MALEIC HYDRAZIDE (102)

EXPLANATION

The compound was first evaluated in 1976. The review of its toxicology in 1996 and the present review of residue aspects are within the CCPR Periodic Review Programme.

The manufacturer submitted information on metabolism and environmental fate, analytical methods, use patterns, supervised trials, and the effects on residues of storage and processing. The Netherlands supplied information on analytical methods, residue trials, and national GAP and MRLs. Germany and Poland provided information on GAP and MRLs.

IDENTITY

ISO common name: maleic hydrazide

Chemical name
IUPAC: 6-hydroxy-2*H*-pyridazin-3-one; 1,2-dihydropyridazine-3,6-dione
CA: 6-hydroxy-3(2*H*)-pyridazinone; 1,2-dihydro-3,6-pyridazinedione

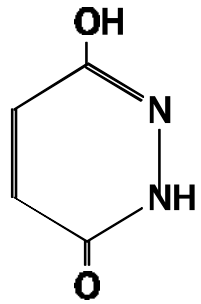
CAS No: 123-33-1

CIPAC No: 310

Synonymes: MH

Molecular formula: $C_4H_4N_2O_2$

Structural formula:



Molecular weight: 112.1

Physical and chemical properties

Pure active ingredient

Vapour pressure: $<10^{-5}$ Pa at 25°C, purity 99.7% (Knauppila *et al.*, 1989)

Melting point: 298-300°C at 99.9% purity (Anon., 1989a)

Octanol/water partition coefficient (log P_{OW}):		-0.68 at pH 5 -2.01 at pH 7 -2.42 at pH 9, purity 99.6% (Kerish and Parkins, 1985)
Solubility:	methanol	4.179 g/l
	water	4.507 g/l
	toluene	<1 mg/l
	hexane	<1 mg/l
		at 25-26°C, 99.6% purity (Jewell, 1989)
Specific gravity:		1.61 g/cm^3 (Sweetapple, 1988)
Hydrolysis (45°C, dark):		stable at pH 3, 6 and 9 after 61 days (Lacadie, 1976)
Hydrolysis (80°C, dark):		stable at pH 3, 6 and 9 after 30 days (Lacadie, 1976)
Photolysis (water, at 25°C):		essentially stable at pH 5 and 7 for 30 days, half-life 15.9 days at pH 9 (Fackler, 1993) degradation products: maleic acid, succinic acid (Schocken, 1994)
Photolysis (in air):		stable at 20°C after irradiation for 7 days (Riggs, 1995a)
Dissociation constant:		pK_a 5.62 at 20 $\pm$ 1°C (Book and Thomas, 1988)
pH (25°C):		3.61 at 0.4% in water 4.32 of 1% in water/dioxane, 50:50 (Mattschei, 1989)
Oxidation:		Slight increase in temperature during the first 30 min after mixing with $KMnO_4$ (Sanders, 1990)

Technical material

Purity:	>99%
Melting range:	300-302°C (Riggs, 1995b)
Thermal stability in air:	stable at 55°C in water-saturated air for 14 days (Riggs, 1995c)
Stability in presence of 315L stainless steel:	stable at 20°C for 16 weeks (Riggs, 1995d)
Storage stability:	stable at 25°C for 1 year (Thomson, 1990)

Formulations

Maleic hydrazide (as the potassium salt) is formulated as dispersible granules (SG, GR) and as liquid formulations (SL, SC).

METABOLISM AND ENVIRONMENTAL FATE

Animal metabolism

Caley and Cameron (1990) and Caley *et al.* (1990a) studied the metabolism of [^{14}C]maleic hydrazide in male and female Sprague-Dawley rats at a target level of 2 mg/kg bw given as a single intravenous dose, a single oral dose or an oral dose after 14 daily doses of unlabelled maleic hydrazide at 2 mg/kg/day, and given at a target level of 100 mg/kg as a single oral dose.

After either intravenous or oral administration radioactivity was eliminated rapidly during the first 24 hours (Table 1). The main route of elimination was via the urine with more than 40% of the administered dose excreted within 4 hours. Excretion in the urine was faster initially after intravenous dosing but the mean total excretion was similar in all dose groups (76.71 to 86.97%). The total elimination in the faeces was between 9.4 and 14.4% of the oral doses and 6.3% and 5.1% of the intravenous dose in males and females respectively. Radioactivity in the expired air accounted for less than 0.5% of the administered dose. The levels of radioactivity in all the tissues and organs combined accounted for less than 0.01% of the total administered dose. Less than 0.5% of the administered radioactivity remained in the carcase.

Table 1. Excretion of [^{14}C]maleic hydrazide after oral and intravenous administration to rats.

Ref.	Administration method, Dose	Time, h	Mean % of administered dose					
			Urine		Faeces		Total	
			Male	Female	Male	Female	Male	Female
Caley *et al.*, 1990;	Intravenous 2 mg/kg	0-4 0-24 0-168	65.2 78.2 80.3	59.5 85.3 87.0	X 5.3 6.3	X 4.4 5.1	65.2 83.4 86.6	59.5 89.7 92.1
Caley and Cameron, 1990	Oral 2 mg/kg	0-4 0-24 0-168	43.8 82.8 83.4	54.8 77.1 78.5	X 12.4 13.0	X 9.7 10.5	43.8 95.1 96.3	54.8 86.8 89.0
	Multiple Oral 2 mg/kg	0-4 0-24 0-168	44.4 75.8 77.1	53.3 74.8 76.7	X 13.3 14.4	X 11.2 13.5	44.4 89.1 91.5	53.3 86.0 90.2
	Oral 100 mg/kg	0-4 0-24 0-168	47.5 78.9 80.0	45.0 78.4 80.7	X 9.0 9.4	X 11.0 11.5	47.5 87.9 89.4	45.0 89.4 92.3

X = no faeces available

The urine contained two compounds: the major component was maleic hydrazide and the minor was tentatively identified as its sulfate conjugate. Because of poor chromatography the identification of faecel metabolites could not be confirmed but there were at least two components, possibly maleic hydrazide and fumaric acid.

Hawkins *et al.* (1984) studied the percutaneous absorption of [^{14}C]maleic hydrazide in rabbits. A liquid formulation of the potassium salt was applied to the shaved backs of New Zealand White rabbits for a 4-hour exposure period at 16 mg/kg bw. Urine was collected for periods of 0-4, 4-24, 24-48, 48-72 and 72-96 hours. Faeces were collected at 24-hour intervals for 96 hours. The rabbits were killed at 96 hours. ^{14}C was measured in the urine, faeces, cotton wool swabs (used for removing the residual material from the dose sites after completing the exposure), dressings and carcases. Most of the radioactivity was eliminated in the urine, 24% and 39% of the total applied dose in males and females respectively (Table 2). Urinary elimination was rapid during the first 24

hours, accounting for 22% and 38% of the administered dose in males and females respectively. Less than 0.2% was excreted in the faeces. The total absorption of maleic hydrazide was calculated to be 26% and 40% of the applied dose in males and females respectively. Most of the urinary radioactivity (88% to 96.5%) was associated with unchanged maleic hydrazide.

Table 2. Mean excretion of radioactivity in the urine and faeces of rabbits after topical application of [^{14}C]maleic hydrazide (Hawkins *et al.*, 1984).

Time, h	^{14}C, % of applied					
	Male		Female		Male and female	
	Mean	SD	Mean	SD	Mean	SD
Urine						
0-4	2.6	4.5	12.5	22	7.5	15
4-24	19	13.5	25	14	22	13
24-48	1.6	0.38	0.77	0.38	1.2	0.57
48-72	0.38	0.18	0.89	1.15	0.64	0.79
72-96	0.14	0.12	0.11	0.06	0.13	0.09
Cage washings						
0-48	1.4	2.4	0.00	0.00	0.69	1.7
48-96	0.84	1.3	0.58	0.76	0.71	0.94
Faeces						
0-24	0.19	0.17	0.13	0.10	0.16	0.13
24-48	0.00	0.00	0.02	0.04	0.01	0.03
48-72	0.00	0.00	0.00	0.00	0.00	0.00
72-96	0.00	0.00	0.02	0.04	0.01	0.03
Dressings	11	5.7	12	8.9	11.5	6.7
Dose washings[1]	54	14	40	16.1	47	16
Total	91.15		92.02		91.55	
Systemic absorption[2]	26.15		40.02		33.05	

[1] Recovered from cotton wool swabs
[2] Urine, faeces and cage washings
SD = standard deviation

Lactating goats. Cameron *et al.* (1992) examined the metabolism of maleic hydrazide in a non-pregnant lactating goat dosed twice daily by gavage with 7.5 mg/kg bw [^{14}C]maleic hydrazide after milking for 32 days. Urine and faeces were collected 12 hours after each dosing and milk immediately before each dosing and immediately before slaughter. Liver, kidney, fat (renal and subcutaneous), muscle, bile and plasma were collected at slaughter and whole blood immediately before slaughter. All tissues were sequentially extracted with methanol/water (90:10) and acetonitrile/water (90:10). After concentration, the extracts were heated at 60°C for 4 hours with 4 M HCl, then evaporated and reconstituted in 90:10 methanol/water. A sample of liver was hydrolysed by incubation with 4 N NaOH at 60°C for 24 hours. Liver was also digested with protease by incubating with pepsin in 0.1 M HCl for 96 hours at 37°C. A subsample of milk extract was combined with 0.1 M sodium acetate (pH 5) containing β-glucuronidase with sulfatase activity added and incubated at 37°C for 17 hours.

Approximately 87% of the administered dose was recovered in the urine, faeces, cage wash, tissues and milk (Table 3). The main route of elimination was in the urine, which accounted for approximately 63% of the administered dose.

Table 3. ^{14}C in urine, faeces, cage wash, milk and tissues from a goat administered [^{14}C]maleic hydrazide.

Ref.	Sample	Interval, h	Total recovered, % of administered dose
Cameron, *et al.*, 1992	Urine	12 24 48 72 84 (total)	8.02 7.30 16.87 18.63 12.12 (62.94)
	Faeces	12 24 48 72 84 (total)	0.06 1.65 6.10 7.31 8.03 (23.15)
	Cage wash	12 24 48 72 84 (total)	0.04 0.09 0.08 0.08 0.21 (0.50)
	Milk	12 24 36 48 60 72 84 96 108 (total)	0.00 0.002 0.015 0.008 0.025 0.011 0.027 0.014 0.022 (0.13)
	Tissues	(total)	(0.06)
	TOTAL		86.78

The ^{14}C in milk increased from 0.2 mg/kg as maleic hydrazide (pm, day 1) to 0.88 mg/kg (am, day 4), and decreased to 0.67 mg/kg within 24 hours of the final dose. Only 0.06% of the administered dose was recovered from the tissues, in which the highest levels of radioactivity were observed in the liver (1.3 mg/kg) and kidneys (3.3 mg/kg). The results are shown in Table 4.

Table 4. ^{14}C in milk, blood, bile and tissues from a goat administered [^{14}C]maleic hydrazide.

Ref.	Sample	Interval, h	^{14}C, mg/kg as maleic hydrazide
Cameron *et al*., 1992	Milk	12 24 36 48 60 72 84 96 108	0.00 0.20 0.54 0.61 0.79 0.79 0.88 0.85 0.67
	Subcutaneous fat	slaughter	0.19
	Renal fat	slaughter	0.11
	Muscle (fore)	slaughter	0.44
	Muscle (hind)	slaughter	0.44
	Kidney	slaughter	3.3
	Liver	slaughter	1.3
	Whole blood	slaughter	0.63
	Bile	slaughter	1.3
	Plasma	slaughter	0.71

The nature of the radioactive residues in the tissues and milk in extracted and hydrolysed samples is shown in Table 5. In the kidneys the major metabolite, accounting for 91% of the ^{14}C, was a polar compound, postulated to be a conjugate. Acid hydrolysis of this yielded maleic hydrazide and a relatively non-polar component with an HPLC retention time of 15 min. In liver approximately 43% of the ^{14}C was not extractable with methanol or acetonitrile, but protease treatment increased the extractable residues to approximately 98%. After acid hydrolysis, the level of the polar conjugate in liver decreased with a corresponding increase in maleic hydrazide and two metabolites with HPLC retention times of 10 and 15 minutes. The 10 minute retention time is similar to that of fumaric acid. Maleic hydrazide and the polar conjugate were also identified in muscle and fat after acid hydrolysis. Approximately 13% of the ^{14}C in milk was identified as maleic hydrazide, and enzyme treatment indicated that the major polar components were sulfate conjugates. Maleimide did not co-chromatograph with any unknown metabolites in milk.

Table 5. Radioactive residues in extracted and hydrolysed tissues and milk from a goat treated with [^{14}C]maleic hydrazide.

Report	Sample	^{14}C, mg/kg as maleic hydrazide						
		MH [1]	Conjugate[2]	Unknown 1[3]	Unknown 2[4]	Other	Un-extractable	Total
Cameron *et*	Extracted							
al., 1992	Kidney	nd	2.77	nd	nd	0.19	0.07	3.03
	Liver	nd	0.51	nd	0.04	0.06	0.56	1.17
	Muscle	0.03	0.26	nd	0.05	<0.01	0.01	0.36
	Fat	nd	0.16	nd	0.01	0.01	<0.01	0.19
	Milk	0.11	0.39	0.06	0.14	<0.01	0.03	0.74
	Acid-hydrolysed							
	Kidney	0.96	1.79	nd	0.13	0.03	0.07	2.98
	Liver	0.16	0.16	0.10	0.13	0.07	0.56	1.18
	Muscle	0.15	0.05	0.05	0.15	0.02	0.01	0.43
	Fat	0.05	0.07	0.01	0.03	0.02	<0.01	0.19
	Enzyme-hydrolysed							
	Milk	0.38	0.05	0.05	0.25	0.02	0.03	0.78
	Protease-hydrolysed							
	Liver	0.25	0.43	nd	0.09	0.01	0.06	0.84
	Protease- and acid-hydrolysed							
	Liver	0.30	0.28	nd	0.27	0.03	0.06	0.94

nd = not detected
[1] maleic hydrazide
[2] Conjugate had a retention time of approximately 8 min
[3] HPLC retention time 10 min, later identified as fumaric acid
[4] HPLC retention time 15 min, tentatively identified as pyridazinone

Cameron and Johnston (1995) subjected goat milk extracts to HPLC analysis after storing the milk at about -20°C for periods up to 18 months. The stability of the radiolabelled components under these storage conditions was determined and a major unknown metabolite was identified as 3-pyridazinone.

The profile of radioactivity observed in enzyme-deconjugated milk extracts confirmed the stability of the radiolabelled components. Three main components were detected by radio-HPLC after each storage period. The main compound was eluted at the same retention time as maleic hydrazide and represented about 50.5% of the radioactivity after 1 month and 67.5% after 18 months. A less polar compound now known to be 3-pyradizinone accounted for 32.8% after 1 month and 22.1% after 18 months and the third, more polar, component represented 7.2% after 1 month and 10.4% after 18 months. A further component seen in milk extracts at 1 month and representing 6.8% of the injected radioactivity was not observed at the later time: its disappearance was considered to result from the breakdown of polar conjugated material, probably as a result of more efficient enzymatic deconjugation.

Lactating cows. Jackson and Hall (1992a) dosed twelve lactating cows intrarumenally in 4 groups of 3 animals each twice daily for 28 days at 0, 0.45, 1.36 and 4.5 mg/kg bw/day with [^{14}C]maleic hydrazide. Milk was collected daily throughout the dosing period and the cows were slaughtered 6 hours after the final dose. The levels of ^{14}C in the milk are shwon in Table 6 and in the edible tissues in Table 7.

The ^{14}C in the milk reached a plateau after 3-4 days of about 0.02 mg/kg as maleic hydrazide from the low dose, 0.06 mg/kg from the medium dose, and 0.2 mg/kg from the high dose, indicating a linear relationship between dose and residue.

Table 6. ^{14}C in milk from lactating cows.

Ref.		Mean ^{14}C, mg/kg as maleic hydrazide		
	Days	0.45 mg/kg bw/day	1.35 mg/kg bw/day	4.5 mg/kg bw/day
Jackson and Hall, 1992a	1-3	0.011-0.016	0.033-0.049	0.12-0.2
	4	0.018	0.055	0.21
	8	0.02	0.062	0.2
	9-28	0.019-0.021	0.052-0.064	0.19-0.22

Table 7. ^{14}C in tissues from lactating cows.

Ref.	Sample	Mean ^{14}C, mg/kg as maleic hydrazide		
		0.45 bw/day	1.35 bw/day	4.5 bw/day
Jackson and Hall, 1992a	Liver	0.08[a]	0.24[c]	0.8[d]
	Kidney	0.34[a]	1.0[c]	3.9[d]
	Muscle	0.02[a]	0.09[c]	0.2[d]
	Fat	0.05[b]	0.1[d]	0.4[e]

LOD a 0.0, b 0.03, c 0.04, d 0.1, c 0.3 mg/kg

Jackson and Hall (1992b) dosed groups of ten hens (average body weight 2 kg) dosed with [^{14}C]maleic hydrazide at 1, 3 and 10 mg/kg bw/day. The test solution was administered by gavage twice daily for 28 days. Eggs were collected daily and liver, kidneys, muscle (breast and thigh), abdominal fat and skin with associated fat were collected at slaughter.

Egg yolks and whites were separated and daily samples in each dose group were pooled. Tissue samples were also pooled. The levels of ^{14}C are shown in Tables 8 and 9. The residue levels were too low for the identification of metabolites.

Table 8. ^{14}C in pooled samples of egg whites and yolks from hens treated with ^{14}C-maleic hydrazide for 28 days.

Ref.	Days	Mean ^{14}C, mg/kg as maleic hydrazide					
		1 mg/kg bw/day		3 mg/kg bw/day		10 mg/kg bw/day	
		White	Yolk	White	Yolk	White	Yolk
Jackson and Hall, 1992b	1	0.0028	<0.001	0.028	0.001	0.156	0.01
	2	0.0088	0.001	0.045	0.010	0.181	0.04
	3	0.0115	0.004	0.051	0.019	0.192	0.07
	4	0.0124	0.007	0.054	0.031	0.189	0.10
	5	0.013	0.010	0.057	0.042	0.210	0.14
	6	0.0127	0.013	0.061	0.051	0.208	0.17
	7 to 14	0.013 to 0.0152	0.015 to 0.018	0.053 to 0.057	0.057 to 0.062	0.19 to 0.203	0.20 to 0.23
	15 to 28	0.0126 to 0.0147	0.018 to 0.019	0.055 to 0.069	0.060 to 0.073	0.190 to 0.203	0.20 to 0.23

Table 9. ^{14}C in tissues from hens treated with [^{14}C]maleic hydrazide for 28 days.

Ref.	Sample	Mean ^{14}C, mg/kg as maleic hydrazide		
		1 mg/kg bw /day	3 mg/kg bw/day	10 mg/kg bw/day
Jackson and Hall, 1992b	Liver	0.016	0.059	0.19
	Kidney	0.059	0.235	0.78
	Breast muscle	0.022	0.080	0.27
	Thigh muscle	0.014	0.059	0.18
	Abdominal fat	0.006	0.020	0.06
	Skin and fat	0.022	0.060	0.18

Maleic hydrazide is rapidly metabolized by hens. The ^{14}C reached plateaux in egg whites after 5 days and yolks after about 8 days of 0.01-0.02 mg/kg from the low dose, 0.05-0.07 mg/kg from the mid dose, and 0.19-0.23 mg/kg from the high dose. The tissue residues were highest in the kidneys (0.06-0.8 mg/kg) and lowest in abdominal fat (0.006-0.06 mg/kg). Radioactive residues in the muscle, liver and skin ranged from 0.01-0.02 mg/kg at the low dose yo 0.18-0.27 mg/kg at the high dose. The residues were not high enough to identify metabolites.

Johnston *et al.* (1993) dosed six laying hens twice daily for 3½ days by gavage with [^{14}C]maleic hydrazide at 15 mg/kg bw/day (equivalent to 196 ppm in the diet). The excreta were collected daily and the cage rinse was retained. Eggs were collected daily and separated into whites and yolks. Liver, kidney, muscle (breast and thigh), abdominal fat pad, skin with associated fat, heart, lungs, spleen, whole blood and plasma were collected at slaughter.

The ^{14}C levels in the eggs, tissues, excreta and cage rinse are shown in Table 10. The maximum residues in egg whites and yolks were 0.33 and 0.23 mg/kg as maleic hydrazide respectively. The residues in the tissues ranged from 0.04 to 0.2 mg/kg. Approximately 98% of the administered dose was recovered in the excreta and cage rinse within 24 h after the final dose. The distribution of extractable and unextractable ^{14}C in tissues and eggs is shown in Table 11.

Table 10. ^{14}C in eggs, tissues, excreta and cage rinse from hens treated with [^{14}C]maleic hydrazide for 3½ days.

Report	Sample	Hours after first dose	^{14}C	
			mg/kg as maleic hydrazide	% of administered dose
Johnston et al., 1993	Egg white	24 78 72 96 120	0.023 0.295 0.293 0.334 0.201	0.001 0.008 0.009 0.010 0.006
	Egg yolk	24 48 72 96 120	<0.01 0.07 0.12 0.18 0.23	<0.001 0.002 0.001 0.002 0.003
	Abdominal fat	slaughter[1]	0.04	<0.001
	Heart	slaughter	0.10	<0.001
	Kidney	slaughter	0.20	0.002
	Liver	slaughter	0.13	0.005
	Lung	slaughter	0.12	0.001
	Breast muscle	slaughter	0.11	
	Thigh muscle	slaughter	0.09	
	Spleen	slaughter	0.10	<0.001
	Skin with fat	slaughter	0.07	
	Plasma	slaughter	0.13	
	Whole blood	slaughter	0.09	
	Excreta	24 48 72 96 (total)		27.16 27.09 27.63 14.42 (96.30)
	Cage wash	24 48 72 96 (total)		0.35 0.38 0.67 0.58 (1.98)

[1] 24 hours after final dose

Table 11. Extractable and unextractable radioactive residues from hen tissues and eggs.

Ref.	Sample	mg/kg as maleic hydrazide	% of ^{14}C in sample		
			Extractable	Unextractable	Total
Johnston *et al.*, 1993	Kidney	0.18	74.6	29.9	104.5
	Liver	0.13	71.5	19.2	90.7
	Breast muscle	0.11	78.5	12.7	91.2
	Egg white	0.197	73.4	32.4	105.8
	Egg yolk	0.26	112.1	25.7	137.8

The residues were determined by HPLC. Their distribution is shown in Table 12. In the kidneys after extraction about 21% of the TRR was associated with a nonpolar metabolite, <5% was maleic hydrazide, and about 25% was an unidentified polar compound. The major extractable residue in liver (58% of the ^{14}C) and muscle (64%) was the nonpolar metabolite found in the kidneys. In egg white, the polar metabolite constituted about 32% of the TRR and the nonpolar metabolite about 33%. Maleic hydrazide accounted for about 51% of the ^{14}C in egg yolk, which also contained the unknown polar and nonpolar metabolites. After acid treatment, the level of the polar compound in the kdineys, egg white and yolk extracts decreased with a corresponding increase in maleic hydrazide and/or other compounds. Maleimide did not co-chromatograph with any of the metabolites. Mass spectrometry of the nonpolar metabolite isolated from egg white indicated that it was a conjugate of a methylated maleic hydrazide, probably the O-methyl derivative.

Table 12. Distribution of radioactive residues in tissues and eggs.

Ref.	Sample	Radioactive residues, mg/kg as maleic hydrazide					
		MH	Polar metabolite[1]	Nonpolar metabolite[2]	Other compounds	Unextractabl	Total
Johnston et al., 1993	After extraction						
	Kidney	<0.01	0.06	0.05	0.02	0.10	0.24
	Liver	nd	<0.01	0.07	0.02	0.02	0.12
	Muscle	<0.01	<0.01	0.07	<0.01	0.01	0.11
	Egg white	nd	0.061	0.063	0.004	0.064	0.192
	Egg yolk	0.18	0.03	0.02	0.05	0.07	0.35
	After acid hydrolysis						
	Kidney	0.05	<0.01	0.06	0.01	0.10	0.23
	Liver	<0.01	<0.01	0.06	0.01	0.02	0.11
	Muscle	<0.01	nd	0.05	0.01	0.01	0.08
	Egg white	0.061	nd	0.066	0.005	0.027	0.159
	Egg yolk	0.18	nd	0.05	0.03	0.07	0.33

nd = no HPLC peak MH = maleic hydrazide

[1] Unknown compound with HPLC retention time 8 min.

[2] HPLC retention time 15 min. tentatively identified as conjugae of O-methyl maleic hydrazide

Plant metabolism

The metabolism of [4,5- ^{14}C]maleic hydrazide was investigated in potatoes and onions.

Lengen (1988) treated potato plants with single applications of two maleic hydrazide formulations spiked with 0.007 g of the radiolabelled compound. Tubers and vines were collected 1 and 12 weeks after treatment. The tubers were washed with cold water to remove surface soil and debris and peeled, and the vines were air-dried. The peeled tubers were extracted twice with 20% aqueous methanol and twice with 0.1 N formic acid (pH 4.5). The ^{14}C levels were highest in the vines (mean 202 mg/kg as maleic hydrazide) and at similar levels the tubers and peels (26 and 25 mg/kg). The results are shown in Table 13.

Table 13. ^{14}C in potato tubers, peel and vines harvested 1 and 12 weeks after treatment with two formulations of [^{14}C]maleic hydrazide.

Ref.	Formulation	PHI, weeks	^{14}C, mg/kg as maleic hydrazide		
			Tubers	Peels	Vines
Lengen, 1988	SG	1	32	40	211
		12	24	19	215
	SL	1	19	16	198
		12	30	26	183

About 90% of the ^{14}C in the peeled tubers was extractable with aqueous methanol and formic acid. Maleic hydrazide was the major residue, indicating that only limited metabolism occurred. The glucose conjugate of maleic hydrazide was the main metabolite. The identities were confirmed by thermospray mass spectrometry. Fumaric acid, maleimide and maleic acid were also identified. The results are shown in Table 14.

Table 14. Compounds identified in extracts of potato tubers.

Ref.	Compound	Extractable residues as % of total residues			
		SG		SL	
		1 wk	12 wk	1 wk	12 wk
Lengen, 1988	Maleic hydrazide	84.2	52.0	78.7	75.3
	Maleic acid	nd	1.5	<0.1	0.2
	Fumaric acid	0.7	1.5	1.2	1.8
	MH glucoside	9.4	13.3	7.3	6.4
	Maleimide	0.2	nd	0.2	0.2

nd = not detected

In summary, maleic hydrazide was translocated from the potato foliage to the tubers which contained maleic hydrazide and its glucoside as the major residues. Maleic acid, fumaric acid and maleimide were minor metabolites.

A single application (hand-held sprayer) of [^{14}C]maleic hydrazide at a rate equivalent to 2.3 kg/ha was applied to potato plants which were harvested 1 hour, 2 weeks and 8 weeks after

treatment (Caley *et al.*, 1990b). Excess soil was brushed off and discarded and the tubers were washed in distilled water. Vines were not washed. Potato tubers and vines were radio-assayed. The results are shown in Table 15. After 1 hour virtually 100% of the ^{14}C was in the vines with only 0.04% the tubers. After 8 weeks about 10% of the ^{14}C was in the vines and 90% in the tubers.

Table 15. ^{14}C in rinsed potatoes, wash water and vines at intervals after treatment with [^{14}C]maleic hydrazide.

Ref.	PHI	Sample	Mean ^{14}C, mg/kg as maleic hydrazide
Caley *et al.*, 1990b	1 h	tubers: tissue wash	 0.035 0.009
		vines	109
	2 wks	tubers: tissue wash	 57 0.064
		vines	24.55
	8 wk	tubers: tissue wash	 67 36.4
		vines	7.73

Six tuber samples from the treated plots were harvested at 2 and 8 weeks. Individual and pooled samples (composites of treated tubers and vines) were extracted sequentially with 20% aqueous methanol and 0.1 N formic acid (Table 16). About 80-85% of the ^{14}C was extractable with methanol. HPLC and TLC of the methanol extract yielded single radioactive peaks shown by co-chromatography to be due to maleic hydrazide.

Table 16. Extractable and unextractable radioactive residues in pooled samples of potatoes harvested at intervals after treatment with [^{14}C]maleic hydrazide.

Ref.	PHI, weeks	% of ^{14}C in sample			
		Extracted by		Unextractable	Total
		20% aqueous methanol	0.1 N formic acid		
Caley *et al.*, 1990b	2	85.74	7.41	7.26	100.4
	8	80.77	4.22	12.39	97.4

In summary, maleic hydrazide was translocated from potato leaves to the tubers, with about 60% translocation in 8 weeks. All the radioactivity in the methanol extracts of the tubers was due to maleic hydrazide.

Caley *et al.* (1990c) treated onion tops with a single application of [^{14}C]maleic hydrazide by hand-held sprayer at a rate equivalent to 2.3 kg/ha when about half the tops had fallen. Plants were sampled 1 hour and 2 weeks after treatment. Excess soil was brushed off and discarded. The leaves and bulbs collected 1 hour after treatment were washed with distilled water. The leaves of plants

sampled after 2 weeks were discarded and the bulbs were washed. Samples were oven-dried to a constant weight at 40°C and the radioactivities were expressed on a dry-weight basis. Six of the samples harvested 2 weeks after application and a pooled sample (about 2 g of each) were extracted with 20% aqueous methanol and 0.1 N formic acid.

The results are shown in Table 17. The levels of radioactivity in the bulbs after 2 weeks were about ten times the initial levels.

Table 17. ^{14}C in onion leaves and bulbs after treatment with ^{14}C-maleic hydrazide.

Ref.	PHI	Sample	Mean ^{14}C[1]
Caley *et al.*, 1990c	1 h	leaves	528
		bulbs	14.8
	2 wks	bulbs	113

[1] mg maleic hydrazide equivalents/kg dry weight

^{14}C found in rinsed leaves and bulbs and the wash water is shown in Table 18. The mean proportions of the ^{14}C found in the wash water were about 22 and 51% from the leaves and bulbs respectively after 1 hour and 0.2% from the bulbs after 2 weeks

Table 18. ^{14}C in rinsed onions and wash water 1 hour and 2 weeks after treatment with [^{14}C]maleic hydrazide.

Ref.	Sample harvest	Sample	Mean ^{14}C[1]
Caley *et al.*, 1990c	1 h	Leaves:	
		rinsed tissue	2764
		wash	774
		Bulbs:	
		rinsed tissue	240
		wash	254
	2 wks	Bulbs:	
		rinsed tissue	2390
		wash	4.1

[1] Expressed as total µg maleic hydrazide equivalents

The distribution of ^{14}C in the analytical fractions from the bulbs after 2 weeks is shown in Table 19. About 90% of the ^{14}C was extractable with methanol. The methanol extracts contained a single radioactive compound identified by HPLC and thin-layer co-chromatography as maleic hydrazide.

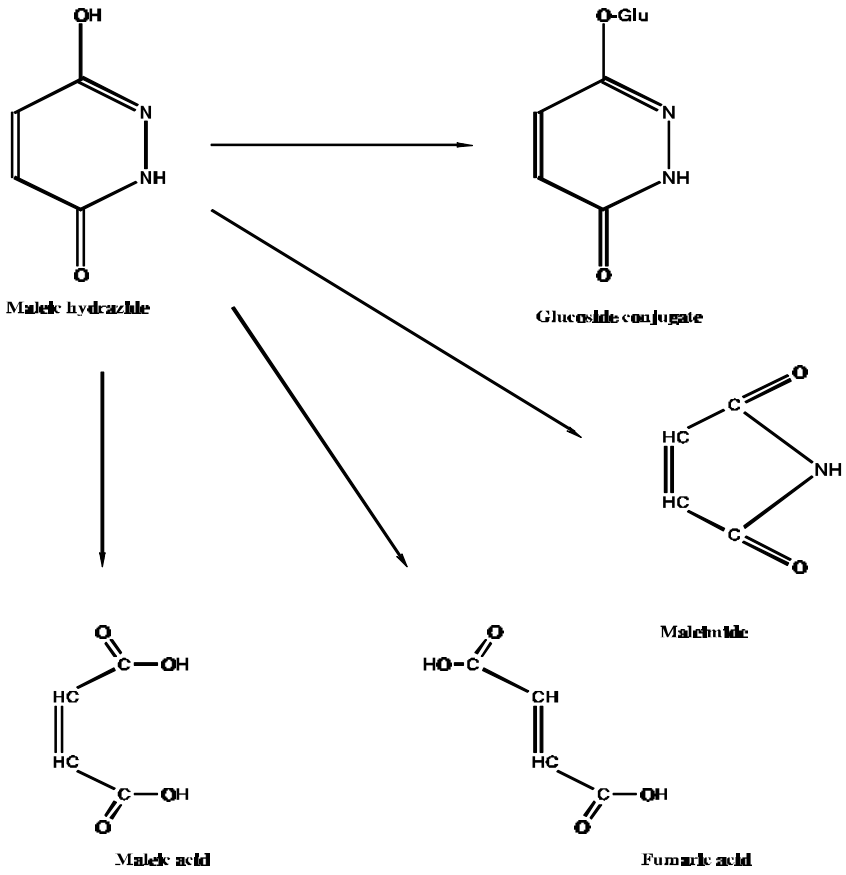
Table 19. Extractable and unextractable radioactive residues in onion bulbs harvested 2 weeks after treatment with [^{14}C]maleic hydrazide.

Sample no.	% of ^{14}C in sample		
	Extracted by	Unextractable	Total

	20% aqueous methanol	0.1 N formic acid		
1	87.19	6.71	1.65	95.55
2	89.45	6.86	1.89	98.20
3	85.71	6.64	1.46	93.81
4	87.43	7.32	1.73	96.48
5	85.38	5.68	1.15	92.21
6	82.32	8.76	2.08	93.16
1-6 pooled	90.62	5.95	2.60	99.17

In summary, maleic hydrazide was translocated from onion tops to the bulbs. The methanol-extractable metabolite in the bulbs harvested 2 weeks after treatment was maleic hydrazide. Proposed metabolic pathways in plants are shown in Figure 1.

Figure 1. Proposed metabolic pathways of maleic hydrazide in plants.



Environmental fate in soil

Aanaerobic degradation

Mackie *et al.* (1991a) investigated the degradation of [^{14}C]maleic hydrazide aged aerobically in loamy sand for 12 hours and then incubated under flooded anaerobic conditions for 60 days. Overall mean recoveries were 93.6-98.3% over the aerobic and anaerobic incubation periods. $^{14}CO_2$ evolution increased to 70.3% 60 days after flooding. Volatile organic ^{14}C was very low (mean $\leq$0.08%). The proportion of ^{14}C extractable with methanol/water decreased with time from 56.6% at day 0 to 3.5% 60 days after flooding. The proportion of the radioactivity in the water decreased from 30% at 30 days to 0.86% at 60 days. Bound radioactivity at 60 days accounted for 22.65% of the applied dose. Maleic hydrazide was degraded steadily to maleic acid, maleimide and an unidentified component, which were detected throughout the incubation period, as well as to $^{14}CO_2$.

Lengen (1986) investigated the distribution of radioactivity in a sandy loam soil incubated with 4.35 mg/kg [^{14}C]maleic hydrazide under anaerobic conditions (Table 20). When anaerobic conditions were established, 13 days of aerobic incubation 19-27% of the applied radioactivity had been evolved as $^{14}CO_2$.

Table 20. Distribution (%) of radioactivity in anaerobic soils treated with [^{14}C]maleic hydrazide.

Ref.	Days incubation	^{14}C, % of TRR					
		CO_2	Other volatiles	Water	Extracted from soil	Bound in soil	Total
Lengen, 1986	0	27.2[1]	<0.01	0.32	16.74	39.04	83.3
	32	19.9	<0.01	4.22	4.65	45.30	74.07
	60	23.8	<0.01	3.72	2.42	44.75	74.69

[1] One sample analysed, duplicate lost

The water phase of the anaerobic samples on day 0 contained less than 0.4% of the radioactivity, suggesting that the ^{14}C residues would not be readily desorbed from the soil. Extraction with isopropanol/water/ammonia removed 16.7% of the applied radioactivity and 39% remained bound. The soil extract was cleaned up on reverse-phase columns and the eluate analysed by HPLC. Additional residues were eluted with 1*N* formic acid and chromatographed on silica gel TLC plates. HPLC showed less than 2% of the ^{14}C as maleic hydrazide and TLC an additional 0.1%. Four other components, each less than 3% of the TRR were also detected.

The extractable soil residues decreased during the 60-day anaerobic incubation to less than 5%, while bound material increased to about 45%. The level of maleic hydrazide decreased to 1.3%, with other products (maleamic acid, maleic/fumaric acids, succinic acid and lactic acid) generally not exceeding 0.6%. The water phase showed a slight increase in ^{14}C activity to about 4% and TLC analysis indicated that it contained less than 1% of the initial ^{14}C as maleic hydrazide.

Aerobic degradation

Mackie *et al.* (1991b) studied the degradation of [^{14}C]maleic hydrazide in soil under aerobic conditions. $^{14}CO_2$, ^{14}C in organic volatiles and levels of radioactivity in the soil were determined throughout the 90-day incubation. Overall mean recoveries ranged from 95.6% to 101% during this period. Cumulative $^{14}CO_2$ evolution rose to 71.6% at 90 days. Organic volatile evolution was <5%. Radioactivity extractable with 1:1 methanol/water decreased from 62.4% at day 0 to 0.44% at 90 days. Bound radioactivity at 90 days accounted for 24.5% of the applied dose.

TLC indicated that maleic hydrazide was rapidly degraded. Maleic acid, maleimide and up to 5 unidentified components were detected in soil extracts throughout the incubation period. The proportions of these compounds were low because of further degradation to $^{14}CO_2$. HPLC analysis

of methanol/water extracts of samples taken during the first 5 days confirmed the presence of maleic hydrazide, maleimide and 3 unidentified components.

The half-life of maleic hydrazide under these conditions was 11 hours.

Mobility

Lengen (1985) determined the adsorption of the potassium salt of [^{14}C]maleic hydrazide to four soils. At equilibrium, log plots of the concentrations in soil against those in the aqueous phase conformed (with correlation co-efficients >0.9) to the Freundlich equation

$$\log S = \log k + 1/n \log C$$

where S is the maleic hydrazide adsorbed to the soil, C the concentration of maleic hydrazide in solution and k and n are the y-intercept and slope, respectively, of the curve. The results were as follows.

Soil	$k_{adsorption}$ (28 h)	$k_{desorption}$ (60-72 h)
Wisconsin sand	0.21	0.39
Washington silt loam	0.23	14.45
Connecticut sandy loam	2.61	2.97
Texas sandy clay loam	0.14	0.6

The k values determined by linear regression analysis indicated low adsorption to soil and thus a rather high potential for leaching.

In the same paper Lengen reported the mobility of [^{14}C]maleic hydrazide (potassium salt) in four leaching columns packed with the same soils. The test material was allowed to age aerobically for 14 days and the treated soils were then added to the tops of the soil columns and leached with 50 cm of water. Only 4.9% of the applied radioactivity was leached from the sandy loam column, and most of the radioactivity remained in the top 15 cm.

Haig *et al.* (1991) obtained different results. The treated soil was allowed to age for 12 hours only (about the half-life of maleic hydrazide under aerobic conditions). Overall mean recoveries from the loamy sand and sand were 102.2% and 103.1% of the applied radioactivity respectively including $^{14}CO_2$ evolved during the 7-day leaching period ($\leq$25%). Leaching was greatest from the sand with 100.8% of the ^{14}C recovered in the leachate, but only 39.8% from the loamy sand. The total extractable radioactivity was generally low for the loamy sand (5.37%) and negligible for the sand (0.22%). Bound residues accounted for 29.3% of the applied dose for the loamy sand and 1.1% for the sand. The results indicate that maleic hydrazide has the potential to leach, but will be degraded rapidly by ageing to products which bind strongly to the soil and are therefore not readily leached.

Field dissipation

Studies were conducted at several sites with the potassium salt.

Lengen and Batorewicz (1986, 1987) showed that maleic hydrazide formulated as an SG dissipated rapidly from field sites in Connecticut and New Mexico (USA). The half-life was estimated to be less than two weeks in a sandy clay loam and 5 days in a clay loam soil.

Dykman (1993 a,b,c) conducted field dissipation studies in California, Washington and North Carolina.

In California a turf sandy loam soil with about 0.6% organic matter was treated at 6.7 kg a.i/ha (1993a). The half-life was 5.3-6 days. The concentration was 3 mg/kg at day 0 and <0.01 mg/kg (the LOD) after 30 days. Residues at 15-30 cm were below the LOD after 14 days.

A Washington state potato field of sandy loam soil with about 0.7% organic matter was treated at 3.4 kg ai/ha (1993b). The half-life was 2.6 days. The concentration started at 0.66 mg/kg and became below the LOD after 14 days. Levels of maleic hydrazide near the LOD were found at 15-30 cm.

In North Carolina a tobacco field of sandy loam clay soil, organic matter about 1.4 %, was treated at 5.04 kg ai/ha (1993c). The half-life was 5.8-7.3 days. The initial maleic hydrazide concentration was 1.6 mg/kg and became lower than the LOD after 27 days.

None of the sites showed residues of maleic hydrazide below 30 cm.

Photolysis

Lengen and Frederick (1985) exposed ^{14}C-maleic hydrazide in sandy loam soil to simulated sunlight. The compound was very stable with about 80% recovery as intact maleic hydrazide after 34 days of exposure.

Environmental fate in water

Lacadie (1976) determined the hydrolysis of [^{14}C]maleic hydrazide in buffered solutions at pH 3, 6 and 9 at 7.2°C and 26.7°C. No hydrolysis was seen in two months.

Lengen and Frederick (1985) found a half-life of 34-52 days under photolytic conditions with simulated sunlight. The main photoproduct was maleic acid.

Fackler (1993) repeated the study by Lengen and Frederick and found a half-life of 15.9 days at pH 9. Maleic hydrazide was stable in all dark control solutions.

Schocken (1994) exposed aqueous solutions of [^{14}C]maleic hydrazide at a nominal concentration of 12 mg/l in pH 9 buffer to artificial sunlight for 85 days with a 12-hour light and 12-hour dark cycle each day. The main photoproducts were maleic and succinic acids.

Residues in rotational crops

Caley *et. al.* (1990) investigated the degradation of [4,5-^{14}C]maleic hydrazide in field-grown rotational wheat. The compound was applied once to a sandy loam soil at a rate of 0.3 g/m^2 (equivalent to 3 kg/ha) and wheat was planted 30 and 92 days after treatment. Forage was collected 5 weeks after emergence, and whole plants were collected at maturity of the grain and separated into grain, chaff and straw. Soil cores (22 cm) were taken before and after application, before sowing, and at each harvest. The cores were separated into 0-11 cm and 12-22 cm sections. The TRRs in the soil samples on a dry weight basis are shown in Table 21. Most of the recovered radioactivity was in the upper core sections (top 11 cm).

Table 21. ^{14}C in soil sampled at various intervals after treatment with [^{14}C]maleic hydrazide.

Ref.	Time of sampling	^{14}C, mg/kg as maleic hydrazide, mean and (range)			
		92-day planting		30-day planting	
		Upper section	Lower section	Upper section	Lower section

Ref.	Time of sampling	^{14}C, mg/kg as maleic hydrazide, mean and (range)			
		92-day planting		30-day planting	
		Upper section	Lower section	Upper section	Lower section
Caley *et al.*, 1990d	Before sowing wheat	1.25 (0.32-1.94)	0.10 (0.01-0.22)	2.28 (0.03-5.52)	0.05 (0.02-0.12)
	At first harvest	0.88 (0.21-1.55)	0.06 (0.01-0.16)	1.18 0.4-1.51)	0.03 (0.01-0.13)
	At final harvest	2.25 (0.62-7.08)	1.13 (0.03-5.96)	1.13 (0.17-2.71)	0.06 (0.02-0.1)

Whole plants from the 92-day planting contained radioactive residues similar to the controls and those from the 30-day planting showed that the uptake of [^{14}C]maleic hydrazide was limited. The radioactivity was distributed throughout the plants with slightly higher levels in the straw and chaff than the grain. The results are shown in Table 22.

Table 22. ^{14}C in wheat harvested from plots treated with [^{14}C]maleic hydrazide 92 and 30 before planting.

Ref.	Planting interval	Time of sampling	Mean total ^{14}C, mg/kg dry wt as maleic hydrazide			
			Straw	Grain	Chaff	Whole plant
Caley *et al.*, 1990d	92 days	5 weeks post emergence	X	X	X	0.03
		maturity	0.08	0.02	0.02	0.06[1]
	30 days	5 weeks post emergence	X	X	X	0.29
		maturity	0.04	0.02	0.05	0.04[1]

X No analysis
[1] Calculated from residdues in individual plant components

The mean levels of radioactivity in the soil decreased from 2.5 mg/kg as maleic hydrazide at application to 0.88 mg/kg at the first harvest of the wheat. The residues in the wheat were too low for identification. The ^{14}C in whole plants planted 92 and 30 days after soil treatment corresponded to 0.03 and 0.29 mg/kg respectively 5 weeks after emergence and 0.06 and 0.04 mg/kg at maturity of the grain. The straw, grain and chaff contained 0.04-0.08 mg/kg, 0.02 mg/kg and 0.02-0.05 as mg/kg respectively at maturity.

Ling and Burnett (1995) treated sandy loam soil at the maximum combined label rate of 6.6 kg ai/ha. ^{14}C residues were 0.26 mg/kg as maleic hydrazide in the forage of wheat planted 30 days after treatment (DAT) and 0.08 mg/kg in forage after planting 120 DAT. Residues were not detected in forage from 274 DAT and 364 DAT plantings.

^{14}C residues in the straw were 0.52 mg/kg from 30 DAT plantings and 0.22 mg/kg from 120 DAT. Residues in the straw from 274 and 364 DAT plantings were 0.03 and 0.02 mg/kg respectively.

^{14}C residues in the grain were 0.36 mg/kg from 30 DAT, 0.2 mg/kg from 120 DAT, 0.024 mg/kg from 274 DAT and 0.019 mg/kg from 364 DAT plantings.

In the grain samples from 30 DAT and 120 DAT crops, 47.5% and 56% of the ^{14}C respectively was shown to be incorporated into glucose. An additional 12% was released from each sample by hydrolysis with a proteinase enzyme, indicating incorporation into or association with protein.

The extracted radioactive material was found to be very polar, nonionic and of low molecular weight. The parent compound could not be conclusively identified, but may have been present at levels of no more than 0.02 mg/kg in the 30 DAT forage and straw.

Acid hydrolysis with 1*N* HCL released a significant amount of activity from forage and straw, but the component(s) could not be separated from the matrix. This may again indicate incorporation into the tissues.

METHODS OF RESIDUE ANALYSIS

Analytical methods

Crops

The method of Lane (1963) involves reduction with zinc and hydrolysis in hot alkali to hydrazine. The hydrazine is isolated by distillation and determined colorimetrically as the azine after the addition of *p*-dimethylaminobenzaldehyde. The procedure is useful for determining residues of total maleic hydrazide and its conjugates. The available recovery data are shown in Table 23.

Table 23. Recovery of maleic hydrazide from various crops (Lane, 1963).

Sample	Fortification level, mg/kg	Recovery range, %	Mean recovery, %	Standard deviation	
				%	mg/kg
Cranberries	4	53 - 95	70	15	0.6
French fries	85	75 - 95	87	8.6	7.3
Mashed potatoes	28	74 - 87	83	3.9	1.1
Onions	10	70 - 106	81	15	1.5
Peaches	1.3	54 - 115	92	23	0.3
Potatoes	39	67 - 113	85	18	6.9
Potato chips	44	84 - 96	91	5	2.2

Newsome (1980) analysed plant material for residues of maleic hydrazide and its ß-D-glucoside by HPLC. Both maleic hydrazide and the glucoside were extracted with methanol and the extract was concentrated. The residues were cleaned up by passage through different cation-exchange columns (Amberlite XAD-2 and Dowex 50 resins for maleic hydrazide; Amberlite XAD-2, Dowex 1 and Dowex 50 resins for the glucoside) to separate the compounds from one another and from co-extractives. The glucoside was then hydrolysed with ß-glucosidase and the maleic hydrazide residues were determined by HPLC with detection by light absorption at 313 nm. The

average recoveries of maleic hydrazide at 1-50 mg/kg and of the glucoside at 2-50 mg/kg from beets, carrots, potatoes and turnips were both 87%. The LOD was 1 mg/kg.

King (1983) determined residues of maleic hydrazide in potatoes by gas chromatography after oxidation with aqueous lead dioxide to 3,6-pyridazinedione in the presence of cyclopentadiene. Potato samples were extracted with methanol and partitioned with chloroform containing cyclopentadiene and a suspension of freshly precipitated lead dioxide. The chloroform layer was removed and the aqueous fraction again partitioned with chloroform. The chloroform fractions were combined and evaporated to dryness. Residues maleic hydrazide were determined by GLC with EC detection on a DB17 packed column. Recoveries from potato samples fortified at 0.1, 0.5, 1, 5 and 10 mg/kg were 95.7, 94.0, 91.5, 87.9 and 90.4% respectively. The mean recovery of maleic hydrazide (as the Diels-Alder adduct) was 91.7% and the coefficient of variation was 3.1%. The limit of determination was 0.1 mg/kg. Samples containing conjugates were not analysed.

Harrison *et al.* (1989) used two monoclonal antibodies specific for maleic hydrazide to develop an enzyme immunoassay. Detection limits ranged from 0.11 to 1.3 mg/kg maleic hydrazide but the method was not validated for plants.

The official method of analysis for maleic hydrazide in The Netherlands (Anon., 1996) is based on the method of Lane (1963). The hydrazine produced by treatment with zinc in strong alkali is steam-distilled and the *p*-dimethylaminobenzaldehyde derivative is measured by spectrophotometry at 455 nm. In onions the LOD was 1 mg/kg with a mean recovery of 68.5% (n = 16, standard deviation 6%).

Animal products

Doran and McGuire (1996) employed proteolytic enzymes to solubilize maleic hydrazide from its bound form in animal tissues. The extracted maleic hydrazide was then determined by HPLC with UV detection. At fortification levels of 0.2 mg/kg, recoveries were 90-96% from cow milk and 68-88% from eggs. Beef liver spiked with 1 mg/kg showed recoveries of 52-79%.

Soil

Batoroewicz (1986) developed an HPLC method with electrochemical detection. The compound was soxhlet-extracted with water, the extract was concentrated to an appropriate volume, centrifuged and injected onto the HPLC column. Recoveries from clay loam and sandy clay loam soils fortified at 1 mg/kg were 60-70%.

Kennedy (1997a) extracted maleic hydrazide from soil with methanol/water (50:50) and quantified the residue by direct injection onto a reversed-phase HPLC column with an electrochemical detector. The mean recovery was 105% at fortification levels of 0.005, 0.025, 0.05 and 0.1 mg/kg with a relative standard deviation of 6.9%. The LOD was 0.005 mg/kg.

Water

Kennedy (1997b) cleaned up ground-water samples by liquid/liquid partition with dichloromethane. After concentration the residue was determined by HPLC with electrochemical detection. Validation at fortification levels of 0.0001, 0.0005, 0.001 and 0.002 mg/l showed a mean recovery of 92% with a relative standard deviation of 8.8%.

Stability of pesticide residues in stored analytical samples

Dykeman (1993d) tested the stability of maleic hydrazide in potato tubers stored for 12 months at about -20°C (Table 24).

Table 24. Stability of maleic hydrazide in frozen potatoes (Dykeman, 1993).

Months storage	Fortification level, mg/kg	% remaining	% remaining mean
0	25	96	100
	40	104	
1	30	84	79
	30	73	
3	20	107	110
	20	113	
6	20	111	113
	20	115	
12	20	76	84
	20	92	

Jacobson and Wight (1992a,b) tested the stability of maleic hydrazide in frozen onions and potatoes fortified at 20 mg/kg (Table 25).

Table 25. Stability of maleic hydrazide in frozen onions and potatoes fortified at 20 mg/kg (Jacobson and Wight, 1992a,b). Controls showed <1.2 mg/kg in potatoes and <0.2 in onions in all samples.

Months storage	Sample	% remaining	
		potatoes	onions
0	stored 1	113	98
	stored 2	79	98
	analytical[1] 1	77	118
	analytical 2	93	107
1	stored 1	86	53
	stored 2	103	49
	analytical 1	93	76
	analytical 2	87	73
2	stored 1	113	115
	stored 2	100	115
	analytical 1	56	113
	analytical 2	87	99
4	stored 1	80	115
	stored 2	113	83
	analytical 1	101	77
	analytical 2	72	111
6	stored 1	97	121
	stored 2	116	116
	analytical 1	97	81
	analytical 2	118	121

[1]Control sample spiked at 20 mg/kg and analysed immediately

Cameron and Johnston (1995) determined the profile of radioactivity in enzyme-deconjugated goat milk extracts during storage at about -20°C for about 18 months. Three main components were observed in the extracts at each analysis by radio-HPLC. The major component was eluted at the same retention time as maleic hydrazide and represented about 50.5% of the injected ^{14}C after 1 month and 67.5% after 18 months. A less polar component now known to be 3-pyradizinone accounted for 32.8% after 1 month and 22.1% after 18 months and a third more polar component represented 7.2% after 1 month and 10.4% after 18 months. The results confirmed the stability of the radiolabelled components in goat milk stored under these conditions.

Johnston and Cameron (1996) dosed laying hens with [^{14}C]maleic hydrazide at 3 mg/kg bw/day, extracted samples of pooled liver, kidney and egg yolk from selected hens with methanol or methanol/water (80:20) then analysed them by HPLC. The extracts were stored at about -20°C for 30 months. The profiles of radioactivity in samples analysed within about 1 month of collection and after storage for about 30 months were very similar, indicating that no deterioration of the ^{14}C residues had occured during storage.

USE PATTERN

The potassium salt of maleic hydrazide as the potassium salt is a growth regulator used to suppress sprouting in storage bulb vegetables and potatoes, to control suckers on tobacco and volunteer potatoes in following crops, and as a grass growth retardant in amenity and non-crop situations. It is also used on carrots. Tables 26 summarizes the use patterns.

Table 26. Registered uses of maleic hydrazide, application rates expressed as free maleic hydrazide.

Crop/Country	Form	Application				PHI, days
		Timing	Rate, kg ai/ha	Spray conc. kg ai/hl	No.	
Carrots Denmark	SL	BBCH 49	1.8-2.2		1	14
Garlic France	SG	when 10% leaves fallen but still green	2.4		1	10
Grass (non-fodder) Denmark	SL	BBCH 21-25, grass 5-10 cm high	5.4		1	NA
UK	SC	when grass is beginning to grow	4.6			NA
Onions France	SG	before leaves fall over (necking) and still green	2.4		1	10
Greece	SL	mature plants	2.3		1	15
Denmark	SL	BBCH 49	1.4-1.6		1	14
Netherlands	SL	at necking when tops are still green	2.3		1	28
Poland	EC SG	about 2 weeks before harvest	2.0 2.4	0.68 0.8	1 1	
Spain	SL	late stage	2.7	0.45	1	
UK	SG SC	10-50% necking 50 % necking	1.5-2.4 2.3-3.0		1 1	7 4
Potatoes France	SG	when 80% of tubers have reached 35-40mm	3.0		1	21
Denmark	SL	BBCH 49	3.1		1	14
Poland	EC SG	about 4-6 (EC) or 3-5 (SG) weeks before harvest	2.6 3	0.43-0.87 0.5-1.0	1 1	
UK/Ireland	SG	when smallest tubers are not less than 2.5 cm long, not for use on seed potatoes	3.0		1	21

Crop/Country	Form	Application				PHI, days
		Timing	Rate, kg ai/ha	Spray conc. kg ai/hl	No.	
Shallots France	SG	before leaves fall over (necking) and still green	2.4		1	10
Tobacco Greece	SL	mature plants	1.1-1.6		1	7
Italy	SC GR	after flowering	1.8-2.3 1.7-2.5	0.3-0.37 0.3-0.5	1 1	
Spain	SL	late stage	2.7	0.45	1	

RESIDUES RESULTING FROM SUPERVISED TRIALS

The results of supervised residue trials on crops are shown in Tables 27-31. Residues, application rates and spray concentrations have been expressed as maleic hydrazide and have generally been rounded to two significant figures or, for residues below 0.1 mg/kg, to one significant figure. Only when residues were detected in control samples are they recorded in the Tables. Multiple values from single trials are from replicate field samples. Underlined residue values were used for the estimation of maximum residue levels and/or STMRs.

Bulb vegetables

Garlic. Critical GAP: 1 x 2.4 kg ai/ha, PHI 10 days (France). One trial was conducted in France in 1992 with single applications of maleic hydrazide at either 2.4 or 3.6 kg ai/ha (Table 27).

Table 27. Residues of maleic hydrazide in garlic, France.

Year	Application				PHI, days	Residues, mg/kg	Reference, analytical method
	Form	No	kg ai/ha	kg ai/hl			
1985	600 SG	1	2.4		10 30 (S) 60 (S) 90 (S)	 5.5 7.0 5.0	Anon., 1990a; (S) = Storage, days, before analysis no information on analytical method
1992	600 SG	1 1	2.4 3.6		7 7 control	2.4, <u>2.7</u> 5.4, 6.3 0.22, 0.13	Anon., 1993a; GLC

Shallots. Critical GAP: 1 x 2.4 kg ai/ha, PHI 10 days (France). Five trials were conducted in France (1998-1992). In the trial in 1988, samples were analysed by GLC and by a colorimetric method. In three of the trials the samples were analysed or re-analysed after storage for 5-11 months (Table 28).

Table 28. Residues of maleic hydrazide in shallots, France, 1988-92.

Year	Application				PHI, days	Residues, mg/kg	Reference, remarks analytical method
	Form	No	kg ai/ha	kg ai/hl			
1988	600 SG	1	2.4		5 17 18 19 28	<u>9.5</u> (8.4) 2.4 (5.0) 8.5 (6.3) 10 (7.0) 2.6 (4.1)	Anon., 1989b, 1993b,c GLC () 2nd analysis colorimetric

Year	Application				PHI, days	Residues, mg/kg	Reference, remarks analytical method
	Form	No	kg ai/ha	kg ai/hl			
1989	600 SG	1	2.4		52 (S) 240 (S)	7.6 4.0	Anon., 1990a; (S) = Storage, days, before analysis
		1	2.4		52 (S) 240 (S)	11 2.8	no information on analytical method
		1	2.4		52 (S) 240 (S)	8.6 4.0	
1990, site 1	600 SG	1	2.4	0.3	18 150 (S) 270 (S) 330 (S)	 14 <0.1 8.7	Anon., 1990b; (S) = Storage, days, before analysis No information on analytical method
		1	2.4		26 150 (S) 270 (S) 330 (S)	 13 14 13	
		1	2.4		35 150 (S) 270 (S) 330 (S)	 5.0 20 10	
1990, site 2		1	2.4	0.3	21 150 (S) 270 (S) 330 (S)	 13 <0.1 4.9	Anon., 1990b; (S) = Storage, days, before analysis no information on analytical method
		1	2.4		30 150 (S) 270 (S) 330 (S)	 <0.5 <0.5 <0.5	
		1	2.4		38 150 (S) 270 (S) 330 (S)	 7.0 21 4.2	
1992	600 SG	1	2.4	0.48	7	2.6, 3.9 4.0, 4.2 4.3, <u>4.5</u>	Anon., 1993b, c; GLC
		1	3.6	0.72	7	7.7, 7.9 5.7, 7.8 6.9, 7.1	

<u>Onions</u>. Critical GAP: 1 x 3.0 kg ai/ha, PHI 4 days (UK). The results of trials in France, The Netherlands, the UK and the USA are shown in Table 29.

Table 29. Residues of maleic hydrazide in onions. The results in parentheses are suspect.

Country Year	Application				PHI, days	Residues, mg/kg	Reference, remarks, analytical method
	Form	No	kg ai/ha	kg ai/hl			
UK, 1983	600 SG	1	2.3	0.75	15	<0.5, 0.8, 3.6, <u>3.7</u>	Tomkins, 1983 Colorimetric
	180 SL	1	2.3	0.75	15	3.0, 3.4, 6.2, <u>7.5</u>	

Country Year	Application Form	No	kg ai/ha	kg ai/hl	PHI, days	Residues, mg/kg	Reference, remarks, analytical method
UK, 1984	600 SG	1	2.1	1.5	(21 25	2.8) (control 3.7) 2.7	Tomkins, 1984 Colorimetric SG and SL were applied to separate plots in the same trial
	SL	1	3.0	1.5	(21 25	4.0) (control 3.7) 2.2	
UK, 1985	600 SG	1	3.0	0.75	(23 (128 S 12 129 (S) 212 (S)	16) 4.9) (control 20) <u>5.5</u> 7.0 7.7	Tomkins, 1985a Colorimetric (S) = Storage, days, before re-analysis Samples at days 12, 129, 212 are replicates
UK, 1993	800 SG	1 1	2.4 3.6		7 7	2.7,4.6, <u>4.8</u> 5.9, 6.4, 7.0	Anon., 1993d, 1994 GLC
USA, 1992	269SL						Jacobson and Wight, 1992a Colorimetric
CA		1	2.2	0.19	10	1.0	
OR (No1)		1	2.2	0.76	10	6.3	
OR (No2)		1	2.2	0.77	10	0.38	
OR (No3)		1	2.2	1.5	10	0.40	
WA		1	2.2	0.77	10	1.1	
ID		1	2.2	0.24	10	4.0	
CO (No1)		1	2.2	0.19	10	0.95	
CO (No2)		1	2.2	0.19	10	0.89	
CO (No3)		1	2.2	2.4	10	1.3	
TX		1	2.2	0.24	10	0.94	
MI (No1)		1	2.2	0.19	10	4.3	
MI (No2)		1	2.2	0.19	10	3.9	
NY (No1)		1	2.2	0.24	10	3.0	
NY (No2)		1	2.2	1.9	10	4.8	
NY (No3)		1	2.2	0.24	10	7.5	
Netherlands 1977		1 1	2.3 2.3	0.46 0.46	35 191 (S) 39 187 (S)	3.8 3.7 4.2 3.4	Olthof, 1998 Colorimetric (S) = Storage, days, before analysis
Netherlands 1989	180 SL	1	1.1	0.22	29	0.38,0.43	Pritchard, 1993 GLC
		1	1.1[1]	0.22	29	1.1, 1.2	
		1	1.1[2]	0.22	29	0.50,0.84	
		1	1.6	0.32	29	7.3, 11	
		1	1.6[1]	0.32	29	2.0, 2.0	
		1	1.6[2]	0.32	29	1.6, 1.9	
		1	2.3	0.45	29	1.6, 4.9	
		1	2.3[1]	0.45	29	0.84, 3.2	
		1	2.3[2]	0.45	29	2.1, 3.1	
Netherlands 1990	180 SL	1	1.1	0.22	21	1.2, 1.3	Pritchard, 1993 GLC
		1	1.1[1]	0.22	21	0.15,0.68	
		1	1.1[2]	0.22	21	0.43,0.51	
		1	1.6	0.32	21	0.51,0.54	
		1	1.6[2]	0.32	21	0.68,1.4	
		1	2.3	0.45	21	2.1, 2.8	
		1	2.3[2]	0.45	21	1.6, 1.7	
	un-	1	4[3]		21	0.73,0.78	
	known	1	6[3]		21	0.93, 2.3	
		1	8[3]		21	0.76, 1.4	
Netherlands 1991	600 SG	1	1.5	0.3	30	0.54,0.92	Pritchard, 1993 GLC
		1	1.5[1]	0.3	30	0.84, 1.5	
		1	2.4	0.48	30	0.62, 1.7	
		1	2.4[1]	0.48	30	2.4, 5.4	

Country Year	Application				PHI, days	Residues, mg/kg	Reference, remarks, analytical method
	Form	No	kg ai/ha	kg ai/hl			
	180 SL	1 1 1	1.1 1.1[1] 1.1[1]	0.22 0.22 0.22	30 30 30	0.49,0.61 0.75,1.2 0.43,0.92	
		1 1 1	1.6 1.6[1] 1.6[2]	0.32 0.32 0.32	16 30 16 30 30	2.4, 3.3 0.36,0.83 1.1, 1.6 0.47, 1.8 0.82, 1.3	
		1 1 1	2.3 2.3[1] 2.3[2]	0.45 0.45 0.45	16 30 16 30 30	0.61,2.4 1.0, 1.7 2.0, 2.3 1.0, 2.3 1.5, 7.8	
	un-known	1 1 1	4[3] 6[3] 8[3]		30 30 30	0.55, 1.0 1.1, 2.2 0.95, 4.0	
France, 1987	600 SG	1	2.4	0.48	8 150 (S) 210 (S) 8 150 (S) 210 (S) 13 150 (S) 210 (S)	 9.0 0.05 5.3 0.41 5.0 0.25	Anon., 1987 analytical method: no information PHI 8 or 13 days, (S) = Storage, days, before analysis
France, 1992	600 SG	1 1	2.4 3.6	0.48 0.72	7 7	0.1, 0.17 3.4, 3.7 2.9, 3.5 3.3, 3.8 4.8, 5.0 3.3, 4.0	Anon., 1993b,c; GLC

[1] + Surfactant Primawett (0.125 l)
[2] + Surfactant Exell (0.5 l)
[3] 4, 6 and 8 kg of formulated product "Allirem". No further information

Root and tuber vegetables

Carrots. Critical GAP: 1 x 2.2 kg ai/ha, PHI 14 days (Denmark). No residue data were received.

Parsnips. No information on GAP was received. Residue trials were carried out in the UK (Table 30).

Table 30. Residues of maleic hydrazide in parsnips.

Country	Application				PHI,	Residues,	Reference, remarks
Year	Form	No	kg ai/ha	kg ai/hl	days	mg/kg	analytical method
UK, 1987	600 SG	1	3.0	0.9	23	19 (2)	Tomkins, 1987
			3.0	1.2	23	26, 27	Colorimetric method
			6.0	1.8	23	13, 45	
			9.0	2.7	23	31, 45	

Potatoes. Critical GAP: 1 x 3.1 kg ai/ha, PHI 14 days (Denmark). Residue trials were conducted in the UK and the USA (Table 31).

Table 31. Residues of maleic hydrazide in potatoes.

Country	Application				PHI,	Residues,	Reference, remarks
Year	Form	No	kg ai/ha	kg ai/hl	days	mg/kg	analytical
UK, 1982 Cambridge-shire, site 1	600 SG	1	3	0.75	unknown		Anon., 1983
					0 (S)	14	Colorimetric
					30 (S)	15	PHI unknown
					90 (S)	6.8	(S) = storage, days, before
					180 (S)	7.2	analysis
UK, 1982 Cambridge-shire, site 2	600 SG	1	3		unknown		Anon., 1983
					0 (S)	22	Colorimetric
					30 (S)	29	PHI unknown
					90 (S)	14	(S) = storage, days, before
					180 (S)	17	analysis
UK, 1982 Essex	600 SG	1	3		unknown		Anon., 1983
					0 (S)	17	Colorimetric
					30 (S)	13	PHI unknown
					90 (S)	13	(S) = storage, days, before
					180 (S)	12	analysis
UK, 1982 Kent, site 1	600 SG	1	3		unknown		Anon., 1983
					0 (S)	10	Colorimetric
					30 (S)	15	PHI unknown
					90 (S)	11	(S) = storage, days, before
					180 (S)	7.7	analysis
UK, 1982 Kent, site 2	600 SG	1	3		unknown		Anon., 1983
					0 (S)	8.2	Colorimetric
					30 (S)	8.6	PHI unknown
					90 (S)	4.7	(S) = storage, days, before
					180 (S)	7.9	analysis
UK, 1982 Midlands	600 SG	1	3	2.3	unknown		Anon., 1983
					0 (S)	25	Colorimetric
					30 (S)	34	PHI unknown
					90 (S)	14	(S) = storage, days, before
					180 (S)	13	analysis
UK, 1985 Worcester-shire	600 SG	1			28		Anon., 1985
			0.5		150 (S)	5.3	Colorimetric
							(S) = storage, days, before
					32		analysis
		1	0.5		150 (S)	1.0	
		1	0.5		150 (S)	1.6	
		1	0.5		150 (S)	2.7	
		1	0.5		150 (S)	2.1	
		1	0.5		150 (S)	2.2	

Country Year	Application				PHI, days	Residues, mg/kg	Reference, remarks analytical
	Form	No	kg ai/ha	kg ai/hl			
UK, 1985 Cambridge-shire, site 1	600 SG	1 1	3 3	9.1 aerial 0.66 ground	36 166 (S) 36 180 (S)	7.0 4.6 8.5 7.0	Tomkins, 1985b Colorimetric (S) 5 = storage, days, before re-analysis
UK, 1985 Cambridge-shire, site2	600 SG	1	3	0.75 ground	53 170 (S)	14 12	
UK, 1985 Cambridge-shire	600 SG	1 1	3 3	9.1 aerial 0.66 ground	36 166 (S) 36 180 (S)	4.8 2.3 11 7.3	
UK, 1985 Notting-hamshire	600 SG	1	3	1.1 ground	34 170 (S)	29 36	
UK, 1985 Lincoln-shire, site 1	600 SG	1 1	3 3	9.1 aerial 0.53 ground	40 162 (S) 40 180 (S)	12 16 8.0 9.5	
UK, 1985 Lincoln-shire, site 2	600 SG	1	3	0.75 ground	40 180 (S)	3.9 3.0	
UK, 1985 Lincoln-shire, site 3	600 SG	1	3	0.75 ground	55 182 (S)	14 12	
UK, 1985 Lincoln-shire, site 4	600 SG	1	3	0.75 ground	48 182 (S)	6.5 11	
UK, 1985 Norfolk	600 SG	1	3	1.5 ground	40 197 (S)	16 15	
UK, 1985 Derby, site2	600 SG	1	3	1.4 ground	32 control 170 (S) control	20 4.2 12 10	
UK, 1985 Derby, site1	600 SG	1	3	0.67 ground	21 162 (S)	8.9 19	
UK, 1991 York	600 SG	1	3	0.67	45	5.5[1] 4.7[2]	Anon., 1991 [1] GLC [2] Colorimetric
UK, 1991 Lincolnshire	600 SG	1	3	0.75	41	8.7[1] 5.4[2]	
UK, 1991 Doncaster	600 SG	1	3	0.75	42	9.5[1] 6.5[2]	
UK, 1991 Cambridge-shire, site 1	600 SG	1	3	0.75	23	9.5[1] 8.4[2]	
UK, 1991 Cambridge-shire, site 2	600 SG	1	3	0.75	69	11[1] 9.4[2]	
UK, 1991 Cambridge-shire, site 3	600 SG	1	3	0.77	57	14[1] 11[2]	
UK, 1993 Gloucester-shire, 2 sites	134 SL	1 1	3.1 3.1	0.78 0.78	28 29	13 9.3	Patel, 1994 GLC

Country Year	Application Form	No	kg ai/ha	kg ai/hl	PHI, days	Residues, mg/kg	Reference, remarks analytical
UK, 1992 Kent, 2 sites	600 SG	1 1	3 3	0.86 0.86	30 30	5.7 4.3	Knight, 1994 GLC
UK, 1992 Doncaster	600 SG	1	3	0.6	44	8.7	
UK, 1992 York	600 SG	1	3	0.67	68	10	
UK, 1992 Northamp-tonshire	600 SG	1	3	0.75	55	5.9	
UK, 1992 Suffolk	600 SG	1	3		32	13	
USA, 1991 CA	269 SL	1	3.4	0.8	21	2.7, 3.8, 12	Jacobson and Wight, 1992b Colorimetric
OR		1	3.4	1.1	21	5.2, 6.4, 1.7	
WA (No 1)		1	3.5	1.1	21	11, 15, 20	
WA (No 2)		1	4.4	1.5	21	6.4, 8.4, 15	
WA (No 3)		1	3.0	3.6	21	<1.2, 2.3, 3.0	
ID (No 1)		1	3.3	1.2	21	18, 22, 26	
ID (No 2)		1	3.4	1.2	21	7.7,11, 11	
ID (No 3)		1	3.1	3.6	21	6.5, 8.5, 9.1	
ND		1	2.9	1.2	21	13,26,36	
WI		1	3.4	0.98	21	<1.2, 2.6, 2.7	
MI		1	3.4	1.0	21	10, 15, 15	
NY		1	3.4	1.2	21	15, 20, 35	
ME		1	3.4	1.2	21	34, 48, 61	
ME		1	3.4	3.6	21	36, 41, 41	

Animal products

Feeding studies with unlabelled maleic hydrazide were not reported but metabolism studies on cows (Jackson and Hall, 1992a) and hens (Jackson and Hall, 1992b) were conducted for 28 days with dosing at 0.45, 1.35 or 4.5 mg/kg bw/day. Residues of maleic hydrazide reached a plateau in the milk after 3-4 days of 0.02 mg/kg and in eggs after 5-8 days of 0.01-0.02 mg/kg.

FATE OF RESIDUES IN STORAGE AND PROCESSING

In storage

The post-harvest storage stability of maleic hydrazide was determined in shallots, onions and potatoes. The storage conditions were not reported in detail for most of the trials but were equivalent to commercial practice. The results are shown above in Tables 28, 29 and 31.

Shallots. Table 28 includes 3 storage trials for 8 months (Anon., 1990a) and 6 for 5, 9 or 11 months (Anon., 1990b).

Onions. Table 29 includes 1 storage trial for 5 months (Tomkins, 1985a), 2 for 6 months (Olthof, 1998) and 3 for 5 -7 months (Anon., 1987).

Potatoes. Table 31 includes 17 storage trials for 6 months (Anon., 1983; Tomkins, 1985b).

In a storage study by Dykeman (1993d) potatoes were sprayed at an application rate of 4.4 kg ai/ha and harvested 21 days later. Samples were placed in refrigerated storage for 1 year. The recorded temperatures were 7-12°C for 6 months and 3-9°C for 6 months. Residues of maleic hydrazide were determined by a colorimetric method (Table 32).

Table 32. Effect of refrigerated storage on residues of maleic hydrazide in potatoes (Dykeman. 1993d).

Storage period, months	Residues, mg/kg, in replicate samples			Mean, mg/kg (Std. Dev.)
	1	2	3	
0	30, 36	25, 26	33	30 (4.6)
1	23	24	20	22.3 (2.1)
3	25	26	30	27 (2.6)
6	21	17	18	18.7 (2.1)
12	16	17	17	16.7 (0.58)

Byast (1988) determined the residues of maleic hydrazide in peeled tubers and potato peels before and after storage for 1 year (Table 33). T-tests to compare the means of fresh and stored samples revealed no significant differences among the means. The residues were determined by the HPLC method of Newsome (1980).

Table 33. Residues of maleic hydrazide in peeled potatoes and peels at harvest an after 1 year storage (Byast, 1988).

Field site (UK)	Sample	No. of samples	Mean residues, mg/kg	
			at harvest	after storage
Scott	Peeled tubers	3	8.0	8.9
	Peels	3	4.4	1.8
Renshaw	Peeled tubers	3	11	16
	Peels	3	7.5	6.9
Richardson	Peeled tubers	3	8.8	8.4
	Peels	3	5.2	4.8
Hay	Peeled tubers	3	10	7.7
	Peels	3	3.9	2.5
Greens	Peeled tubers	3	3.6	3.8
	Peels	3	1.4	2.6

In processing

Potatoes from supervised trials carried out in the UK (Table 31) were processed. Analyses were by the GLC method of King (1983).

(Anon., 1991). For boiling, whole potatoes were washed in flowing water for 2 min at room temperature, steam peeled, mechanically sliced and boiled for 5 min at 100°C. For crisping, whole potatoes were washed for 2 min, steam peeled, mechanically chipped, blanched at 80°C for 1.5 min and fried for 9 min at 180°C.

(Patel, 1994). Whole potatoes were washed for 2 min at room temperature, pricked with metal forks and microwaved in ½ kg batches for 15 min at 1800 watts.

(Knight, 1994). To produce baked potatoes, whole potatoes were washed in flowing water for 2 min at room temperature and baked in 12 kg lots in electric ovens for 80 min at 200°C. For crisping, whole tubers were washed for 2 min, steam peeled, re-washed for 3 min, mechanically sliced, blanched in water at 80°C for 1.5 min and fried in 1 kg lots for 9 min at 180°C. Chips were produced similarly, but fried in 4 kg lots in fresh oil for 10 min at 180°C.

The results are shown in Table 34. The mean processing factors were boiled tubers 0.52, microwaved tubers 1.2, baked tubers 1.35, crisps 0.0265 and chips 0.92.

Table 34. Processing studies on potatoes.

Ref.	Sample	Residues, mg/kg	Processing factor
Anon., 1991	RAC	5.5	
	boiled tuber	3.5	0.64
	RAC	8.7	
	boiled tuber	3.5	0.40
	RAC	9.5	
	Crisps	0.23	0.02
	RAC	9.5	
	Crisps	0.33	0.03
	RAC	11	
	Chips	15	1.36
	RAC	14	
	Chips	13	0.92
Patel, 1994	RAC	13	
	microwaved tuber	16	1.23
	RAC	9.3	
	microwaved tuber	11	1.18
Knight, 1994	RAC	5.7	
	baked tuber	4.5, 7.1, 7.3, 9.5	0.79, 1,2, 1.3, 1.7
	RAC	4.3	
	baked tuber	4.4, 6.3, 6.6, 7.8	1.02, 1.5, 1.5, 1.8
	RAC	8.7	
	Crisps	<0.1, 0.18, 0.38, 0.64	<0.01, 0.02, 0.04, 0.07
	RAC	10	
	Crisps	0.26, 0.29	<0.01 (2), 0.026, 0.029
	Chips	7, 10, 11, 12	0.7, 1, 1.1, 1.2
	RAC	5.9	
	Chips	4.7, 5.5,	0.8, 0.92, 0.93, 1.05

Ref.	Sample	Residues, mg/kg	Processing factor
		5.4, 6.2	
	RAC	12.8	
	Chips	7.6, 9.3, 10 (2)	0.59, 0.73, 0.78 (2)

Jacobson and Wight (1992c) carried out trials in the USA. The potatoes were sprayed with 3.4 kg ai/ha and tubers were harvested after a PHI of 21 days. The samples were steamed-peeled and washed. 18 and 56 kg were used for producing chips and potato granules respectively. The wet peel was dried. The RAC and peel samples were analysed by the colorimetric method after distillation and the processed fractions by HPLC with electrochemical detection (Table 35). The processing factors for producing granules and chips were 3-4, notably higher than the processing factors for chips in the studies summarized in Table 34.

Table 35. Processing studies on potatoes (Jacobson and Wight, 1992c).

Location	Sample	Residues, mg/kg	Processing factor
Washington	RAC[1]	5.4	
	RAC[2]	7.4	
	Wet peel	1.5	0.2
	Dry Peel	23	3.1
	Granules	29	3.9
	Chips	22	2.97
North Dakota	RAC[1]	23	
	RAC[2]	19	
	Wet peel	3.2	0.17
	Dry Peel	64	3.4
	Granules	70	3.7
	Chips	63	3.3

[1]Samples collected and frozen at harvest
[2]Sampled after cool storage immediately before processing. Processing factors derived from these residues

Byrd and Patel (1992) processed potatoes to crisps. The frozen tubers were thawed for 18 hours at room temperature, washed in flowing water for 2 min, peeled, mechanically chipped, blanched at 80°C for 1.5 min and fried for 9 min at 180°C in vegetable oil. The residues (Table 36) were determined by the GLC method of King, 1983.

Table 36. Processing studies on potatoes (Byrd and Patel, 1992).

Sample	Sample weight, kg	Residues		Processing Factor
		mg/sample	mg/kg	
Raw potato	5.74	5.47	31.4	
Thaw water	0.3	30.9	9.3	
Washed potato	5.5	8.25	45.4	1.4
Peeled potato	4.9	8.76	42.9	1.3
Peel	0.5	0.44	0.2	0.006
Water from peeling	100	0.25	25	
Sliced potato	4.8	2.18	10.5	0.33
Holding water	16	1.79	28.6	
Blanched potato	4.85	0.50	2.4	
Blanch water	15	1.8	27	
Cooling water	65	0.31	20.1	

Sample	Sample weight, kg	Residues		Processing Factor
		mg/sample	mg/kg	
Crisps	0.55	0.33	0.18	0.0057
Oil	18.4	0.30	5.52	

Residues in the edible portion of food commodities

Residues in peeled potato tubers are included in the processing studies described above. All the other residues reported in the Tables of supervised trials were in the edible fractions. No other studies of residues in edible portions of commodities were reported.

RESIDUES IN FOOD IN COMMERCE OR AT CONSUMPTION

Data on residues in ware potatoes (Table 37) were received from The Netherlands (Olthof, 1998).

Table 37. Residues of maleic hydrazide in potatoes in commerce; Netherlands, 1996.[1]

Samples analysed	Samples whithout residues (LOD = 1 mg/kg)	Samples with residues <MRL	Samples with residues >MRL	MRL,mg/kg
43	42	1	-	50

[1] Report AM9511GF7 (1997), Inspectorate of Public Health, Amsterdam, The Netherlands

NATIONAL MAXIMUM RESIDUE LIMITS

The following national MRLs were reported to the Meeting.

Country	Definition of the residue	Commodity	MRL, mg/kg
European Union		Carrots	0.2*
		Spring onions	0.2*
		Other bulb vegetables	10
		Early potatoes	1*
		Ware potatoes	50
		Other fruit and vegetables	1*
Germany	Maleic hydrazide and its conjugates, expressed as maleic hydrazide	Bulb vegetables except spring onions	10
		Stored potatoes	50
		Other food of plant origin	1
Netherlands	Maleic hydrazide	Garlic	10
		Onions	10
		Shallots	10
		Ware potatoes	50
		Other food commodities	1*
Poland	Maleic hydrazide	Onion. Bulb	10
		Other food commodities of plant origin	1

* at or about the LOD

APPRAISAL

Maleic hydrazide (6-hydroxy-2*H*-pyridazin-3-one) was first reviewed in 1976. At the request of the manufacturer, it was scheduled for the CCPR Periodic Review Programme. Its toxicology was evaluated in 1996 and it is now evaluated for residues.

The Meeting received information on animal and plant metabolism, environmental fate, analytical methods, updated GAP, supervised residue trials and the effect on residues of processing.

Maleic hydrazide is a plant growth regulator. It is formulated (as the potassium salt) as dispersible granules (SG, GR) and as liquid formulations (SL, SC). It main uses are for suppression of sprouting in stored potatoes and bulb vegetables, the control of suckers on tobacco and of volunteer potatoes in following crops and as a grass growth retardant in non-crop situations.

The absorption, distribution, metabolism and excretion of [^{14}C]maleic hydrazide has been studied in rats, rabbits, cows, a goat and hens.

Maleic hydrazide was well absorbed when administered orally to rats. Elimination was rapid and mainly via the urine (77-87% of the administered dose). Elimination via the faeces and expired CO_2 was less than 14% and 0.5% respectively. Very low levels of the test material were found in the carcase (<0.5% of the dose). No differences in the rate or route of elimination were noted between males and females. The major urinary component was maleic hydrazide (45-70%) and a minor metabolite was tentatively identified as its sulfate conjugate.

Maleic hydrazide was absorbed through rabbit skin at a rapid rate after a 4-hour topical exposure. The absorbed radioactivity was rapidly eliminated, almost entirely in the urine and in most cases during the first 24 hours after application. Approximately 90% of the urinary radioactivity excreted in the first 24 hours was identified as maleic hydrazide. The total dermal absorption of the radiolabelled material was calculated to be 26% of the total applied dose in males and 40% in females.

Most of the total radioactive residue (TRR) in cows dosed with [^{14}C]maleic hydrazide at 3 levels (0.45, 1.36, 4.5 mg/kg bw/day) was found in the kidneys. In milk, radioactive residues reached a plateau after 3-4 days of treatment, at a level of 0.02 mg/kg in the low-dose group. Radioactive residues in the low-dose animals were 0.34 mg/kg in the kidneys and ranged from <0.05 mg/kg in the fat and muscle to 0.08 mg/kg in the liver.

In a goat [^{14}C]maleic hydrazide was excreted in the urine (approximately 63% of the administered dose), faeces (23%) and milk (0.13%). Only 0.06% of the administered dose was recovered from the tissues (fat, muscle, kidneys, liver, blood and bile). Most of the radioactivity in the tissues and milk was in a conjugate, which was hydrolysed to maleic hydrazide and 2 relatively nonpolar compounds. One of these, observed in the liver, muscle and fat, co-chromatographed with fumaric acid. The residues of the parent before hydrolysis were 0.11 mg/kg in milk, 0.03 mg/kg in muscle and undetectable in the kidneys, liver and fat. More maleic hydrazide was identified after enzymatic hydrolysis in the milk (0.38 mg/kg) and after acid hydrolysis in the tissues (kidneys 0.96, liver 0.16, muscle 0.15 and fat 0.05 mg/kg).

Maleic hydrazide was rapidly metabolized by hens. Approximately 98% of the administered ^{14}C was recovered in the excreta within 24 hours after dosing laying hens for 3.5 days. Maleic hydrazide was the major component of egg yolk (0.18 mg/kg, 69% of the TRR) but was not present in muscle. An unidentified nonpolar metabolite was the major component of the residue in the liver (60% of the TRR) and was also present in the kidneys, muscle, egg white and egg yolk. Mass spectrometry of the nonpolar metabolite isolated from egg white indicated that it was a conjugate of a methylated maleic hydrazide. A polar compound was present in the kidneys and eggs. After acid

treatment, the level of this compound in extracts decreased, with a corresponding increase in maleic hydrazide and some unidentified compounds.

Six hens were dosed daily for 28 days with [^{14}C]maleic hydrazide at 1, 3 and 10 mg/kg bw/day. The TRR reached a plateau in egg whites after 5 days of administration and in egg yolks after about 8 days. The plateau levels in egg whites and yolks were 0.01-0.02 mg/kg from the low dose, 0.05-0.07 mg/kg from the mid dose and 0.19-0.23 mg/kg from the high dose. The highest TRR was observed in the kidneys (0.06 mg/kg in the low-dose group) and the lowest in abdominal fat (0.006 mg/kg in the low-dose group). Radioactive residues in muscle, liver and skin were 0.01 to 0.02 mg/kg from the low dose.

Information on the metabolism of maleic hydrazide in plants was provided for potatoes and onions. Maleic hydrazide is rapidly absorbed by foliage and translocated to growing shoots and roots.

Approximately 99% of the radioactivity in potato plants harvested 1 hour after treatment was in the vines. In plants harvested 8 weeks after treatment 61% was in the tubers. Most of the TRR in potato tubers consisted of maleic hydrazide (52-84%), with lower levels of a glucose conjugate (6.4-13%).

Leaves of onions harvested 1 hour after treatment contained approximately 87% of the total radioactivity. At 2 weeks after application, the levels of radioactivity in the bulbs were about 10 times those at the first harvest. The residues in the methanol-extractable fraction were identified as maleic hydrazide (no glucose conjugate was identified).

Maleic hydrazide is degraded rapidly in soil and is efficiently mineralized to CO_2 under aerobic conditions (half-life 11 hours). Degradation proceeds via the initial formation of maleamide resulting from the elimination of one of the nitrogens, followed by further conversion to maleamic acid, maleic and fumaric acids which will yield lactic acid and succinic acid and finally CO_2. Most of the radioactivity remaining in the soil is in the form of firmly bound residues. Maleic hydrazide has a high leaching potential but if it is allowed to age for a number of days after application it will be degraded rapidly and bind strongly to the soil, which will minimize leaching. The dissipation of maleic hydrazide in the environment is attributed to both aerobic and anaerobic degradation. Photolysis and hydrolysis may make limited contributions.

In a metabolism study on rotational crops wheat was planted 30 and 92 days after treatment of the soil with [^{14}C]maleic hydrazide in the field. Total radioactive residues in wheat forage, grain, chaff and straw ranged from 0.02 mg/kg to 0.29 mg/kg expressed as maleic hydrazide. The residues were too low to permit identification.

A further rotational wheat study showed that the residues in the grain are incorporated into glucose or associated with protein.

Analytical methods for total residues of maleic hydrazide in plants are based on reduction with zinc and hydrolysis in hot alkali to hydrazine. The hydrazine is isolated by distillation and determined colorimetrically as the azine by the addition of *p*-dimethylaminobenzaldehyde. These procedures are useful for determining total maleic hydrazide. The LOD for onions was 1 mg/kg.

Maleic hydrazide and its ß-D-glucoside can be determined by HPLC. Both maleic hydrazide and the glucoside are extracted from plant tissue with methanol and the extract is concentrated. Maleic hydrazide and the glucoside are cleaned up separately by passage through different cation-exchange columns. The glucoside is then hydrolysed with ß-glucosidase and maleic hydrazide is determined by HPLC with detection by light absorption at 313 nm. The average recovery of maleic

hydrazide from beets, carrots, potatoes and turnips fortified at 1 to 50 mg/kg was 87%. The LOD was 1 mg/kg. The same average recovery of the glucoside was obtained at levels from 2 to 50 mg/kg.

A gas-chromatographic method involves oxidation of maleic hydrazide with aqueous lead dioxide to 3,6-pyridazinedione in the presence of cyclopentadiene. The reaction product is determined by GLC with an ECD. The mean recovery of maleic hydrazide (as the Diels-Alder adduct) from potato samples fortified at 0.1, 0.5, 1, 5 and 10 mg/kg was 92% and the coefficient of variation was 3.1%. The limit of determination was 0.1 mg/kg. This method quantifies free extractable maleic hydrazide but not its conjugates.

An enzyme immunoassay based on two monoclonal antibodies specific for maleic hydrazide has been developed but the method has not been validated for plant samples.

HPLC with electrochemical detection has been used for the determination of maleic hydrazide in soil and water. The LODs were 0.005 mg/kg for soil and 0.0001 mg/l for water.

Proteolytic enzymes have been employed to solubilize maleic hydrazide from its bound residues in animal products, which occur as glucuronide and sulphate conjugates. Both types of conjugate will release maleic hydrazide on acid hydrolysis, so methods for the analysis of maleic hydrazide are also suitable for some of its conjugates if these are first hydrolysed. In view of the susceptibility of both conjugates to hydrolysis, it was assumed that maleic hydrazide glucoside would serve as a standard for the validation of methods for the glucuronide and sulphate conjugates. The extracted maleic hydrazide was analysed by HPLC with UV detection. Recoveries at fortification levels of 0.2 mg/kg of maleic hydrazide and its glucose conjugate (expressed as maleic hydrazide) were 90-114% for cow milk, 72-94% for liver and 68-80% for eggs.

The Meeting noted that the method was validated by fortifying animal products with the glucoside conjugate of maleic hydrazide, a plant metabolite. Furthermore, metabolism in goats indicated that a large proportion of conjugated metabolites were not released by acid hydrolysis. The Meeting could not confirm the validity of the method, based on HCL/pepsin hydrolysis, for residues in animal products arising from residues in feed.

In a study of the storage stability of maleic hydrazide and its metabolites in milk at -20°C, 33 and 22% of the applied radioactivity was identified as 3-pyridazinone after 1 and 18 months storage respectively.

Information was submitted on the stability of maleic hydrazide residues in stored analytical samples of potatoes and onions. The Meeting concluded that the compound is stable for at least six months in potatoes and onions.

The metabolism studies with a root or tuber vegetable (potato) and a bulb vegetable (onion) showed that the metabolic pattern is similar in these crops. Maleic hydrazide is degraded slowly in plants and is the major residue identified in studies of plant metabolism. Maleic hydrazide glucoside was the main metabolite in potatoes (6-13% of the total ^{14}C) and did not occur in onions.

The Meeting concluded that the definition of the residue in plants for compliance with MRLs and for the estimation of dietary intake should be maleic hydrazide *per se.*

For animal products an appropriate definition would be the sum of free and conjugated maleic hydrazide, but metabolism in goats produced a large proportion of conjugated metabolites from which the exocons were not released by acid hydrolysis.

In a storage stability study of maleic hydrazide and its metabolites in milk, 3-pyridazinone accounted for 33 and 22% of the applied radioactivity after 1 and 18 months storage but the relevance of free and conjugated pyridazinone to the definition of the residue could not be estimated from the data submitted. Furthermore, no validated analytical method for the metabolites, including pyridazinone, is available. From the limited data reported the Meeting could not recommend a definition of the residue in animal products.

The octanol/water partition coefficient of maleic hydrazide at natural pH (log P_{OW} = –0.68 at pH 5 and –2.01 at pH 7) shows that the compound is hydrophilic. The Meeting concluded that the compound is not fat-soluble.

Information was made available to the Meeting on registered uses of maleic hydrazide and on supervised residue trials on garlic, shallots, onions and potatoes.

Garlic, shallots and bulb onions. The reported GAP is 1 x 2.3-3.0 kg ai/ha, with PHIs (days) of 4 or 7 in the UK, 10 in France, 15 in Greece and 28 in The Netherlands. Labels give the following directions.

> Apply one or two weeks before harvest and not later than 50% necking.
> Do not apply less than one week before harvesting.
> Avoid spraying edible onions too early, if spraying is done earlier than two weeks before maturity, spongy bulbs may result.

One trial on garlic (1 x 2.4 kg ai/ha, PHI 10 days) approximated French GAP (1 x 2.4 kg ai/ha, PHI 10 days). The residues in duplicate samples were 2.4 and 2.7 mg/kg. In one further trial, residues of 5.0 to 7.0 mg/kg were determined after storage times of 30-90 days, but no information on the analytical method used was available.

Five trials on shallots in France were carried out at the registered application rate of 1 x 2.4 kg ai/ha. In two of them, the residues were 9.5 and 4.5 mg/kg after PHIs of 5 and 7 days. No information on the analytical method used was available for the other trials.

Seven residue trials on onions were carried out in the UK (1 x 2.1-3.6 kg ai/ha, PHI 7-25 days). Ten of 37 Dutch trials were at approximately the registered application rate (1 x 2.3 kg ai/ha), but the PHIs ranged from 16 to 39 days. Three French trials at 1 x 2.4-3.6 kg ai/ha were reported. Fifteen trials were conducted in the USA (1 x 2.2 kg ai/ha, PHI 10 days), but no GAP was reported.

In general, the residues after short and long PHIs were of the same order, as the decrease of the residues is offset by translocation of the compound from the onion tops to the bulbs and the uptake of residues by roots from the soil. No degradation of residues was observed after storing bulbs for 5-11 months after harvest.

Because the use pattern and growing conditions of bulb onions, garlic and shallots are alike, the Meeting agreed to extrapolate the residue data for onions (application 1 x 2.3-3 kg ai/ha) to garlic and shallots.

On the basis of the label recommendation that application should be at the earliest two and at the latest one week before harvest, the residues at PHIs from 5 to 17 days were used for the evaluation. In the case of replicates, only the highest result was selected. The residues in onions, shallots and garlic in rank order were 2.3, 2.4, 2.7, 3.7, 3.7, 4.5, 4.8, 5.5, 7.5 and 9.5 mg/kg. The Meeting estimated STMRs of 4.1 mg/kg and maximum residue levels of 15 mg/kg for garlic, bulb onions and shallots. The estimate of 15 mg/kg confirms the current CXL for onion, bulb.

Potatoes. The reported GAP is 1 x 2.6-3.1 kg ai/ha, with PHIs of 14 days in Denmark and 21 days in France and the UK. The label recommendation for application states: "The last few flowers may still be apparent but most of the blossom will already have fallen. A few of the lowest leaves may be turning yellow but the haulm must be predominantly green and actively growing."

The label recommendation indicates that the PHI could range from about 4 to 10 weeks. The metabolism studies on potatoes show that the residue level in the tubers depends on the time available for translocation of maleic hydrazide from the treated leaves to the tubers, so the critical GAP should not be linked to the registered PHIs of 14 or 21 days.

A total of 14 trials were carried out in the USA (1 x 2.9-3.5 kg ai/ha, PHI 21 days) but no GAP was reported. A number of trials from 1985 to1992 in the UK complied with GAP (1 x 3.0 kg ai/ha). The residues in the tubers at PHIs from 21 to 69 days were 3.9, 4.3, 4.8, 5.5, 5.7, 5.9, 6.5, 7.0, 8.0, 8.5, 8.7, 8.7, 8.9, 9.3, 9.5, 9.5, 10, 11, 11, 12, 13, 13, 14, 14, 14, 16 and 29 mg/kg. In the 1985 trials the residues were determined again after storage for about six months. The residues in the stored samples were 2.3, 3.0, 4.6, 7.0, 7.3, 9.5, 11, 12, 12, 15, 16, 19 and 36 mg/kg.

In six trials in the UK in 1982 residues were measured during the storage of field-treated potatoes for 180 days. The field treatment complied with UK GAP but the PHIs were not reported. The residues in rank order at the four sampling intervals 0 days 8.2, 10, 14, 17, 22 and 25 mg/kg, 30 days 8.6, 13, 15, 15, 29 and 34 mg/kg, 90 days 4.7, 6.8, 11, 13, 14 and 14 mg/kg and 180 days 7.2, 7.7, 7.9, 12, 13 and 17 mg/kg. The median values were 15.5, 15, 12 and 9.95 mg/kg for the 0, 30, 90 and 180 days storage periods respectively.

The Meeting based its evaluation on the highest data population, the residues in stored potatoes in the 1985 UK trials, and estimated an STMR of 11 mg/kg and a maximum residue level of 50 mg/kg.

No residue data were reported on carrots.

Animal feeding studies

The exposure of farm animals to maleic hydrazide residues will arise from its use on potatoes with a maximum residue level of 50 mg/kg and an STMR of 11 mg/kg.

Dairy and beef cattle. Because the residue could not be satisfactorily defined the Meeting could not estimate maximum residue levels for cattle milk, meat or edible offal.

Poultry. A 28-day feeding study with [^{14}C]maleic hydrazide at dose levels of 1, 3 and 10 mg/kg bw/day was submitted. As potatoes are a minor feedstuff (less than 10% of diet, according to US data), the Meeting concluded that further studies and the estimation of maximum residue levels for residues in poultry commodities resulting from feed were not necessary.

Processing studies were conducted on potatoes in the UK to determine the effect of washing, peeling, microwave baking, oven baking, boiling and frying on residues of maleic hydrazide. Mean processing factors were 0.52 for boiling, 1.2 for microwave baking, 1.35 for oven baking, 0.0265 for frying crisps and 0.92 for frying chips. A further study in the USA showed a mean processing factor for granules and chips of 3.5 and for dry peels of 3.25. A third study demonstrated that washing and peeling do not reduce the residues (processing factors were 1.4 or 1.3).

Since washing, peeling and microwave or oven baking do not change the residue content substantially, the Meeting estimated only STMRs of 5.7 mg/kg (0.52 x 11) for boiled potatoes and 0.29 mg/kg for crisps (0.0265 x 11). As fried potatoes may be prepared in widely varying ways with

different processing factors (means 3.5 and 0.92 in the trials), the Meeting estimated STMRs for chips of 38.5 mg/kg (3.5 x 11) for US commercial practice and 10.12 (0.92 x 11) for UK commercial practice for the assessment of dietary intake.

RECOMMENDATIONS

On the basis of the data from supervised trials the Meeting estimated the maximum residue levels and STMR levels listed below. The maximum residue levels are recommended for use as MRLs.

Definition of the residue in plant commodities for compliance with MRLs and for estimation of dietary intake: maleic hydrazide.

Commodity		Recommendation		
CCN	Name	New	Previous	STMR, STMR-P
VA 0381	Garlic	15	-	4.1
VA 0385	Onion, Bulb	15	15	4.1
VR 0589	Potato	50	50	11
	Potato crisps			0.29
	Potato chips			38.5[1] 10.12[2]
	Potato, boiled			5.7
VA 0388	Shallot	15		4.1

[1]US commercial practice
[2]UK commercial practice

FURTHER WORK OR INFORMATION

Desirable

Further information on the nature of the residues in farm animals.

DIETARY RISK ASSESSMENT

The International Estimated Dieatary Intakes of maleic hydrazide for the five GEMS/Food regional diets based on the STMRs for garlic, bulb onions, shallots and boiled potatoes, were in the range of 1 to 8% of the ADI. The Meeting concluded that the intake of residues of maleic hydrazide resulting from its uses that have been considered by the JMPR is unlikely to present a public health concern.

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