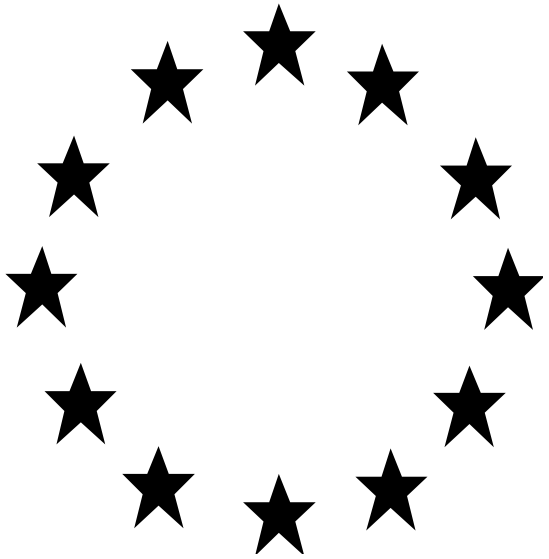


Final addendum to the

Additional Report

- public version -

Additional risk assessment provided by the rapporteur Member State the United Kingdom for the existing active substance

MALATHION

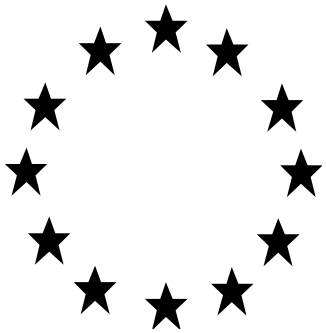
according to the Accelerated Resubmission Procedure laid down in Commission Regulation (EC) No. 33/2008

June 2009

Table of contents

Addendum to Volume 3	May 2009	3
	B.8 Environmental fate and behaviour	
Addendum 2 to Volume 3	June 2009	10
	B.6 Toxicology and metabolism	
	B.7 Residues data	

Council Directive 91/414/EEC



Malathion

Addendum to the Additional Report

May 2009

B.8 Environmental Fate and Behaviour

This addendum to the Additional Report has been prepared by the UK RMS to address the points of clarification raised in the malathion reporting table (rev 1-1). Where reference is made to the original Additional Report these references relate to the version of February 2009.

Point 4 (4):

EFSA: At step 4 PECsw including mitigation measures have been implemented for malathion. FOCUS landscape and mitigation indicated that spray drift inputs should not be mitigated by more than 95%. For the uses assessed in the additional report this equates to a no spray buffer zone somewhere between 30 and 35m for calculations with 1 application and ca. 30m for calculations with 4 applications. So the buffer zone of 40m provides too much spray drift mitigation. Simulations implementing a 30m no spray buffer zone and 4 applications would therefore appear to be needed still, for the EU level assessment that EFSA has to present in the conclusion to be in line with the noted guidance.

As stated above, in the original Additional Report PECsw were calculated at STEP 4 with a 40 m buffer zone. In light of the EFSA comment consideration has been given to the level of spray drift mitigation provided by a 40m buffer zone. Table B.8.1 contains the FOCUS drift values resulting from both 1 and 4 applications of 1.2 kg a.s/ha to fruiting vegetables. These are compared with the mass loading per drift event mitigated by 95%, and the mass loading mitigated with a 40m buffer zone.

It is noted that in the Reporting Table the Notifier has calculated PECsw by using the 95% drift mitigation values, without specifying the measure to be applied to mitigate risk. It is suggested that in accordance with the FOCUS Landscape and Mitigation Report it would then be the responsibility of the Member States to decide which mitigation measures were appropriate at a National product approval level. Whilst the UK RMS considers this approach has some benefits, we have taken the approach of calculating PECsw for a specified buffer zone distance using the standard FOCUSsw models in order to demonstrate the actual mitigation required.

Table B.8.1 Comparison of FOCUS drift values (1 and 4 x 1.2 kg a.s/ha to fruiting vegetables) with 95 % mitigation and 40m buffer zone mitigation.

Scenario	Number of applications	FOCUS drift value (mg/m^2 of surface water area)	95% drift mitigation (mg/m^2 of surface water area)	40m buffer zone drift mitigation (mg/m^2 of surface water area)	40m buffer provides greater than 95% mitigation?
D6 ditch	1 application	2.3129	0.1156	0.0888	Yes
	4 applications	1.5562	0.0778	0.0581	Yes
R2, R3, R4 stream	1 application	2.0597	0.1030	0.1066	No
	4 applications	1.3823	0.0691	0.0697	No

For the R2, R3 and R4 stream scenarios (both 1 and 4 applications) the 40m buffer zone mitigates spray drift by less than 95%. The use of a 40 m buffer zone for those scenarios and water body will therefore be in accordance with the recommendations of the FOCUS Landscape and Mitigation Report.

For the D6 ditch scenario the 40 m buffer provides greater than 95% drift mitigation and a comparison of drift values mitigated by 95% with mitigation provided by other buffer zone distances was therefore required. Table B.8.2 shows that to achieve less than 95% drift mitigation a 30 m buffer zone (1 application) or a 25 m buffer zone (4 applications) is required.

Table B.8.2 Comparison of FOCUS drift values for D6 ditch (1 and 4 x 1.2 kg a.s/ha to fruiting vegetables) with 95 % mitigation and 25m, 30m and 35m buffer zone drift mitigation.

Scenario	Number of applications	Mass loading per drift event (mg/m^2)				
		FOCUS drift value	95% drift mitigation	25 m buffer	30m buffer	35 m buffer
D6 ditch	1 application	2.3129	0.1156	0.1395	0.1171	0.1010
	4 applications	1.5562	0.0778	0.0917	0.0768	0.0661

It was therefore appropriate to re-calculate PECsw at STEP 4 for the D6 ditch scenario with a 30 m buffer (1 application) and 25 m buffer (4 applications) and use the highest of those PECs in the Risk Assessment.

In addition, as the STEP 4 surface water PECs reported in the original Additional Report were calculated based on an interval between applications of only 7 days, it was necessary to re-calculate the STEP4 PECs for all scenarios with an interval between applications of 10 days, to properly reflect the proposed GAP. The GAP modelled is detailed in Table B.8.3.

Table B.8.3 Application rate and timing modelled using the FOCUS surface water scenarios.

Rate of application	1 x 1.2 kg a.s/ha and 4 x 1.2 kg a.s/ha
Crop	Vegetables, fruiting
Interval between applications	10 days
Start of application window	D6 = 7 May R2 = 7 May

	R3 = 18 May R4 = 4 May

The input values for malathion were the same as detailed in the additional report and for completeness are copied below in Table B.8 4.

Table B.8.4 Input parameters used in the FOCUS surface water modelling.

Input parameter	Malathion
Molecular mass (g/mol)	330
Vapour pressure (Pa)	4.4×10^{-4} at 25°C
Water solubility (mg/L)	148 at 25°C
K_{foc} (ml/g)	217
Freundlich Exponent (1/n)	0.94
DT_{50} in soil (days)	0.17 at 20°C [a]
DT_{50} in water (days)	0.38 at 20°C‡
DT_{50} in sediment (days)	1000
Max in soil (%)	-
Max in water/sediment (%)	-

‡ Value for whole water/sediment system

[a] = In the additional report it is stated by the UK RMS that the malathion DT50 in soil of 0.17 days was the shortest (0.17-0.25, n=4). However, after a comment from the Notifier in the Reporting Table it is confirmed here that 0.17 days is the normalised geometric mean DT50 in soil.

Table B.8.5 FOCUS STEP 4 PECsw for malathion following application of either 1 or 4 applications of 1.2 kg a.s/ha and the appropriate buffer zone to mitigate drift by <95%

Mitigation	Number of applications	D6	R2	R3	R4
		Ditch (µg/l)	Stream (µg/l)	Stream (µg/l)	Stream (µg/l)
25 m buffer zone	1	-	-	-	-
	4	0.301	-	-	-
30 m buffer zone	1	0.380	-	-	-
	4	-	-	-	-
40 m buffer zone	1	-	0.288	0.365	0.620
	4	-	0.393	0.240	0.620

The highest PEC for each scenario/water body from either 1 or 4 applications was used in the Risk Assessment and those are detailed in Table B.8.6.

Table B.8.6 FOCUS STEP 4 PECsw for malathion used in the Risk Assessment.

Mitigation	D6	R2	R3	R4
	Ditch	Stream	Stream	Stream
30 m no spray buffer zone	0.380 µg/l (1 application)	-	-	-
40 m no spray buffer zone	-	0.393 µg/l (4 applications)	0.365 µg/l (1 application)	0.620 µg/l (1 and 4 applications)

It is noted by the UK RMS that altering the interval between applications from 7 days to 10 days had a relatively large impact on the PECsw calculated at STEP 4. For the R4 scenario the peak PECsw changed from 1.997 µg/l (as reported in the Additional Report) to 0.620 µg/l. The R4 scenario peak PEC was identified in the original additional report as being driven by runoff and further consideration was therefore given to the dates of applicaton selected by the Pesticide Application Timing calculator and the peaks of exposure. With a 7 day interval between applications the first two applications occured on 4 and 11 May and the peak PECsw occured on 15 May after a runoff event. When the application interval was changed to 10 days (but the application window was kept the same as used with the 7 d interval) only 1 application was made (on 4 May) prior to a runoff event and consequently the peak PEC was much lower (0.620 µg/l on 9 May).

In order to test the sensitivity of the model to the application dates the UK RMS repeated FOCUS surface water modelling with a 10 day interval but changed the start of the application window from 4 May to 11 May. This meant that, like with the original modelling with a 7 day application interval, an application occured 4 days before a run-off event on 15 May, and a higher peak PECsw of 1.824 µg/l occured on 15 May. These results for R4 stream have been tabulated below (Table B.8.7) to illustrate the sensitivity of the model to application dates and individual Member States may wish to consider this issue further during National product authorisations.

Table B.8.7 PECsw for R4 stream with 7 and 10 day application interval and an application window starting on either 4 or 11 May.

Scenario	Start of application window	Application dates	Peak PEC (µg/l)
R4 – 7 day interval	4 May	4 May	1.997 occurred on 15 May
		11 May	
		27 May	
		6 June	
R4 – 10 day interval	4 May	4 May	0.620 on 9 May
		27 May	
		6 June	
		16 June	
R4 – 10 day interval	11 May	11 May	1.824 on 15 May.
		27 May	
		6 June	
		16 June	

The final PECsw with either 30m or 40m buffer zone, as detailed in Table B.8.6, were compared with the toxicity endpoints. The Toxicity Exposure Ratios are shown in Table B.8.8.

Table B.8.8 TERs for aquatic organisms at FOCUS STEP 4

Scenario	Water body	Test organism	Time scale	Toxicity endpoint (µg/L)	Buffer zone distance (m)	PEC (µg/L)	TER	Annex VI trigger
D6	Ditch	Fish	Acute	40	30	0.380	105	100
R2	Stream	Fish	Acute	40	40	0.393	102	100
R3	Stream	Fish	Acute	40	40	0.365	110	100
R4	Stream	Fish	Acute	40	40	0.620[a]	**65**	100
						1.824[b]	**22**	100
D6	Ditch	Fish	Chronic	21	30	0.380	55	10
R2	Stream	Fish	Chronic	21	40	0.393	53	10
R3	Stream	Fish	Chronic	21	40	0.365	58	10
R4	Stream	Fish	Chronic	21	40	0.620[a]	34	10
						1.824[b]	12	10
D6	Ditch	Aquatic invertebrates	Mesocosm	5	30	0.380	13	3*
R2	Stream	Aquatic invertebrates	Mesocosm	5	40	0.393	13	3*
R3	Stream	Aquatic invertebrates	Mesocosm	5	40	0.365	14	3*

Scenario	Water body	Test organism	Time scale	Toxicity endpoint (µg/L)	Buffer zone distance (m)	PEC (µg/L)	TER	Annex VI trigger
R4	Stream	Aquatic invertebrates	Mesocosm	5	40	0.620[a]	8	3*
						1.824[b]	**2.7**	3*
D6	Ditch	Aquatic invertebrates	Mesocosm	5	30	0.380	13	5*
R2	Stream	Aquatic invertebrates	Mesocosm	5	40	0.393	13	5*
R3	Stream	Aquatic invertebrates	Mesocosm	5	40	0.365	14	5*
R4	Stream	Aquatic invertebrates	Mesocosm	5	40	0.620[a]	8	5*
						1.824[b]	**2.7**	5*

* The trigger value is based on the assessment factor agreed at the expert meeting.
[a] = Application window beginning 4 May
[b] = Application window beginning 11 May

From the above, it can be concluded that the risk to aquatic life is acceptable for most scenarios providing that a 30 or 40 m buffer zone is implemented.

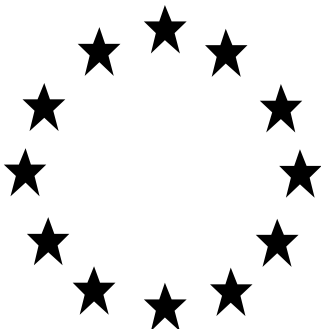
Point 4 (5):

EFSA: A case is made that groundwater exposure from the protected ornamental use will be covered by the simulations that were in the original DAR and the EFSA conclusion addendum for the originally requested (no longer maintained) uses on apples and strawberries. In principle this seems reasonable. However as no maximum number of treatments per year is stipulated in the GAP table for the use in protected ornamentals, the case cannot be accepted without an upper limit being stipulated for the number of applications allowed.

The EFSA conclusion provides the results of groundwater modelling (<0.1 µg/l for all scenarios) for a GAP of 6 x 2.16 kg a.s/ha to strawberries. Interception of 60% was assumed and applications were made in July and August for all scenarios except Jokioinen where the last 2 applications were in September.

The proposed individual rate of application to ornamentals is 0.114 kg a.s/ha and in light of the EFSA comment consideration has been given to the number of applications to ornamentals which would be covered by the groundwater modelling referred to above. If, as a worst case, it is assumed that there is no interception by ornamental plants, a calculation of number of applications at 0.114 kg a.s/ha compared to those to strawberries (6 x 0.864 kg a.s/ha after interception of 60%) shows that 45 applications could be made to ornamentals for the maximum total dose to be within the maximum total dose applied to strawberries in the modelling.
As the maximum acceptable number of applications would in fact be even higher due to interception by the ornamental crop, the UK RMS does not consider it necessary to state a maximum number of applications for this use in this case due to the extremely large margins of safety demonstrated by the existing strawberry GAP.

Council Directive 91/414/EEC



Malathion

Addendum 2 to the Additional Report

June 2009

B.6 Toxicology and metabolism

Evaluation Table Open point 2.11
RMS to revise the difference in the potency of malaoxon and malathion based on the overall database.

Comparative toxicity of Malathion and Malaoxon

Malaoxon, a major plant and minor technical impurity has been assessed in a 14 day range finding study and a 24-month toxicity/carcinogenicity study in rats.

Tables 1-5 summarises the data on cholinesterase inhibition in these studies (the end point critical in determining reference values).

Table 1 Summary of cholinesterase activity in 4 week study in the rat with malathion

Parameter			DOSE GROUP (ppm)									
Cholinesterase IU/ml	Control		males					females				
	males	females	50 5.7	100 10.4	500 51.9	10000 1035.9	20000 2008.2	50 5.7	100 11.6	500 57.6	10000 1134.4	20000 2192.6
Plasma	0.564	1.517	0.518	0.585	0.544	0.406**	0.229**	1.603	1.737	1.634	0.834	0.340*
(% of control)	-	-	(91.8)	(103.7)	(96.5)	(72.0)	(40.6)	(105.7)	(114.5)	(107.7)	(55.0)	(22.4)
RBC	8.6	7.5	8.6	8.3	8.2	7.1**	7.2**	7.5	7.6	7.4	7.0	6.8
(% of control)	-	-	(100.0)	(96.5)	(95.3)	(82.6)	(83.7)	(100.0)	(101.3)	(98.7)	(93.3)	(90.7)
Brain	10.3	10.9	9.9	9.7	10.1	9.2*	7.6**	10.6	10.3	10.7	9.0**	7.9**
(% of control)	-	-	(96.1)	(94.2)	(98.1)	(89.3)	(73.8)	(97.2)	(94.5)	(98.2)	(82.6)	(72.5)

Table 2 Summary of cholinesterase activity in 14 day range finding study in the rat with malaoxon

Cholinesterase Activity		Dose group (ppm (mg/kg bw/day))											
		control		males					females				
		males	females	10 1.1	25 3.0	100 12.1	2500 293.1	3500 387.3	10 1.1	25 3.1	100 12.5	2500 281.6	3500 294.7
Plasma (IU/ml	**wk1**	0.613	1.194	0.607	0.596	0.554**	0.093**	0.115**	1.058	1.094**	0.88**	0.134**	0.106**
% of control				(99.0%)	(97.2%)	(90.4%)	(15.2%)	(18.8%)	(88.6%)	(91.6%)	(73.7%)	(11.2%)	(8.9%)
	term	0.714	1.214	0.673	0.62	0.601	0.083**	0.067**	1.23	1.201	0.992	0.082**	-
				(94.3%)	(86.8%)	(84.2%)	(11.6%)	(9.4%)	(101.3%)	(98.9%)	(81.7%)	(6.8%)	-
RBC (IU/ml)	**wk1**	8.3	8	8.2	8	7.4*	6.8**	6.5**	8.3	8.3	7.5	7	6.7*
% of control				(98.8%)	(96.4%)	(89.2%)	(81.9%)	(78.3%)	(103.8%)	(103.8%)	(93.8%)	(87.5%)	(83.8%)
	term	7.5	7	7.2	7	6.4	5.7**	6.2*	7.3	7.3	6.5	6.4	-
				(96.0%)	(93.3%)	(85.3%)	(76.0%)	(82.7%)	(104.3%)	(104.3%)	(92.9%)	(91.4%)	-
Brain (IU/g)	**term**	10	9.9	10	10	10	6.3**	2.5**	9.7	9.6	9.8	3.3**	-
% of control				(100.0%)	(100.0%)	(100.0%)	(63.0%)	(25.0%)	(98.0%)	(97.0%)	(99.0%)	(33.3%)	-

* statistically significant

Table 3 Summary of effects in 90 day study in the rat

Parameter			DOSE GROUP (ppm)									
Cholinesterase	**Control**		**males**					**females**				
	males	**females**	**100 6.6**	**500 34.4**	**5000 339.6**	**10000 679.6**	**20000 1389.6**	**100 7.9**	**500 39.3**	**5000 383.8**	**10000 784.0**	**20000 1597.0**
Plasma (IU/ml)	0.575	3.388	0.571	0.562	0.478	0.387	0.201	3.368	3.279	1.9	0.971	0.311
(% of control)	-	-	(99.3)	(97.7)	(83.1)*	(67.3)**	(35.0)**	(99.4)	(96.8)	(56.1)*	(28.7)**	(9.2)*8
RBC (IU/ml)	1.1	1.2	1	0.9	0.4	0.4	0.3	0.9	0.9	0.5	0.4	0.4
(% of control)	-	-	(90.9)	(81.8)**	(36.4)**	(36.4)**	(27.3)**	(75.0)	(75.0)	(41.7)**	(33.3)**	(33.3)**
Brain (IU/g)	11.4	11.5	10.8	11.2	10.4	9.9	9.1	11.7	11.2	10.3	9.5	6.4
(% of control)	-	-	(94.7)	(98.2)	(91.2)**	(86.8)**	(79.8)**	(101.7)	(97.4)	(89.6)*	(82.6)**	(55.7)**

Table 4 Summary of cholinesterase activity in 2 year study in the rat with malathion

Cholinesterase activity		controls		Dose Group (ppm)							
		male	female	male				female			
				100/50 7/2	500 29	6000 359	12000 739	100/50 8/3	500 35	6000 415	12000 868
Plasma IU/ml (% of control)	**3 months**	0.623	2.928	0.609	0.631	0.456**	0.292**	2.868	2.76	1.449**	0.566**
		-	-	(97.8%)	(101.3%)	(73.2%)	(46.9%)	(98.0%)	(94.3%)	(49.5%)	(19.3%)
	6 months	0.633	3.33	0.621	0.591	0.481**	0.299**	3.327	3.305	1.777**	0.654**
		-	-	(98.1%)	(93.4%)	(76.0%)	(47.2%)	(99.9%)	(99.2%)	(53.4%)	(19.6%)
	12 months	0.737	3.319	0.698	0.736	0.615*	0.419**	3.581	2.879	2.053**	1.004**
		-	-	(94.7%)	(99.9%)	(83.4%)	(56.9%)	(107.9%)	(86.7%)	(61.9%)	(30.2%)
	termination	1.869	3.495	1.615	1.327**	0.675**	c	3.475	1.02	1.374**	0.389**
		-	-	(86.4%)	(71.0%)	(36.1%)	-	(99.4%)	(29.2%)	(39.3%)	(11.1%)
RBC IU/ml (% of control)	**3 months**	0.9	1.46	1.17**	1.01	0.47**	0.47**	1.1**	1.02**	0.62**	0.49**
		-	-	(130.0%)	(112.2%)	(52.2%)	(52.2%)	(75.3%)	(69.9%)	(42.5%)	(33.6%)
	6 months A[#]	0.75	0.99	0.72	-	-	-	0.85	-	-	-
		-	-	(96.0%)	-	-	-	(85.9%)	-	-	-
	6 months B[#]	1.03	1.37	1.16	0.97	0.59**	0.44**	1.38	1.37	0.77**	0.62**
		-	-	(112.6%)	(94.2%)	(57.3%)	(42.7%)	(100.7%)	(133.0%)	(56.2%)	(45.3%)
	12 months	1.43	1.5	1.43	1.33	0.78**	0.6**	1.52	1.29*	0.83**	0.74**
		-	-	(100.0%)	(93.0%)	(54.5%)	(42.0%)	(101.3%)	(90.2%)	(55.3%)	(49.3%)
	termination	1.16	1.35	1.11	0.96	0.66**	c	1.34	0.99**	0.76**	0.65**
		-	-	(95.7%)	(82.8%)	(56.9%)	-	(99.3%)	(85.3%)	(56.3%)	(48.1%)
Brain IU/g (% of control)	**3 months**	10.77	10.75	10.82	10.71	9.43**	9.1**	10.78	9.62	9.12	6.72
		-	-	(100.5%)	(99.4%)	(87.6%)	(84.5%)	(100.3%)	(89.5%)	(84.8%)	(62.5%)
	6 months	10.02	9.99	9.85	9.8	8.85**	8.16**	9.68	9.75	8.27	5.05
		-	-	(98.3%)	(97.8%)	(88.3%)	(81.4%)	(96.9%)	(97.6%)	(82.8%)	(50.6%)
	12 months	9.93	9.89	9.83	9.69	8.85**	8.45**	10.09	10.58	8.7	7.17
		-	-	(99.0%)	(97.6%)	(89.1%)	(85.1%)	(102.0%)	(107.0%)	(88.0%)	(72.5%)
	termination	10.76	10.73	10.59	10.44	7.41**	c	10.69	10.58	8.78	3.52
		-	-	(98.4%)	(97.0%)	(68.9%)	-	(99.6%)	(98.6%)	(81.8%)	(32.8%)

Table 5 Summary of cholinesterase activity in 2 year study in the rat with malaoxon

Cholinesterase activity		**control**		**males**			**females**		
		males	**females**	**20 1**	**1000 57**	**2000 114**	**20 1**	**1000 58**	**2000 141**
Plasma (IU/ml) (% of control)	3 months	0.531	2.559	0.525	0.132**	0.092**	2.583	0.355*	0.14**
		-	-	(98.9%)	(24.9%)	(17.3%)	(100.9%)	(13.9%)	(5.5%)
	6 months	0.615	3.201	0.588	0.124**	0.071**	3	0.419**	0.139**
		-	-	(95.6%)	(20.2%)	(11.5%)	(93.7%)	(13.1%)	(4.3%)
	12 months	0.74	3.422	0.787	0.193*	0.087**	3.359	0.611*	0.196**
		-	-	(106.4%)	(26.1%)	(11.8%)	(98.2%)	(17.9%)	(5.7%)
	Term	1.603	3.119	1.619	0.306**	0.151**	3.651	0.526*	0.316**
		-	-	(101.0%)	(19.1%)	(9.4%)	(117.1%)	(16.9%)	(10.1%)
RBC (IU/ml) (% of control)	3 months	1.06	1.25	0.93	0.4**	0.45**	1	0.47**	0.53**
		-	-	(87.7%)	(37.7%)	(42.5%)	(80.0%)	(37.6%)	(42.4%)
	6 months	1.15	1.29	0.91**	0.39**	0.43**	1.04**	0.56**	0.52**
		-	-	(79.1%)	(33.9%)	(37.4%)	(80.6%)	(43.4%)	(40.3%)
	12 months	1.25	1.43	1.08	0.49**	0.44**	1.18	0.58**	0.49**
		-	-	(86.4%)	(39.2%)	(35.2%)	(82.5%)	(40.6%)	(34.3%)
	Term	1.25	1.32	1.12	0.68**	0.7**	1.1	0.72**	0.71**
		-	-	(89.6%)	(54.4%)	(56.0%)	(83.3%)	(54.5%)	(53.8%)
Brain (IU/g) (% of control)	3 months	10.45	10.57	10.25	9.51	8.53**	10.38	9.34**	2.3**
		-	-	(98.1%)	(91.0%)	(81.6%)	(98.2%)	(88.4%)	(21.8%)
	6 months	10.22	10.29	10.49	10.03	9.05**	10.43	9.64**	3.97**
		-	-	(102.6%)	(98.1%)	(88.6%)	(101.4%)	(93.7%)	(38.6%)
	12 months	11.45	11.27	11.24	10.58	9.46**	11.27	10.67*	4.26**
		-	-	(98.2%)	(92.4%)	(82.6%)	(100.0%)	(94.7%)	(37.8%)
	Term	10.73	10.77	10.61	7.52**	2.82**	10.63	9.26	4.04**
		-	-	(98.9%)	(70.1%)	(26.3%)	(98.7%)	(86.0%)	(37.5%)

* statistically significant ($p < 0.05$)
** statistically significant ($p < 0.01$)

Using the available data to make a direct comparison of the toxicity of malathion and malaoxon is hampered by the different sampling times and different dosing levels employed in the various studies.

Comparing the 4 week malathion study with the 14 day malathion study; for example malathion produced significant inhibition (ca 80-90% of controls) of both RBC and Brain cholinesterase at a dose of 10000 ppm (1035.9 and 1134 mg/kg bw/day for males and females respectively). For malaoxon significant inhibition (30-85% of controls, although the 33.3% inhibition of brain cholinesterase appears in females at odds with the RBC inhibition in females of 91.4%) of both RBC and Brain cholinesterase was seen at a dose 2500 mg/kg bw/day (293.1 and 281.6 mg/kg bw/day for males and females respectively). Comparing these dose levels malaoxon is at least 4 fold more toxic than malathion though likely greater as the malaoxon study is half the duration of the malathion study. It's worth noting both these studies only had 5 rats/sex/dose.

Probably a better comparison in terms of short term exposures is to look at the 3 month study with malathion, the 3 month time point in the malathion 2 year study and the 3 month time point in the malaoxon 2 year study.

In the 3 month study with malathion a statistically significant reduction RBC cholinesterase (87.7% of controls) was seen in males at a dose of 500 ppm (equivalent to 34.4 mg/kg bw/day). While a dose of 5000 ppm (339.6 and 383.8 mg/kg bw/day for males and females respectively) produced significant reductions in RBC and Brain cholinesterase (RBC 36.4 and 41.7% of controls in males and females respectively; Brain 91.2 and 89.6% of controls in males and females respectively).

At the 3 month time point in the malathion 2 year study both RBC cholinesterase was significantly reduced in females at the lowest dose test 100 ppm (8 mg/kg bw/day).

At the 3 month time point in the malaoxon 2 year study both RBC and Brain cholinesterase were significantly reduced (RBC 37.7 and 37.6% of controls in males and females respectively; Brain 91.0 and 88.4% of controls in males and females respectively) at a dose of 1000 ppm (57 and 58 mg/kg bw/day for males and females respectively).

Comparing the 3 month study with malathion and the 3 month time point in the malaoxon 2 year study there appear around a 6-7 fold difference in toxicity between malathion and malaoxon.

Considering the terminal measurement in the 2 year studies with malathion and malaoxon it can be seen that both compounds produce a similar level of brain cholinesterase inhibition (ca 30-40% of controls) at dose of 12000ppm for malathion (739 and 868 mg/kg bw/day for males and females respectively) and 2000 ppm (114 and 141 mg/kg bw/day for males and females respectively) for malaoxon a 6-7 fold difference in toxicity.

Therefore comparing both short term and long term data with similar levels of RBC and Brain cholinesterase inhibition it appears that malaoxon is 6-7 fold more toxic than malathion.

In the FAO report on malathion (1997) LD50 values in rodents for malathion were quoted as ranging between 1000-10,000 mg/kg bw, the observed differences probably being due to impurities, while the LD50 for malaoxon was 100-220 mg/kg/day. In the DAR a batch of malathion with a known isomalathion level (0.44 % w/w) had an LD50 value 1857-2057 mg/bw day (both sexes). Therefore comparing the acute data it appears that malaoxon is 10-20 fold more toxic than malathion. However the reliability of the malaoxon LD50 is unknown.

B.6.14 Exposure data (IIIA 7.2)

Evaluation Table open point 2.10
RMS to present in an addendum worker exposure estimates with and without the use of PPE, also according to EUROPOEM II (as it was not presented in the additional report) and considering one application.

At PRAPeR TC 11 (4 June 2009) a request was made for the RMS to provide a revised exposure assessment for re-entry workers which also considered the exposure of workers who may be using PPE (protective gloves). The revised assessment was also to consider the exposure arising from a single treatment of 'Malathion 440 g/L EW'. These open points are addressed in the exposure assessment presented below.

AOEL / Dermal absorption

The short term systemic AOEL for malathion (0.2% isomalathion) is 0.03 mg/kg bw/day determined from the 90 day rat study and applying an

assessment factor of 1000 (see EFSA Scientific Report (2006) 63, 1-87, Conclusion on the peer review of malathion / Appendix 1 – list of endpoints (p54).

The dermal absorption values assumed for 'Malathion 440 g/L EW' are in line with those agreed for the 440 g/l emulsion oil in water formulation previously considered for Annex 1 listing (Fyfanon). These are 5% and 15% for the concentration and dilution respectively (see EFSA Scientific Report (2006) 63, 1-87, Conclusion on the peer review of malathion (p16)). The 15% value is used in the worker assessment for exposure to a dry foliar residue.

B.6.14.3 Worker exposure (IIIA 7.2.3)

Worker exposure for Malathion 440 g/L EW has been evaluated for use on field strawberries and protected ornamental crops (see Addendum 3 of the DAR (9 September 2005). The exposure assessments were considered to demonstrate an acceptable scenario for workers re-entering protected ornamentals when malathion was applied at the critical GAP. For outdoor strawberries, an acceptable scenario was given where a 24 hour re-entry interval was observed. The acceptable scenarios are described in the EFSA Scientific Report (2006) 63, 1-187, Conclusion on the peer review of malathion Appendix 1 – list of endpoints (p55).

For this re-submission the critical GAP for strawberry has been reduced to 1.2 kg a.s./ha and a revised worker re-entry exposure assessment is presented for this change in GAP. No further evaluation of worker exposure from application to ornamentals is necessary as no changes to the GAP for ornamentals has been proposed.

Worker activities

The original exposure assessment assumes worker re-entry into field strawberries immediately after the final application to perform harvesting activities. This assumption is considered by the applicant to be overly conservative as the critical GAP specifies a PHI of 3 days before harvest. Therefore, the applicant has proposed worker re-entry can be considered for 2 possible scenarios.

1. Crop inspection immediately after application
2. Harvest activities at the PHI of 3 days

This evaluation agrees these are the realistic re-entry scenarios to be considered.

B.6.14.3.1 Estimation of worker exposure using the EUROPOEM re-entry model

a) Crop inspection

It is assumed that a worker re-enters the crop soon after application to carry out crop inspection activities. The duration of this activity is 2 hours and it is assumed there is no degradation of malathion after the final application. Calculations also assume a TC of 3000 cm^2

(EUROPOEM value for hand harvesting strawberries), a 60 kg worker and 15% dermal absorption.

As dislodgeable foliar residue (DFR) studies with malathion are not available, for a Tier 1 assessment DFR is predicted from conservative default assumptions which assume a DFR of 3 μg/cm^2 per kg as/ha applied.

D = DFR x TC x WR x AR x P

D = Dermal Exposure [µg a.s./person*d]
DFR = Dislodgeable Foliar Residue per 1 kg a.s./ha [µg a.s./cm² x ha/kg a.s.]
= 3 µg a.s./cm² x ha/kg a.s.
TC = Transfer Coefficient [cm²/person/h]
= 3000 [cm²/person/h]
WR = Work Rate [2 hours/day]
AR = Application Rate (1.2 kg a.s./ha)
P = Penetration Factor for Clothing (= 1) which assumes no clothing such as a long sleeved shirt is taken into account

D = 3 x 3000 x 2 x 1.2 x 1

D = **21.6 mg a.s./person/day**

Assuming 60 kg body weight and 15 % dermal absorption, systemic exposure is estimated to be 0.054 mg/kg bw/day, i.e.180% of the short-term systemic AOEL.

This is for a single application of malathion.

b. Hand-harvesting

It is assumed that a worker re-enters the crop 3 days after the final application to carry out hand harvesting. The duration of this activity is 8 hours and it is assumed there is no degradation of malathion after the final application. Calculations also assume the same TC, a 60 kg worker and 15% dermal absorption.

As dislodgeable foliar residue (DFR) studies with malathion are not available, for a Tier 1 assessment DFR is predicted from conservative default assumptions which assume a DFR of 3 μg/cm^2 per kg as/ha applied.

D = DFR x TC x WR x AR x P

D = Dermal Exposure [µg a.s./person*d]
DFR = Dislodgeable Foliar Residue per 1 kg a.s./ha [µg a.s./cm² x ha/kg a.s.]
= 3 µg a.s./cm² x ha/kg a.s.
TC = Transfer Coefficient [cm²/person/h]
= 3000 [cm²/person/h]
WR = Work Rate [2 hours/day]
AR = Application Rate (1.2 kg a.s./ha)
P = Penetration Factor for Clothing (= 1) which assumes no clothing such as a long sleeved shirt is taken into account

D = 3 x 3000 x 8 x 1.2 x 1

D = **86.4 mg a.s./person/day**

Assuming 60 kg body weight and 15 % dermal absorption, systemic exposure is estimated to be 0.216 mg/kg bw/day, i.e.720% of the short-term systemic AOEL.

This is for a single application of malathion.

Summary

Based on a Tier 1 assessment using the EUROPOEM re-entry model the predicted exposures for crop inspection and hand-harvesting are 180% of the AOEL and 720% of the AOEL respectively.

As this product may be applied up to 4 times in a programme of treatments (10 day interval between treatments), if levels of DFR accumulate between treatments, levels of exposure could be higher than those which have been predicted. Also there is the potential for DFR to decline after treatment (crop inspection) and after the 3 day harvest interval (hand harvesting). Further refinement of the exposure assessment is therefore required.

B.6.14.3.2 Refinement of cumulative DFR to establish suitable re-entry interval for unprotected workers performing inspection activities assuming 15% dermal absorption

For crop inspection, dermal exposure has been estimated using the following equation:

$DFR_0 = AR * n * 3\ \mu g/cm^2$

Where:
DFR_0 = Dislodgeable foliar residue immediately after application
AR = Application rate
n = number of applications
(1 kg/ha is assumed to be equivalent to 3 $\mu g/cm^2$)

This equation can be refined where suitable data are available for residue decline and assuming workers would not enter the treated crop immediately after application but would enter after the proposed waiting period. In practice persons would not be expected to re-enter treated crops until spray deposits are dry. The refinement using first order kinetics is proposed as follows:

$DFR_t = DFR_0 * e^{(-0.693/DT50) * t}$
Where:
DFRt = Dislodgeable foliar residue at time t
DT50 = Decline rate of foliar residue

According to the proposed GAP for strawberry, a maximum of 4 applications with an interval of 10 days is proposed for SEU. Residue data generated on strawberries in Southern Europe (2007 trials) (presented in Table B.7.7) are further summarised below.

Table 6.41 Residues of malathion on strawberry (mg/kg)

Interval (days)	Trial 1		Trial 2		Trial 3		Trial 4	
	Malathion only	Total malathion *	Malathion only	Total malathion *	Malathion only	Total malathion *	Malathion only	Total malathion *
Directly after spraying	0.65	0.74	0.41	0.46	0.30	0.36	0.32	0.35
1	0.12	0.19	0.09	0.14	0.06	0.11	0.09	0.12
3	0.05	0.09	0.07	0.10	0.05	0.07	0.05	0.07

* Total malathion = Malathion + Malaoxon + Desmethyl malathion expressed as malathion equivalent residues

The applicant concludes from these residue trials that the rate of decline of malathion is rapid and similar to total residues of malathion, malaoxon and desmethyl malathion (expressed as malathion equivalents). The applicant suggests this supports the conclusion that the inclusion of desmethyl malathion would not significantly increase the persistence of malathion residues on crops. Based on these data the applicant notes that the DT50 in plants for malathion would be significantly less than 1 day.

This evaluation agrees the strawberry residue trials conducted in 2007 indicate that residues in strawberries decline significantly after one day. However, in these trials the metabolites MMCA and MDCA were not determined in the analysis of total malathion. In the 2008 strawberry residue trials malathion residues were only measured at day 0 and 3 days after treatment. These data (also shown in Table B.7.7) show a similar rate of decline to the 2007 trials at the 3 day time point for parent malathion (average 82% decline in 2007 trials and 87% decline in 2008 trials). However, total malathion residues declined by only 55% on average for the correct residues definition i.e. parent malathion plus its metabolites malaoxon, desmethyl malathion, MMCA and MDCA being determined in the samples. As the metabolites MMCA and MDCA are of toxicological significance these metabolites must be considered in the assessment of re-entry exposure.

Data from an apple metabolism study (McEwen 2004) which are summarised in Addendum 1 to the DAR (Tables 7.1 – 23 and 7.1 – 24, p46-47) provide information on the presence of malathion and malathion metabolites on leaf and crop surfaces. In this study four 2-3 year-old apple trees (var. Gala), were treated each with 100 ml of malathion solution containing [14C]-malathion at three occasions corresponding to an application rate of 1.8 kg a.i./ha at each timing. The first treatment took place 7 weeks prior to harvest, with two further treatments made at 14 day intervals. Untreated trees served as controls.

The total radioactive residues (TRR) in surface wash extract measured two hours after the final application accounted for 24.5%

TRR (0.89 mg/kg) of which >95% was attributed to parent malathion (0.85 mg/kg) based on HPLC analysis. The TRR in surface wash was shown to decline to 3.5% TRR (0.089 mg/kg) by Day 7, 1.7% TRR (0.048 mg/kg) by Day 14 and 1.82% TRR (0.03 mg/kg) by Day 21. Malathion was also shown to decline rapidly in surface wash extract over this period. The distribution of malathion between the crop surface and homogenate indicates approximately 66% of the total (parent) malathion to be available on the surface immediately after application which declined to around 10 -30% by Day 7-21. HPLC results combining MMCA, MDCA and DMM show residues in surface wash extracts are low, ranging from 0.76% TRR (0.028 mg/kg) in surface wash extracts at Day 0 (3% of the total TRR) then declining to 1.1% TRR (0.018 mg/kg) by Day 21. The TLC results reported by McEwen (2004), combining MMCA and MDCA also confirm residues of these metabolites in surface wash extracts to be low. The TRR ranged from 0.005 mg/kg (0.13% TRR) in surface wash extracts at Day 0 declining to 0.003 mg/kg (0.2% TRR) by Day 21. TLC results for DMM range from 2.84% TRR (0.103 mg/kg) at Day 0, declining to 0.68% TRR (0.011 mg/kg) after Day 21. In contrast, the quantitative results from homogenates after surface washing (HPLC and TLC data) demonstrate that the majority of the TRR related to the malathion metabolites MMCA and MDCA is within the crop and therefore not available as surface residues.

Surface residues immediately prior to the final application in the apple metabolism study show the total radioactive residue (TRR) in the surface wash extract was 2.9% TRR (0.051 mg/kg) which comprised of 6 components the largest of which was malathion at 1.83% (0.032 mg/kg). These data suggest the accumulation of dislodgeable foliar residues following sequential applications (14 day interval) would not be significant. This conclusion is supported by experimental work conducted in the US in 2006 and reported by Yanhong Li *et al*. In this study two applications of malathion were applied to outdoor strawberry plants. Leaf samples were collected from Day 1 to Day 5, and from Day 13 to Day 17 after the first application and on Day 8 and Day 11 after the second application. Measurements of DFR were made using both leaf punch samples and from whole leaf samples. The results from this study also showed a rapid decline in malathion DFR after application, with the day 13 DFR measurements being below the limit of detection (reported as 1 ppm).

To summarise, from the surface wash data DFR are concluded to be predominantly malathion with residues of MMCA and MDCA metabolites being typically <0.01 mg/kg. The significance of these metabolites at these levels on the dermal exposure of re-entry workers is expected to be negligible. The available data from residues and DFR trials on strawberry and metabolism data on apple suggest the accumulation of DFR from successive treatments of malathion would be negligible if a 10 day interval between applications is observed. These data also suggest DFR of malathion at the time of harvest would be significantly lower than the DFR immediately after the final application where the proposed PHI of 3 days is observed.

Assessment

Assuming first order dissipation, the applicant has derived a DT50 value for malathion of 0.5 days using data from the apple metablolism study. This calculation applies best fit kinetics according to the methods reported by Timme and Frehse (1986). Applying simple first order kinetics to these apple metabolism data gives a longer half life of 3.3 days. There are a number on uncertaines in using etiher of these values. The data are based on

surface wash residues for apple fruit therefore it is uncertain what differences may occur between apple and strawberry plants and between the smooth surface of apple fruit and the surface of strawberry fruit and leaves. Secondly, these data are a small (unreplicated) dataset and crucially, there are no data for the 1 and 2 day timepoints to show the actual pattern of degradation over the period immediately after the final treatment. Using a non linear fit of these data (see figure 1) a half life of 1.86 days ($r^2 = 1$) is calculated.

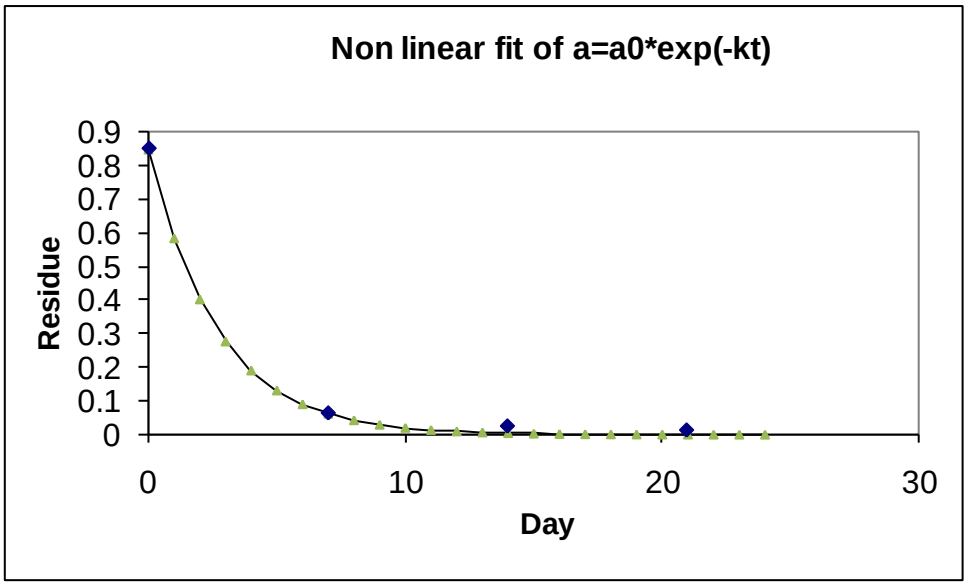


Figure 1 Plotted dissipation of malathion from apple metabolism data (McEwen 2004) based on non linear (first order) degradation

DFR dissipation curves vary in form and shape, and are often biphasic, reflecting different rate processes, chemical-physical influences and partitioning (Whitmyre *et al* 2004). Using data for melon, grape and peach foliage, the use of biphasic kinetics resulted in more robust r^2 values for the regression curves that describe foliar dissipation of endosulfan compared to use of simple first-order kinetics (Whitmyre *et al* 2004).

Using the information given above exposure to workers re-entering crops treated with a programme of 4 treatments of 'Malathion 440 g/L EW'is predicted for crop inspection (2 hours exposure) and hand-harvesting (8 hours exposure). The calculations presented at (a) and (b) assume a half life of 0.5 days. Assessments have also been produced which assume a calculated half-life of 3.3 days (linear fit, first order degradation) and 1.86 days (non linear fit, first order degradation). All estimates are summarised in Table 6.42 and presented in B.6.15 (Operator and Worker Exposure estimates).

a. Crop inspection

$$\text{Worker Exposure} = \frac{\text{DFR } (\mu g/cm^2) \times \text{TC } (cm^2/h) \times \text{T (h)} \times \text{Dermal Absorption (\%)}}{\text{Bw (kg)} \times 1000}$$

Using the half life (DT_{50}) value of 0.5 days and a re-entry interval of 1 day after the final treatment, a refined cumulative DFR can be estimated as follows:

DFR following 4th application = $3.6 * e^{(-0.693/0.5)*1} = 0.9003\ \mu g/cm^2$

Worker exposure = [0.9003 x 3000 x 2 x 0.15]/60000

Worker exposure = 0.0135 mg/kg bw/d (45% of the AOEL)

b. Hand harvesting (3 days after final application)

$$\text{Worker Exposure} = \frac{\text{DFR } (\mu g/cm^2) \times \text{TC } (cm^2/h) \times \text{T (h)} \times \text{Dermal Absorption (\%)}}{\text{Bw (kg)} \times 1000}$$

Using the worst case DT_{50} of 0.5 day and a re-entry interval of 3 days, a refined cumulative DFR can be estimated as follows:

DFR following 4th application = $3.6 * e^{(-0.693/0.5)*3} = 0.0563\ \mu g/cm^2$

Worker exposure = [0.0563 x 3000 x 8 x 0.15]/60000

Worker exposure = 0.0034 mg/kg bw/d (11% of the AOEL)

Table 6.42 Summary of exposure assessments assuming different degradation rates for the dissipation of malathion DFR from plant surfaces

Scenario	Assumed Half-life (days)	Predicted systemic exposure (mg/kg bw/day)	% of the AOEL
Crop Inspection	0.5	0.0135*	45
Harvest	0.5	0.0034	11
Crop Inspection	1.86	0.039	129
Harvest	1.86	0.072	241
Crop Inspection	3.3	0.054	181
Harvest	3.3	0.131	437

*Assumes re-entry occurs 24 hours after the final application is made

These assessments show a variety of outcomes depending on which half-life is used to decline Malathion DFR between treatments and after the final treatment. For endosulfan, Whitmyre *et al* (2004) found biphasic kinetics was a more accurate predicter of daily DFR than first order kinetics when describing the overall dissipation. Whitmyre *et al* (2004) concluded that first order kinetics may overestimate DFRs and, potentially, post application worker exposures. The data for Malathion DFR reported by Yanhong Li *et al* suggests malathion DFR also follow a biphasic rather than a first order dissipation, hence the assessments presented above may be overestimates of exposure. It should be recognised however, that actual DFR data for the proposed use on strawberry are not available and there are uncertaines associated with using the apple metabolism data to refine the tier 1 assessment. A more robust calculation of DFR dissipation cannot be achieved from the available information.

B.6.14.3.3 Refinement of re-entry assessment incorporating the use of protective gloves by workers involved in crop inspection and hand harvesting

The report of the EUROPOEM re-entry working group states that the bare hand scenario for (straw)berries results in a (arithmetic mean) TC value of 2,500 cm^2/hr for hands. The report concludes that taking into account the crop height and cropping pattern of strawberries there is likely to be very low exposure to the rest of the body. Adding the forearms, which are described as representing skin as well, gives a TC value of 3,670 cm^2/hr although it is noted that this figure is higher than comparable ones but may be explained by the inexperience of the pickers. From these assumptions the TC of 3,000 cm^2/hr is suggested by EUROPOEM for workers hand picking strawberries. As this TC

value is based on bare hand exposure with little contributed by other body parts, the benefit from using PPE for hand-harvesting strawberries would be limited to the hands.

Work by the UK HSE indicate that the performance of gloves in the field typically results in actual hand exposures >5% of exposure on outside of gloves. Similarly, for a review of the published literature on the performance of PPE reported by TNO (TNO report V7333 Effective Personal Protective Equipment 2007) the authors proposed protection values for gloves of 90% when liquids are handled and 95% when solids are handled. Whilst these values do not relate to protection from a dry dislodgeable foliar residue, a value of 5% appears reasonable for the purpose of refining the assessment.

Using the estimated exposures summarised in Table 6.42 and assuming 95% protection from the use of gloves all predicted exposures are within the systemic AOEL for malathion.

Table 6.43 Summary of exposure assessments assuming different degradation rates for the dissipation of malathion DFR from plant surfaces including consideration of PPE

Scenario	Assumed Half-life (days)	Predicted systemic exposure (mg/kg bw/day)	% of the AOEL – Bare hands	Predicted systemic exposure (mg/kg bw/day)	% of the AOEL – Protective gloves worn
Crop Inspection	0.5	0.0135*	45	0.001*	2
Harvest	0.5	0.0034	11	0.0002	1
Crop Inspection	1.86	0.039	129	0.002	7
Harvest	1.86	0.072	241	0.004	12
Crop Inspection	3.3	0.054	181	0.003	9
Harvest	3.3	0.131	437	0.007	22

*Assumes re-entry occurs 24 hours after the final application is made
$ Assumes protective gloves reduce the workers actual dermal exposure by 95%

B.6.14.4 Conclusions

From the available information used to consider the dissipation of malathion DFR after the proposed 4 treatments and 3 day PHI, it is uncertain whether levels of exposure for re-entry workers handling treated crops with bare hands would be within or above the AOEL. Estimates of exposure have been presented which show both outcomes. If protective gloves were used by workers all predicted exposures are within the AOEL. However, as there is no available usage data to show how typical such practice is it is uncertain how representative this scenario is.

To address the uncertainty in the bare hand exposure assessment higher tier data, such as data on dislodgeable foliar residues for the use of Malathion 440 g/L EW in the manner proposed, are required. Alternatively, MS will need to judge from robust usage data if the use of PPE in the exposure assessment is an appropriate refinement. This should be done at MS level.

As a safe use for re-entry workers has been previously identified for workers re-entering treated ornamental plants (roses), these data are not required to support the Annex 1 listing of malathion.

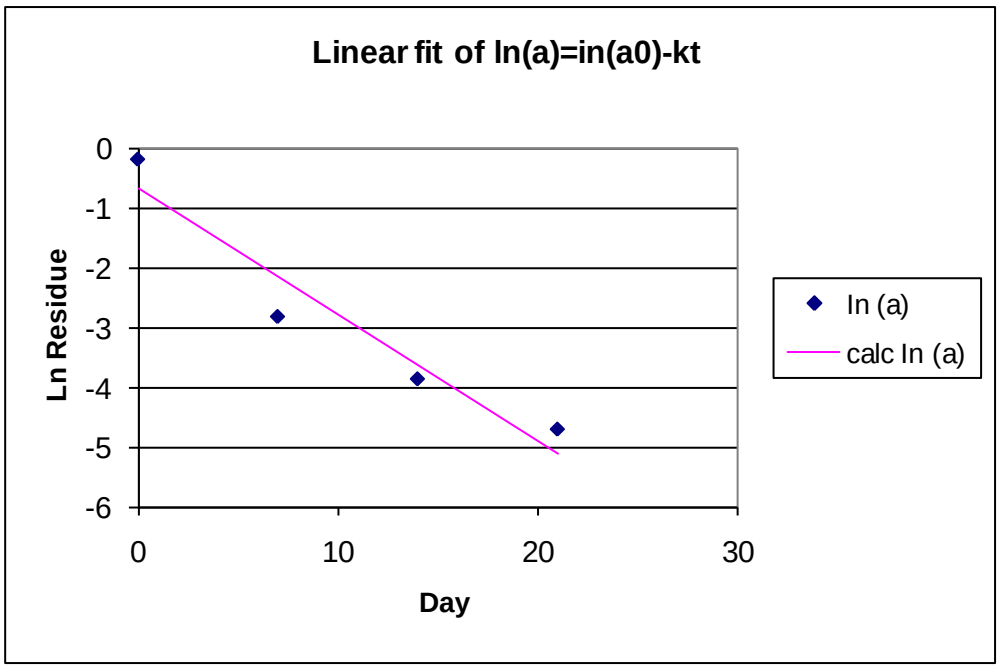
References

1. van Hemmen *et al* (2002). Post-application exposure of workers to pesticides in agriculture. Report of the re-entry working group, EUROPOEM II project: FAIR3-CT96-1406

B.6.15 - Worker exposure estimates

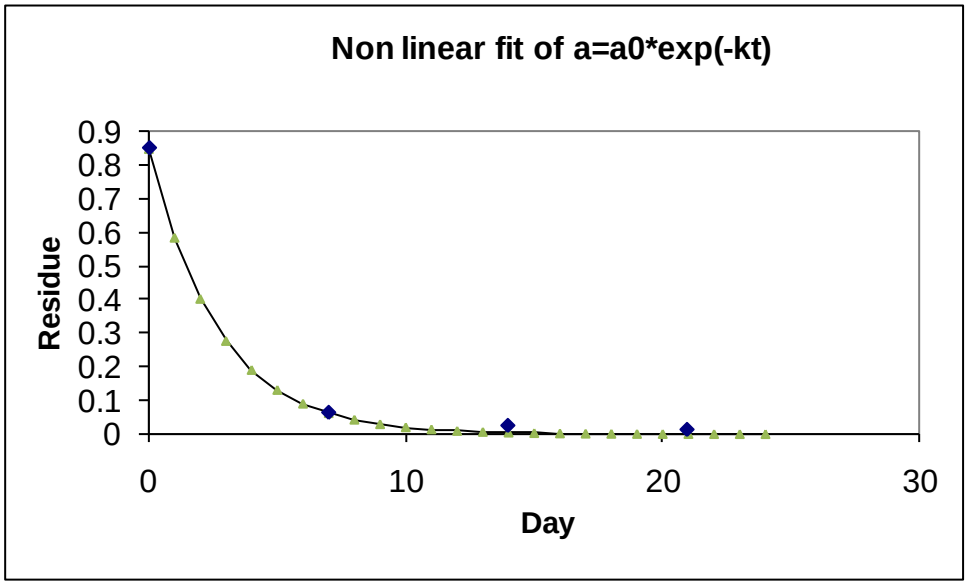
Calculation of half-life values

Linear fit



Half-life = 0.693/k = 3.30 days

Non Linear fit



Half-life = 0.693/k = 1.86 days

Worker exposure - Crop Inspection / 0.5 day half life

Half-life calculator

$N_t = N_o \times (0.5)^{\text{number of half-lives}}$

N_t = amount remaining after specified number of half-lives

N_o = original amount

Number of half-lives = elapsed time ÷ half-life

Application rate (kg a.s./ha)	1.2
Interval between applications	10
Exclusion period	1

Application 1

Nt	No	Time	Half life	No of half-lives
	3.6	31	0.5	62
0.000000000000000078				

Application 2

Nt	No	Time	Half life	No of half-lives
	3.6	21	0.5	42
0.00000000000082				

Application 3

Nt	No	Time	Half life	No of half-lives
	3.6	11	0.5	22
0.00000086				

Application 4

Nt	No	Time	Half life	No of half-lives
	3.6	1	0.5	2
0.9000				

Total Nt	0.900
TC	3000
Duration	**2**
Dermal exp (mg/person)	5.400
% dermal abs	15%
Body weight	60
Systemic exp (mg/kg bw/day)	0.014
AOEL	0.03
% of AOEL	45%

Worker exposure – Hand Harvesting 0.5 day half life

Half-life calculator

$N_t = N_o \times (0.5)^{\text{number of half-lives}}$

N_t = amount remaining after specified number of half-lives

N_o = original amount

Number of half-lives = elapsed time ÷ half-life

Application rate (kg a.s./ha)	1.2
Interval between applications	10
Exclusion period	3

Application 1

Nt	No	Time	Half life	No of half-lives
	3.6	33	0.5	66
0.00000000000000000005				

Application 2

Nt	No	Time	Half life	No of half-lives
	3.6	23	0.5	46
0.00000000000005				

Application 3

Nt	No	Time	Half life	No of half-lives
	3.6	13	0.5	26
0.00000005				

Application 4

Nt	No	Time	Half life	No of half-lives
	3.6	3	0.5	6
0.05625				

Total Nt	0.0563
TC	3000
Duration	**8**
Dermal exp (mg/person)	1.350
% dermal abs	15%
Body weight	60
Systemic exp (mg/kg bw/da	0.0034
AOEL	0.03
% of AOEL	11%

Worker exposure – Crop inspection 1.86 day half life

Half-life calculator

$N_t = N_o \times (0.5)^{\text{number of half-lives}}$

N_t = amount remaining after specified number of half-lives

N_o = original amount

Number of half-lives = elapsed time ÷ half-life

Application rate (kg a.s./ha)	1.2
Interval between applications	10
Exclusion period	1
Half life (days)	1.86

Application 1

Nt	No	Time	Half life	No of half-lives
	3.6	31	1.86	16.66667
0.00003460476516434900				

Application 2

Nt	No	Time	Half life	No of half-lives
	3.6	21	1.86	11.29032
0.00143741084723				

Application 3

Nt	No	Time	Half life	No of half-lives
	3.6	11	1.86	5.913978
0.05972978				

Application 4

Nt	No	Time	Half life	No of half-lives
	3.7	1	1.86	0.537634
2.5212				

Total Nt	2.582
TC	3000
Duration	**2**
Dermal exp (mg/person)	15.494
% dermal abs	15%
Body weight	60
Systemic exp (mg/kg bw/day)	0.039
AOEL	0.03
% of AOEL	129%

Worker exposure – Hand Harvesting 1.86 day half life

$N_t = N_o \times (0.5)^{\text{number of half-lives}}$

N_t = amount remaining after specified number of half-lives

N_o = original amount

Number of half-lives = elapsed time ÷ half-life

Application rate (kg a.s./ha)	1.2
Interval between applications	10
Exclusion period	3
Half life (days)	1.86

Application 1

Nt	No	Time	Half life	No of half-lives
	3.6	33	1.86	17.74194
0.000016				

Application 2

Nt	No	Time	Half life	No of half-lives
	3.6	23	1.86	12.36559
0.000682				

Application 3

Nt	No	Time	Half life	No of half-lives
	3.6	13	1.86	6.989247
0.028335				

Application 4

Nt	No	Time	Half life	No of half-lives
	3.6	3	1.86	1.612903
1.1770				

Total Nt	1.2060
TC	3000
Duration	**8**
Dermal exp (mg/person)	28.944
% dermal abs	15%
Body weight	60
Systemic exp (mg/kg bw/da	0.0724
AOEL	0.03
% of AOEL	241%

Worker exposure – Crop inspection 3.3 day half life

$N_t = N_o \times (0.5)^{\text{number of half-lives}}$

N_t = amount remaining after specified number of half-lives

N_o = original amount

Number of half-lives = elapsed time ÷ half-life

Application rate (kg a.s./ha)	1.2
Interval between applications	10
Exclusion period	1
Half life (days)	3.3

Application 1

Nt	No	Time	Half life	No of half-lives
	3.6	31	3.3	9.393939
0.00535112339470652000				

Application 2

Nt	No	Time	Half life	No of half-lives
	3.6	21	3.3	6.363636
0.04378265964215				

Application 3

Nt	No	Time	Half life	No of half-lives
	3.6	11	3.3	3.333333
0.36150903				

Application 4

Nt	No	Time	Half life	No of half-lives
	4.0	1	3.3	0.30303
3.2110				

Total Nt	3.622
TC	3000
Duration	**2**
Dermal exp (mg/person)	21.730
% dermal abs	15%
Body weight	60
Systemic exp (mg/kg bw/day)	0.054
AOEL	0.03
% of AOEL	181%

Worker exposure – Hand Harvesting 3.3 day half life

$N_t = N_o \times (0.5)^{\text{number of half-lives}}$

N_t = amount remaining after specified number of half-lives

N_o = original amount

Number of half-lives = elapsed time ÷ half-life

Application rate (kg a.s./ha)	1.2
Interval between applications	10
Exclusion period	3
Half life (days)	3.3

Application 1

Nt	No	Time	Half life	No of half-lives
	3.6	33	3.3	10
0.003516				

Application 2

Nt	No	Time	Half life	No of half-lives
	3.6	23	3.3	6.969697
0.028722				

Application 3

Nt	No	Time	Half life	No of half-lives
	3.6	13	3.3	3.939394
0.234653				

Application 4

Nt	No	Time	Half life	No of half-lives
	3.6	3	3.3	0.909091
1.9171				

Total Nt	2.1840
TC	3000
Duration	**8**
Dermal exp (mg/person)	52.415
% dermal abs	15%
Body weight	60
Systemic exp (mg/kg bw/da	0.1310
AOEL	0.03
% of AOEL	437%

B.7 Residues data

Evaluation Table Open point 3.8
RMS to re-assess the confined rotational study, with particular attention to the residue definition established for risk assessment

In the confined rotational crop study only residues in immature crops from the 30 day study could be characterised, for mature crops and immature crops from later plant backs, the majority of the residue was unextractable or polar in nature. On characterisation of the immature crops from the 30 day study, malathion, MMCA and low levels of malaoxon (less than 0.01 mg/kg) were detected, thus supporting the proposed residue definition of malathion plus its metabolite malaoxon, desmethyl-malathion, malathion monocarboxylic acid and malathion dicarboxcylic acid expressed as malathion.

With regards to possible positive residues in crops, the applicant has made a strong case as to why residues would not occur based on DT50's in soil of malathion and its metabolites and strawberries not normally being rotated with other crops. In addition, TRR in crops at harvest were less than 0.12 mg/kg, with the exception of wheat grain (0.15 mg/kg 120 day study – to allow for strawberry plants to be grubbed up and a rotational crop planted) and straw (0.21 mg/kg), for a 1.8N application to bare soil (N rate would be a lot higher with strawberry plants present which would intercepting the majority of the malathion applied, thus as the amount of malathion reaching the soil would be much reduced and in most cases the grubbed up strawberry plant would be removed to prevent volunteers).

To conclude, for the above reasons it is unlikely positive residues of malathion would result in rotational crops from the use on strawberries, however for use on other crops, further data on rotational crops ('cold studies') may be required.

Evaluation Table Open Point 3.9
RMS to reconsider the consumer risk assessment in the light of the results of the current discussions

Two issues were raised that impacted on the consumer risk assessment, malaoxon residues in crops and additional season's residue trials on strawberries. Neither where considered major issues that would prevent Annex 1 listing, due to residues of malaoxon being less than 0.02 mg/kg in strawberries and the consumer risk assessment on the four acceptable residue trials giving individual NEDIs, NESTIs, TMDIs and IESTIs from the consumption of strawberries of less than 8% of the ADI and ARfD of 0.03 and 0.3 mg/kg bw/day respectively.

Malaoxon

Only one of the trials samples contained positive residues of malaoxon of 0.01 mg/kg which is 100 fold lower than the highest total malathion residue of 1.0 mg/kg. With regards to the toxicity of malathion verses malaoxon, the NOAEL in the 2 year rat study for malathion was 30 mg/kg bw and for malaoxon 1 mg/kg bw, thus potentially only 30 times more toxic (**Mammalian toxicology of malaoxon is currently being reviewed which is likely to result in malaoxon being considered to be less than 30 times as toxic as malathion and therefore in the case of strawberries even less reason to carry out a separate risk assessment for malaoxon)**.

Therefore, in the above case, even when allowing for malaoxon being 30 times more toxic (intakes would increase by 23%), the resulting intake is only slightly higher and does not alter the % of the ADI or ARfD accounted for in the NEDI, TMDI, NESTI or IESTI calculations

To conclude, for the above reasons the RMS does not consider a separate risk assessment is required for malaxon, however if residue trials indicated higher % residues of malaoxon compared to malathion, then a separate risk assessment may well be required.

Additional residue trials

Four further trials were requested, analysing the residue trial samples for the full residue definition (malathion plus its metabolite malaoxon, desmethyl-malathion, malathion monocarboxylic acid and

malathion dicarboxcylic acid expressed as malathion), as four of the trial samples were only analysed for malathion plus its metabolite malaoxon, desmethyl-malathion, expressed as malathion.

DATAREQUIREMENTS

Four further residue trials

Four further trials were requested, analysing the residue trial samples for the full residue definition (malathion plus its metabolite malaoxon, desmethyl-malathion, malathion monocarboxylic acid and malathion dicarboxcylic acid expressed as malathion), due to the samples from four out of the eight trials submitted, only analysed for malathion plus its metabolite malaoxon, desmethyl-malathion, expressed as malathion.

Fate of MMCA and MDCA during processing

Further data were requested due to mainly concerns with MDCA (MMCA less concern as it was generally accepted that this degrades to MDCA – confirmation required) and what it degrades to (radiolabel study required), the argument it enters the citric acid cycle, based on the proposed metabolic pathway in plants was not accepted, as this was a processing study not metabolism in plants.