on the day of application to 32 – 49% TRR at final harvest (127 – 195 days after application). Degradates identified in soil at final harvest were 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]urea (10–14% TRR) and 3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)aniline (21 – 30% TRR).

The Meeting concluded that the accumulation of novaluron, or its degradates, in rotational crops from use on primary crops, under typical GAP conditions, is unlikely.

Methods of analysis

The Meeting concluded that adequate analytical methods exist both for the monitoring/enforcement of MRLs and for data gathering in supervised field trials and processing studies. Two methods were developed and validated for the determination of novaluron in plant and animal commodities.

A gas chromatography (GC) method with electron capture detection (ECD) may be used for various plant commodities (apple, cabbage, potato, apple processed commodities, broccoli, tomato, orange processed commodities) and animal commodities (fat, kidney, liver, muscle, milk, egg). Homogenized samples are extracted into aqueous methanol and portioned with hexane. The hexane extract is purified with a solid phase extraction cartridge prior to GC determination. A variation of the method uses a mass selective detector (MSD; ions m/z 337 and m/z 335). The method and its variations have been validated at 0.01 or 0.05 mg/kg for plant commodities and at 0.01 mg/kg for animal commodities.

The GC method was radiovalidated for animal commodities (but not for plant commodities). Samples of liver, fat (mesenteric/abdominal), and thigh muscle and eggs (final day sample only) from the nature of the residue in poultry study (see above) were extracted and analysed according to the GC method. To radiovalidate this method, samples of extracts were radioassayed by LSC and the final post-SPE samples were analysed by TLC with radiodetection. Both methods of analysis gave similar results, with the GC method giving 110 – 120% of the recovery and detection of the metabolism results.

A high performance liquid chromatography (HPLC reverse phase) with ultraviolet detection (UV, 252 nm or 264 nm) method may be used for various plant commodities (apple, pear, peach, maize forage, soya plant and seeds, undelinted cotton seed, cotton foliage, tomato, potato). The method was validated at 0.01 or 0.05 mg/kg. A macerated sample is extracted with acetone and methylene chloride, and the organic layer is exchanged to acetonitrile. A gel permeation step may be used for high oil/fat content samples (e.g., cotton seed). The acetonitrile is extracted with hexane, and the residual acetonitrile extract is purified sequentially on Florisil and silica/Rumsil.

A variation of the HPLC method with tandem mass spectrometer detection (MS/MS) may be used for plant and animal matrices. Matrices are extracted with methanol/water and cleaned-up with hexane extraction and SPE. Analysis is by LC-MS/MS in the negative electrospray ionization mode. Novaluron m/z 491 > 471 is monitored. The method was validated at 0.05 mg/kg for apples and at 0.01 mg/kg for potatoes. An independent laboratory validation showed adequate recoveries of novaluron from milk, muscle, and liver at 0.02, 0.02, and 0.05 mg/kg respectively. Recovery from fat in another study was acceptable at a 0.1 mg/kg fortification

Stability of pesticide residues in stored analytical samples

The stability of novaluron in plant commodities under frozen storage conditions (-18^{o}C) for periods of at least 3 to 12 months was demonstrated. The periods of stability adequately cover the storage intervals for all supervised field trials reported. The following minimum intervals of frozen storage stability were determined: apple, 12 months; pear fruit, 158 days; apple juice, 99 days; potato, 12 months; undelinted cotton seed, 160 days; broccoli, 6 months; tomato, 12 months; orange processed fractions, 8 months.

No storage stability data was presented for animal products. The information in the livestock feeding study indicates that all analyses were completed within 53 days of the first sacrifice. The metabolism studies in ruminants and poultry indicate very little metabolism or degradation of novaluron occurs. The Meeting concluded that the relatively short interval of frozen storage (< 53 days) of the animal feeding study commodities should not have resulted in loss of novaluron residues.

Definition of the residue

The results of the radiolabeled novaluron plant metabolism studies on apple, cabbage, cotton, and potato indicate that novaluron does not metabolize or degrade under typical foliar application conditions. Greater than 90% of the TRR is recovered as novaluron, and no significant metabolites/degradates are found.

In ruminants, orally administered radiolabled novaluron (equivalent to 11 – 12 ppm in the diet) undergoes limited metabolism to 2,6-difluorobenzoic acid and 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoro methoxyethoxy)phenyl]urea, each < 10% TRR. The major component of the TRR was novaluron, ≥ 93% TRR in milk, fat, and muscle and ≥ 73% TRR in liver and kidney. In poultry orally administered novaluron (equivalent to 10 ppm in the diet) for 14 days, virtually no metabolism/degradation of novaluron occurred.

The log of the octanol/water partition coefficient, 4.3, suggests a preferential solubility in fat. In both ruminants and poultry, novaluron accumulated preferentially in fat as opposed to muscle (12 – 16:1 for ruminant; 12:1 for poultry).

The analytical methods determine only novaluron.

The Meeting noted that the residue definition in Australia and in the United States for monitoring/enforcement and for risk assessment purposes is novaluron.

Given the results of the metabolism studies and the capability of the analytical methods, the Meeting concluded that the residue definition for both enforcement and dietary intake considerations

for both plant and animal commodities is novaluron. The Meeting also decided that novaluron is fat-soluble.

Results of supervised trials on crops

Supervised trials were presented for the foliar treatment of a variety of crops worldwide.

Apple and Pear

Trials on apples were conducted in Chile (GAP of foliar applications using a 100 g/L EC formulation at a rate of 0.07 kg ai/hL and a PHI of 14 days), USA and Canada (GAP foliar applications, at a rate of 0.37 kg ai/ha using a 75 g/kg WG formulation and a PHI of 14 days). The number of applications was not specified. One trial was not within 30% of GAP (0.005 kg ai/hL and 11 day PHI) with a residue of 0.17 mg/kg.

The GAP for apples in the USA is foliar application of a 75 g/kg WG formulation at 0.37 kg ai/ha. No more than 4 applications may be made per season and no more than 1.1 kg ai/ha may be applied per season. The rate per hectare is maintained regardless of water volume or tree size with a maximum spray concentration of 0.05 kg ai/hL for trees over 3 metres in height and a maximum of 0.08 kg ai/hL for trees less than 3 metres in height. The PHI is 14 days.

Many of the US trials and all of the Canadian trials were conducted with three early season treatments (commencing at petal fall) each at 0.38 kg ai/ha plus three late season treatments (commencing at about 30 days before harvest) each at 0.38 kg ai/ha, for a total of 2.2–2.4 kg ai/ha (2× concentration). The early season applications started at petal fall and continued at 7 day intervals. The time from the final early season application to harvest is 60 – 160 days. There were no apple residue decline studies upon which to estimate the residue attributable to the early season applications. However, several side-by-side trials were conducted in which 6 applications (3 early season plus 3 late season) and 3 applications (3 late season) were applied. It was found that the residues from 6 applications were comparable to those from 3 late season applications: Michigan: 0.81 mg/kg (2.2 kg ai/ha total) and 0.73 mg/kg (1.1 mg/kg ai/ha total); New York, 0.55 and 0.77 mg/kg; Oregon, 0.37 and 0.50 mg/kg; Virginia, 0.65 and 0.67 mg/kg respectively. Therefore, the trials conducted with 6 applications were considered to be at the approximate maximum GAP. The residues from 27 trials at GAP in ranked order were: 0.23, 0.27, 0.35, 0.37, 0.44, 0.44, 0.49, 0.49, 0.50, 0.50, 0.54, 0.55, 0.60, 0.65, 0.67, 0.67, 0.68, 0.71, 0.71, 0.73, 0.75, 0.77, 0.81, 0.86, 0.93, 0.96, and 1.1 mg/kg.

The GAP for pears in the USA is identical to that for apples (above). In eight trials conducted in the US and four trials conducted in Canada, 3 early season applications each at 0.38 kg ai/ha were followed by 3 late season applications each at 0.38 kg ai/ha, for a total seasonal application of about 2.2 kg ai/ha, or 2× the maximum GAP. However, side-by-side trials with apples (above) indicated that the early season use did not contribute to the final residue. Assuming a translation to pears, ten trials were conducted at the approximate maximum GAP, and the residues in ranked order are: 0.18, 0.42, 0.46, 0.47, 0.59, 0.91, 1.0, 1.3, 1.6, and 1.8 mg/kg.

The Meeting decided that the apple and pear residue data, resulting from identical application patterns, were from the same population and combined the data to give the following residues in ranked order: 0.18, 0.23, 0.27, 0.35, 0.37, 0.42, 0.44, 0.44, 0.46, 0.47, 0.49, 0.49, 0.50, 0.50, 0.54, 0.55, 0.59, 0.60, 0.65, 0.67, 0.67, 0.68, 0.71, 0.71, 0.73, 0.75, 0.77, 0.81, 0.86, 0.91, 0.93, 0.96, 1.0, 1.1, 1.3, 1.6, and 1.8 mg/kg. The Meeting estimated an STMR of 0.65 mg/kg and a maximum residue level of 3 mg/kg for pome fruit.

Fruiting vegetables, other than cucurbits

Tomatoes

Supervised field trials for the foliar application of novaluron to tomatoes were reported from Argentina and Brazil. The GAP for Argentina specifies foliar application of a 100 g/L EC foliar

application at 0.005 kg ai/hL, 4 applications, and a 1 day PHI. Two trials were conducted in Argentina, but none were at GAP. Twelve trials were reported from Brazil, where the GAP is for the foliar application of a 100 g/L EC formulation at 0.002 kg ai/hL (0.02 kg ai/ha), with repeat applications as needed and a PHI of 7 days. The residues in ranked order are: < 0.01 (4) and < 0.02 (8). The Meeting estimated an STMR of 0.02 mg/kg and a maximum residue level of 0.02 (*) mg/kg.

Soya bean (immature seeds)

Field trials were reported for the foliar application of novaluron to soya beans (immature seeds) in Brazil. The GAP in Brazil specifies a foliar application of a 100 g ai/l EC formulation at a rate of 0.01 kg ai/ha with a PHI of 53 days. The number of applications is not specified. Eleven trials were conducted at the maximum GAP, and the residues on soya beans in ranked order were: < 0.01 (11) mg/kg. The Meeting estimated an STMR of 0.01 mg/kg and a maximum residue level of 0.01 (*) mg/kg.

Potato

Field trials were reported the EU, Mexico, and the USA for the foliar application of novaluron to potatoes. The GAP for use in Switzerland is a maximum of 2 applications (foliar) of a 100 g ai/L EC formulation at a single application rate of 0.02 kg ai/ha with a 21 day PHI. This GAP may be applied to trials conducted in Europe (Switzerland, Germany, France, Italy and Spain). Fourteen trials were at the GAP of Switzerland, and the residues in ranked order are: < 0.01 (14) mg/kg.

The GAP of Mexico specifies one foliar application of a 100 g/L EC formulation at a rate of 0.015 kg ai/ha with a PHI of 30 days. Two trials were conducted at 0.028 kg ai/ha (about 2×) and a PHI of 14 days, but may be considered as no quantifiable residues were found. The residues in ranked order were: < 0.01 (2) mg/kg.

The GAP of the USA specifies a maximum of 2 applications per season of a 100 g/L EC formulation at a rate of 0.087 kg ai/ha (0.17 kg ai/ha/season) with a PHI of 7 days. Two trials were reported from the USA, where two applications were made at a rate of 0.28 kg ai/ha each (3×). The trials may be considered as no quantifiable residues were found. The residues in ranked order were: < 0.05 (2) mg/kg. The analytical method (GC/ECD) was validated by concurrent fortified sample recoveries at 0.05 mg/kg. However, the same method was validated elsewhere at 0.01 mg/kg, including the method used for the European trials. The limit of quantitation was not adequately established for these USA trials.

The Meeting agreed to combine the non-quantifiable residues for the EU and Mexico, which in ranked order are: < 0.01 (16) mg/kg. The Meeting estimated an STMR of 0.01 mg/kg and a maximum residue level of 0.01 (*) mg/kg.

Oilseeds

Cotton seed

Supervised field trials for the foliar application of novaluron to cotton were conducted in Brazil, Mexico, South Africa, and the USA. The GAP of Brazil specifies foliar application of a 100 g/L EC formulation at a rate of 0.01 kg ai/ha (0.005 kg ai/hL) with a 93 day PHI. Four trials were conducted, three of which were at an exaggerated rate (2×) or a substantially shorter PHI. However, all residues on the cottonseed were below the limit of quantitation. The ranked order of residues found were: < 0.01 (4) mg/kg.

The GAP of Mexico specifies foliar application of a 100 g/L EC formulation at a rate of 0.015 kg ai/ha with a 30 day PHI. Only 1 application is allowed. Two trials were reported, but both were at an exaggerated rate (3×) with quantifiable residues.

The GAP of South Africa specifies the foliar application of a 100 g/L EC formulation at a rate of 0.035 kg ai/ha (0.007 kg ai/hL for ground equipment and 0.12 kg ai/hL for aerial equipment) with no specified PHI and a maximum of 3 applications per season. Two trials are reported, but the PHI is 71 days.

The GAP of the USA specifies the foliar application of a 100 g/L EC formulation at a rate of 0.1 kg ai/ha (0.53 kg ai/hL for aerial equipment and 0.21 kg ai/hL for ground equipment) with a PHI of 30 days. No more than 4 applications and a maximum application of 0.3 kg ai/ha are to be used per season. The re-treatment interval is a minimum of 7 days. The majority of the trials involved 5 applications with a total application of 0.42 kg ai/ha, or 140% of the maximum seasonal rate. The last three applications were made late in the season (3 × 0.1 kg ai/ha, 100% seasonal rate), with a 7 day retreatment interval and with 44 – 80 days between the first two and these three applications. The first two applications were made early season (3 to 4 weeks after crop emergence and 14 days later) at a nominal rate of 0.058 kg ai/ha/application. As the majority of the residue would result from the three late season applications, the trials may be considered to be at GAP.

The residues in ranked order for 16 trials at GAP are: < 0.05 (5), 0.060, 0.066, 0.067, 0.069, 0.10, 0.19, 0.21, 0.22, 0.25, 0.34, and 0.40 mg/kg. The trials from Brazil are considered not to be from the same population as the US trials. The Meeting estimated an STMR of 0.068 mg/kg and a maximum residue level of 0.5 mg/kg.

Primary animal feed commodities of plant origin

Cotton gin trash

Eleven supervised field trials conducted in the US were considered to be consistent with the GAP of the US (see cotton above). The residues in ranked order are: 3.7, 4.0, 4.5, 5.4, 6.7, 7.3, 10, 11, 17, 20, and 27 mg/kg. The Meeting estimated a median of 7.3 mg/kg and a high residue of 27 mg/kg.

Fate of residues during processing

Commercial-type processing studies were reported for apple and cottonseed, and the processing factors and resulting STMR-P values are summarized as follows:

Table 73. Calculated processing factors.

Raw Agricultural Commodity[1]				Processed Commodity				
Commodity	MRL (mg/kg)	STMR (mg/kg)	HR (mg/kg)	Commodity	Processing Factor	MRL (mg/kg)	STMR(P) (mg/kg)	HR(P) (mg/kg)
Apple	3	0.65	1.8	Juice	< 0.1	-	0.065	-
				Wet pomace[2]	7.2	13[3]	4.7[4]	-
Cotton seed (undelinted)	0.7	0.068	0.40	Meal	< 0.6	-	0.041	-
				Hulls	< 0.6	-	0.041	-
				Refined oil	< 0.6	-	0.041	-

[1] Only one processing study was available for each raw agricultural commodity.
[2] Water content (%) was not reported.
[3] 40 mg/kg for apple pomace dry based on a default dry matter content of 40%.
[4] 12 mg/kg for apple pomace dry based on a default dry matter content of 40%.

Farm animal dietary burden

The Meeting estimated the dietary burden of novaluron residues in farm animals on the basis of the diets listed in Appendix IX of the FAO Manual. Calculation from MRLs, highest residues (HR) and STMR-P values provides the levels in feed suitable for estimating MRLs for animal commodities, while calculation from STMR and STMR-P values for feed is suitable for estimating STMR values for animal commodities. The percentage of dry matter is taken as 100% when MRLs and STMR values are already expressed as dry weight.

Table 74. Estimated maximum dietary burden of farm animals.

Commodity	Group	Residue (mg/kg)	Basis of Residue	Dry matter (%)	*Diet content (%)*			Residue contribution (mg/kg)		
					Beef cattle	*Dairy cows*	*Poultry*	Beef cattle	Dairy cows	Poultry
Apple pomace	AB	4.7	STMR-P	40	*40*	*20*	-	4.7	2.4	
Cotton gin trash	AM	27	HR	90	*20*	*20*	-	6	6	
Cotton seed meal	-	0.041	STMR-P	89			*20*			0.01
Cotton seed hulls	AM	0.041	STMR-P	90			-			
Cotton seed	SO	0.40	HR	88	*25*	*25*	-	0.11	0.11	
TOTAL					***85***	***65***	***20***	**11**	**8.5**	**0.01**

The calculated maximum dietary burdens for beef cattle, dairy cows, and poultry are 11, 8.5, and 0.01 ppm, respectively.

Table 75. Estimated STMR dietary burden of farm animals

Commodity	Group	Residue (mg/kg)	Basis of Residue	Dry matter (%)	*Diet content, (%)*			Residue contribution (mg/kg)		
					Beef cattle	*Dairy cows*	*Poultry*	Beef cattle	Dairy cows	Poultry
Apple pomace	AB	4.7	STMR-P	40	*40*	*20*	-	4.7	2.4	
Cotton gin trash	AM	7.3	STMR	90	*20*	*20*	-	1.6	1.6	
Cotton seed meal	-	0.041	STMR-P	89			*20*			0.01
Cotton seed hulls	AM	0.041	STMR-P	90			-			
Cotton seed	SO	0.068	STMR	88	*25*	*25*	-	0.019	0.019	
TOTAL					***85***	***65***	***20***	**6.3**	**4.0**	**0.01**

The STMR dietary burdens for beef cattle, diary cows, and poultry are 6.3, 4.0, and 0.01 mg/kg, respectively.

Farm animal feeding studies

A feeding study was conducted with Friesian cows in which groups received the equivalent of 0, 0.35, 2.6, 8.0, or 26 ppm in the feed for 42 – 44 consecutive days. Average novaluron residues in whole milk on day 42 at the 8 and 26 ppm feeding levels were 0.38 and 1.7 mg/kg; in cream, 6.6 and 14 mg/kg; and in skimmed milk, 0.03 and 0.12 mg/kg. The novaluron maximum residue levels in tissues at the 8 ppm feeding level were: muscle, 0.34 mg/kg; kidney, 0.35 mg/kg; liver, 0.41 mg/kg; subcutaneous fat, 4.4 mg/k; peritoneal fat, 6.8 mg/kg. The novaluron maximum residue levels in tissues at the 26 ppm feeding level were: muscle, 0.56 mg/kg; kidney, 1.2 mg/kg; liver, 1.4 mg/kg; subcutaneous fat, 8.2 mg/kg; peritoneal fat, 13 mg/kg.

Residues were quantifiable at the lowest feeding level (0.35 ppm): milk, 0.04 mg/kg; muscle, 0.05 mg/kg; kidney, 0.06 mg/kg; liver, 0.05 mg/kg; subcutaneous fat, 0.43 mg/kg; and peritoneal fat, 0.56 mg/kg.

Table 76. Novaluron total residues, mg/kg.

Dietary burden *(ppm)*	Cream	Milk	Muscle		Liver		Kidney		Fat	
Feeding level [ppm]	mean	mean	highest	mean	highest	mean	highest	mean	Highest	mean
MRL beef cattle										
(11)			*(0.47/*		*(0.56/*		*(0.48/*		*(9.4/*	
[8/26]			*0.24)*		*0.59)*		*0.51)*		*5.5)*	
			0.34/		0.41/		0.35/		6.8/	
			0.56		1.4		1.2		13	
MRL dairy cattle										
(8.5)	*(7.0)*	*(0.40)*								
[8]	6.6	0.38								
STMR beef cattle										
(6.3)				*(0.19)*		*(0.24)*		*(0.26)*		*(4.1)*
[8]				0.24		0.31		0.33		5.2
STMR dairy cattle										
(4.0)	*(4.3/3.3)*	*(0.20/0.19))*								
[2.6/8]	2.8/6.6	0.13/0.38								

A poultry feeding study was not provided. The nature of the residue in poultry was conducted for fourteen consecutive days at a rate equivalent to 10 ppm in the diet. Novaluron residues in eggs, fat, muscle, kidney, and liver were 0.45, 3.5, 0.31, 0.37 and 0.41 mg/kg, respectively. Residues would most likely be non-quantifiable at the calculated dietary burden level of 0.01 ppm (1/1000 ×).

Maximum residue levels

The Meeting estimated maximum residue levels of 10 mg/kg for meat (fat), 0.7 mg/kg for edible offal, 7 mg/kg for milk fat, and 0.4 mg/kg for milk. The Meeting also estimated the following STMR values: muscle 0.19 mg/kg, fat 4.1 mg/kg, edible offal 0.26 mg/kg, whole milk 0.20 mg/kg, and cream 4.3 mg/kg.

The Meeting estimated maximum residue levels of 0.01 (*) mg/kg for eggs, poultry meat, and poultry edible offal, based on the demonstrated limit of quantification for poultry commodities by the GC/ECD method. Also estimated were STMRs of 0 for eggs, meat, and edible offal and 0.005 mg/kg for poultry fat.

RECOMMENDATIONS

The Meeting estimated the maximum residue levels and STMR values shown below. The maximum residue levels are recommended for use as MRLs.

Definition of the residue

Plants

Definition of the residue (for compliance with MRL and estimation of dietary intake): novaluron.

Animals

Definition of the residue (for compliance with MRL and estimation of dietary intake): novaluron

The residue is fat soluble.

Table 77. Summary of Recommendations.

Commodity		MRL, mg/kg		STMR or	HR,
CCN	Name	New	Previous	STMR-P, mg/kg	mg/kg
JF 0226	Apple juice			0.065	
AB 0226	Apple pomace, dry	40			
FM0812	Cattle milk fat	7		4.3	

Commodity		MRL, mg/kg		STMR or	HR,
CCN	Name	New	Previous	STMR-P, mg/kg	mg/kg
SO 691	Cotton seed	0.5			
OR 691	Cotton seed oil, edible			0.041	
MO 105	Edible offal (mammalian)	0.7		0.26	
PE 0112	Eggs	0.01*		0	
MM 0095	Meat (from mammals other than marine mammals)	10 (fat)		0.19 muscle 4.1 fat	
ML0106	Milks	0.4		0.20	
FP 0009	Pome fruits	3		0.65	
PM 0110	Poultry meat	0.01* (fat)		0 muscle 0.005 fat	
PO 0111	Poultry, Edible offal of	0.01*		0	
VR 0589	Potato	0.01*		0.01	
VP 541	Soya bean (immature seeds)	0.01*		0.01	
VO0448	Tomato	0.02*		0.02	

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes of novaluron, based on the STMRs estimated for 17 commodities, for the five GEMS/Food regional diets were in the range of 7% to 40% of the ADI (see Annex 3 of 2005 JMPR Report). The Meeting concluded that the long-term intake of residues of novaluron resulting from its uses that have been considered by JMPR is unlikely to present a public health concern.

Short-term intake

The 2005 JMPR decided that an acute RfD is unnecessary. The Meeting therefore concluded that the short-term intake of novaluron residues is unlikely to present a public health concern.

REFERENCES

Aikens, P J (2000). ^{14}C-"RIMON": Metabolism in cotton. Huntingdon Life Sciences Ltd. Project ID: MAK549/002671. Makhteshim Chemical Works Ltd., Israel. Report No. R-11087. Unpublished

Aikens, P J (2000). ^{14}C-"RIMON": Hydrolysis under Simulated Processing Conditions. Huntingdon Life Sciences Ltd. Project ID: MAK558/994752 + amendment. Makhteshim Chemical Works Ltd., Israel. Report No. R-11206. Unpublished

Australian Pesticides and Veterinary Medicines Authority, MRL Standard – Maximum Residue Limits in Food and Animal Feedstuff, July 2005, Table 3 (Residue Definition).

Carrancio, L (1999). Determination of Decline Curve of Rimon (Novaluron 10%) in Tomato. Microquim S.A, Argentina. Makhteshim Chemical Works, Ltd., Israel. Report No. R-11446. Unpublished. November17.

Class, T (2001). Independent laboratory Validation of Method for the Determination of Novaluron in Cotton; PTRL Europe GmbH Report B 463 G; R-13888. Makhteshim Agan of North America, Inc., New York. Unpublished. May 2.

Clock-Rust, M (2004). Novaluron (PC Code 124002) – Human Risk Assessment for Proposed Uses on Cotton, Pome Fruit and Potato. PP#2F6430. US EPA, Report DP #295824.

Corden, M T (1998). ^{14}C "RIMON": Metabolism in apples. Huntingdon Life Sciences Ltd. Project ID: MAK429/983248. Makhteshim Chemical Works Ltd., Israel. Report No. R-9768. Unpublished

Corden, M T (1999). ^{14}C-"Rimon" Metabolism in the lactating goat. Huntingdon Life Sciences Ltd. Project ID: MAK 461/984693. Makhteshim Chemical Works Ltd., Israel. Report No. R-9846. Unpublished.

Crowe, A. (1998). ^{14}C "RIMON": Metabolism in potatoes. Huntingdon Life Sciences Ltd. Project ID: MAK438/983684. Makhteshim Chemical Works Ltd., Israel. Report No. R-9803. Unpublished

Gonzalez, R H (2001). Degradation of Residues of Novaluron in Apples. Maipu, R.M., 2000-2001. University of Chile. Makhteshim Chemical Works, Ltd., Israel. Report No. R-14452. Unpublished

ISAGRO, S.p.A. (1989). Method for the Determination of GR 572 (Novaluron) in Apple, Pear, Peach, and Maize for Forage. Report R-8750. Unpublished

Kane, T J (2004). ^{14}C-"Rimon:" Residues in Laying Hens. Report No. MAK 810/ 033178; R-15767. Makhteshim Chemical Works, Ltd., Israel. 15 January. Unpublished.

Koch, D A (2002). Multiresidue Method Testing for Novaluron. ABC Laboratories, Inc. Project ID 47378; Crompton Study No. 2002-02. Makhteshim Agan of North America, New York. Report No. R-15546. Unpublished. Sept. 25.

Lindsell, S R (2001). Independent Laboratory Validation of the Method for the Post-registration Monitoring of Residues of Novaluron in Apples and Potatoes. Huntingdon Life Sciences Ltd. Project ID: MAK 669/012109. Makhteshim Chemical Works Ltd., Israel. Report R-12365. Unpublished. March 14.

Lindsell, S R (2001). Independent Laboratory Validation of the Methodology for the Post-registration Monitoring of Residues of Novaluron in Milk, Muscle and Liver. Huntingdon Life Sciences Ltd. Project ID: MAK 671/012110. Makhteshim Chemical Works, Ltd., Israel. Report No. R-12367. Unpublished. Feb. 23.

Mai, L (1998). STM CR 60: Determination of Novaluron in Plant Materials and Processed Fractions. Analchem Bioassay, Australia. Makhteshim, Australia. Unpublished. R-10587

Munro, S (1999). Novaluron: Investigation into the Stability of Residues in Various Crop Commodities when Stored at Approximately -18°C. Huntingdon Life Sciences Ltd. Project ID: MAK557/994033. Makhteshim Chemical Works Ltd., Israel. Report No. R-11205. Unpublished. Dec. 1

Munro. S (2000). Novaluron and its Chlorophenyl urea and Chloroaniline Metabolites: Development and Validation of Methodology for the Determination of Residues in Soils from Four Sites in Germany and Spain which are to be used for Terrestrial Field Dissipation Trials during 1999-2000. Huntingdon Life Sciences Ltd. Project ID: MAK546/003357 + Amendment. Makhteshim Chemical Works Ltd. Report No. R-11088. Unpublished. Dec 20

Munro, S (2000). Development and Validation of a Method for Post-Registration Monitoring of Residues of Novaluron in Apples and Potatoes. Makhteshim Chemical Works, Ltd., Israel. Report No. MAK 668/01 R-12364 . Unpublished

Munro, S (2001). Development and Validation of Method for Post-registration Monitoring of Resides of Novaluron in Animal Tissues and Milk. Huntingdon Life Sciences Ltd. Project ID: MAK 670/012154. Makhteshim Chemical Works, Ltd., Israel. Report No. R-12366. Unpublished. Feb. 7.

Novaluron – Evaluation Report 672/2003. WHO Specifications for Public Health Pesticides. World Health Organization, Geneva. 2003. R-16922.

O'Conner, J F (2000). ^{14}C-"Rimon" Metabolism in the rat. Huntingdon Life Sciences Ltd. Project ID: MAK 469/980204. Makhteshim Chemical Works Ltd., Israel. Report No. R-10004. Unpublished.

Paden, R (2000). Determination of Magnitude of Residues of Novaluron and Related Metabolites in Cottonseed After Two Applications of Rimon 10EC. Pinnacle Mexico S.A. de C.V. Protocol No. MX99015-4010R. Makhteshim Chemical Works, Ltd., Israel. Report No. R-11217. Unpublished. October 26.

Paden, R. (2003). Determination of the Magnitude of Residues of Novaluron in Potatoes after Two Applications of Rimon 10EC. Pinnacle, Mexico. Makhteshim Chemical Works, Ltd., Israel. Report No. R-14247. Unpublished. Feb. 16.

Redgrave, V A (2001). Rimon Technical: Residues in Milk and Tissues of Dairy Cows. Huntingdon Life Sciences Ltd. Project ID: MAK 605/003999. Makhteshim Chemical Works, Ltd., Israel. Report R-10993. Unpublished.

Redgrave, V A (2001). Rimon Technical: Residues in Tissues of Beef Cattle. Huntingdon Life Sciences Ltd. Project ID: MAK 609/004000. Makhteshim Chemical Works, Ltd., Israel. Report R-10994. Unpublished.

Rose, J E (2001). Method Validation for the Determination of Novaluron in Cotton. PTRL West, Inc. Project ID: AASI AI990801. Makhteshim Agan of North America, Inc., New York. Report No. R-11255. Unpublished. Jan. 3.

Rose, J E (2001). Independent Laboratory Validation of the Analytical Method for Novaluron (Rimon) in Apples. PTRL 993W. Makhteshim Agan of North America, Inc., New York. Report No. R-12608. Unpublished. August 17.

Shaw, D (1998). ^{14}C "RIMON": Hydrolysis under Laboratory Conditions. Huntingdon Life Sciences Ltd. Project ID: MAK 445/973392. Makhteshim Chemical Works Ltd., Israel. Report No. R-9703. Unpublished. May 11.

Shaw, D (2000). ^{14}C-"RIMON": Accumulation In Confined Rotational Crops. Huntingdon Life Sciences Ltd. Project ID: MAK559/002865. Makhteshim Chemical Works Ltd., Israel. Report No. R-11236. Unpublished

Todd, M A (1997). Development and Validation of Method for the Determination of Novaluron in Drinking, Ground, and Surface Waters. Huntingdon Life Sciences Ltd. Project ID: MAK 409/970198. Makhteshim Chemical Works Ltd, Israel. Report No. R-9348. Unpublished. August 26.

Todd, M A (1998). Development and Validation of an Analytical Method for the Determination of Rimon in Apples, Cabbages and Potatoes. Huntingdon Life Sciences Ltd. Project ID: MAK453/972510. Makhteshim Chemical Works, Ltd., Israel. Report No. R-9345. Unpublished. May 7.

Todd, M A (1998). Development and Validation of Method for the Determination of Novaluron Residues in Bovine Tissues (Fat, Kidney, Liver, Muscle), Milk and Eggs. Huntingdon Life Sciences Ltd. Project ID: MAK 454/972535. Makhteshim Chemical Works Ltd., Israel. Report No. R-9346. Unpublished. June 12.

Todd, M A (1999). Novaluron: The Determination of Storage Stability in Apples and Potatoes over a 12 month Period Stored at Approximately -18°C. Huntingdon Life Sciences Ltd. Project ID: MAK470/992503. Makhteshim Chemical Works Ltd., Israel. Report No. R-10014. Unpublished.

Todd, M A (1999). Development and Validation of Analytical Method for the Determination of Residues of Novaluron in Broccoli, Tomatoes, and Orange Processed Fractions. Huntingdon Life Sciences Ltd. Project ID: MAK 499/984521. Makhteshim Chemical Works, Ltd., Israel. Report No. R-10233. Unpublished. July 19.

Tornisielo, V L (1999). Determination of Residues of Rimon 100 (Novaluron) in Cottonseed. *Centro de Energia Nuclear na Agricultura, Universidade de Sao Paolo*. Project No. R73/99. Makhteshim Chemical Works, Ltd., Israel. Report No. R-11391. Unpublished. August 2.

Tornisielo, V L (1999). Determination of Residues of Rimon 100 (Novaluron) in Cottonseed. *Centro de Energia Nuclear na Agricultura, Universidade de Sao Paolo*. Project No. R80/99. Makhteshim Chemical Works, Ltd., Israel. Report No. R-11392.

Tornisielo, V L (1999). Determination of Residues of Rimon 100 (Novaluron) in Tomatoes. *Centro Energia Nuclear na Agricultura, Universidade de Sao Paolo*. Project No. R-26/99. Makhteshim Chemical Works, Ltd., Israel. Report No. R-11387. Unpublished. April 9.

Tornisielo, V L (1999). Determination of Residues of Rimon 100 (Novaluron) in Tomatoes. *Centro Energia Nuclear na Agricultura, Universidade de Sao Paolo*. Project No. R- 69/99. Makhteshim Chemical Works, Ltd., Israel. Report No. R-11388. Unpublished. July 15.

Tornisielo, V L (2000). Determination of Residues of Rimon 100 (Novaluron) in Soybeans. *Centro de Energia Nuclear na Agricultura. Universidade de Sao Paolo*. Project No. R- 64/99. Makhteshim Chemical Works, Ltd., Israel. Report No. R-11389. Unpublished. June 25.

Tornisielo, V L (2000). Determination of Residues of Rimon 100 (Novaluron) in Soybeans. *Centro de Energia Nuclear na Agricultura. Universidade de Sao Paolo*. Project No. R- 65/99. Makhteshim Chemical Works, Ltd., Israel. Report No. R-11390. Unpublished.

Tornisielo, V L (2000). Determination of Residues of Rimon 100 (Novaluron) in Soybeans. *Centro de Energia Nuclear na Agricultura. Universidade de Sao Paolo*. Project No. R- 10/00. Makhteshim Chemical Works, Ltd., Israel. Report No. R-11787. Unpublished. April 11.

Tornisielo, V L (2000). Determination of Residues of Rimon 100 (Novaluron) in Soybeans. *Centro de Energia Nuclear na Agricultura. Universidade de Sao Paolo*. Project No. R-11/00. Makhteshim Chemical Works, Ltd., Israel. Report No. R-11788. Unpublished. Feb. 23.

Tornisielo, V L (2004). Determination of the Residues of Rimon 100 EC (Novaluron) in Tomato Fruit – Piedade SP. *Centro Energia Nuclear na Agricultura, Laboratorio de Ecotoxicologia*. Study No. RF- 0002.034.114.04. R-17895 Makhteshim Chemical Works, Ltd., Israel. Unpublished. October 6.

Tornisielo, V L (2004). Determination of the Residues of Rimon 100 EC (Novaluron) in Tomato Fruit –Sumare, SP. *Centro Energia Nuclear na Agricultura, Laboratorio de Ecotoxicologia*. Study No. RF- 0002.034.116.04. R-17893 Makhteshim Chemical Works, Ltd., Israel. Unpublished. October 6.

Tornisielo, V L (2004). Determination of the Residues of Rimon 100 EC (Novaluron) in Tomato Fruit –Iracemapolis, SP. *Centro Energia Nuclear na Agricultura, Laboratorio de Ecotoxicologia*. Study No. RF- 0002.034.117.04. R-17894 Makhteshim Chemical Works, Ltd., Israel. Unpublished. October 6.

Tornisielo, V L (2004). Determination of the Residues of Rimon 100 EC (Novaluron) in Tomato Fruit – Jaiba, MG. *Centro Energia Nuclear na Agricultura, Laboratorio de Ecotoxicologia*. Study No. RF- 0002.034.115.04. R-17892 Makhteshim Chemical Works, Ltd., Israel. Unpublished. October 13.

Viljoen, A J (1998). Determination of Novaluron Residues in Cottonseed. South African Bureau of Standards (SABS) Report 311/R147. Makhteshim Chemical Works, Ltd., Israel. Report No. R-10715. Unpublished. October 12.

Willard, T R (2001). Magnitude of the Residue of Novaluron in Cotton Raw Agricultural and Processed Commodities. American Agricultural Services Project ID:. AA990801. Makhteshim Agan of North America, New York. Report No. R-11255. Unpublished. January 30.

Willard, T R (2002). Magnitude of the Residue of Novaluron in Pome Fruit Raw Agricultural and Processed Commodities. American Agricultural Services, Inc. Project ID: AA010703. Makhteshim Chemical Works, Ltd. Report No. R-13886. Unpublished. Feb. 25

Willard, T R (2002). Magnitude of the Residue of Novaluron in Cotton Raw Agricultural and Processed Commodities. American Agricultural Services, Inc. Project ID: AA010704. Makhteshim Agan of North America, New York. Report R-13887. Unpublished. Feb. 20.

Willard, T H (2003). Magnitude of the Residue of Novaluron in Cotton Raw Agricultural Commodities – Bridging Study. American Agricultural Services, Inc. Report AA020705. Makhteshim Agan of North America, New York. Report R-15424. Unpublished. August 22.

Willard, T R (2003). Magnitude of the Residues of Novaluron in Apple Raw Agricultural Commodities [Bridging Study]. American Agricultural Services, Inc. Project ID: AA020706. Makhteshim Chemical Works, Ltd. Report No. R-15425. May 13