DODINE (084)

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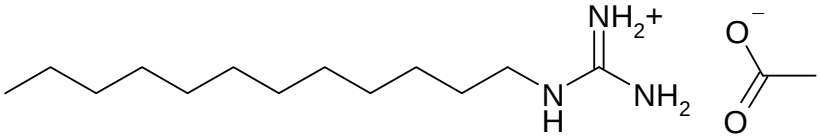
EXPLANATION

Dodine, dodecylguanidine monoacetate, is a fungicide and bactericide that was first evaluated in 1974 for toxicology and residues by the JMPR and subsequently in 1976 and 1977. The most recent toxicological review was in 2000. It was listed under the Periodic Review Programme at the 32nd session of the CCPR, for review by 2002 JMPR, but was re-scheduled for 2003.

The manufacturer provided information on identity, methods of analysis, use pattern, metabolism in plants and farm animals, residue trials on apples, pears, cherries, peaches and plums, storage stability, processing and fate and behaviour in the environment. In addition, the governments of France and the Netherlands provided GAP information.

IDENTITY

Common name:	Dodine (BSI, E-ISO, F-ISO, ANSI), previously called doguadine in France, dodine acetate (BSI, before 1969)
Chemical names IUPAC: CAS:	 1-dodecylguanidinium acetate dodecylguanidine monoacetate
Chemical structure:	
CAS registry No: EEC No: CIPAC No:	[2439-10-3] 219-459-5 101
Molecular formula:	$C_{15}H_{33}N_3O_2$
Structural formula:	
Molecular weight:	287.4 g/mol

Physical and chemical properties

Pure active ingredient

Appearance:	slightly yellow fine powder (Bascou, 1998).
Vapour pressure:	<5.49 x10^{-6} Pa at 50°C, dodine was not detected and therefore it is of very low volatility (Bascou, 1999a).
Melting point:	133.2°C (Bascou, 1998).
Boiling point:	decomposition occurs at about 200°C, before the boiling point is reached (Bascou, 1998).
Density:	0.981 g/ml at 20°C (Bascou, 1998).
Henry's law constant:	calculation to be <1.70 x 10^{-3} Pa m^3 mol^{-1} at 20 °C, dodine was not detected and therefore it is of very low volatility from aqueous solution (Bascou, 1999b)
Solubility in water:	pH 4.9, 0.87 g/l (20.0 ± 0.5°C); pH 6.9, 0.93 g/l (20.0 ± 0.5°C); pH 9.1, 0.79 g/l (20.0 ± 0.5°C) (Bascou, 1999c).
Octanol-water partition coefficient:	at pH 4.6, K_{ow} = 7.7, log P_{ow} = 0.87; at pH 9.3, K_{ow} = 9.1, log P_{ow} = 0.96 (at 20-25 °C, Bascou, 1999d).
Photolysis:	does not undergo photochemical degradation due to low ε (<0.001) at λ >290nm (Maestracci, 1994; van Rijsbergen, 2002a and 2002b; Krips, 2002).
Dissociation constant:	pKa value not available (Bascou, 1999e).

Technical material

Purity:	generally minimum 970 g/kg by titration (FAO, 1988) or 980 g/kg by HPLC analysis. The data below were derived from 982 g/kg material.
Appearance:	slightly yellow fine powder (Bascou, 1998).
Odour:	no characteristic odour (Bascou, 1998).
Melting point:	131.8°C (Bascou, 1998).
Boiling point:	decomposition occurs at about 200°C, before the boiling point is reached (Bascou, 1998).
Solubility in organic solvents	acetone 0.048 g/l ethyl acetate 0.015 g/l ethanol 57.0 g/l acetonitrile 0.044 g/l dicloromethane 0.015 g/l *n*-heptane 0.018 g/l xylene <0.004 g/l *n*-octanol 16.54g/l. All at 20.0 ± 0.5°C (Bascou, 1999c).
Density	0.982 g/ml at 20°C (Bascou, 1998).
Surface tension	27.87 mN/m (Bascou,1998)
pH of aqueous suspension	pH 7.6 for 1% aqueous suspension of technical dodine at 21°C (Bascou, 1999e).
Hydrolysis rate of dodine hydrochloride (97.5% purity)	At pH 4, 7 and 9, in sterile conditions in the dark, no hydrolysis after 30 days at 25 °C. Estimated half life: pH 5, 576 days pH 7, no degradation in HEPES buffer, 914 days in tris pH 9, 1198 days Dodine is stable (Daly et al, 1991).
Photodegradation in air	dodine is very slightly volatile from water to air, in the form of dodecylguanidine, which has $DT_{50} = \leq 3.9$ hours from the Atkinson calculation, $>2.4710^{-11}$ cm^3 $molecule^{-1}$ s^{-1} at 298ºK (Slangen, 2001).

Formulations

Dodine is available in the following formulations:

400 g/l SC (Australia, Belgium, Chile, France, Italy, New Zealand, United Kingdom);
410 g/l SC (Switzerland);
450 g/l SC (Austria, the Netherlands);
500 g/l SC (Hungary, Slovakia, Uruguay);
400 g/kg WG (Italy);
650 g/kg WP (Canada, Chile, Czech Republic, Greece, Poland, Portugal, Slovakia, Spain, Turkey, USA);
900 g/kg WP (Algeria).

METABOLISM AND ENVIRONMENTAL FATE

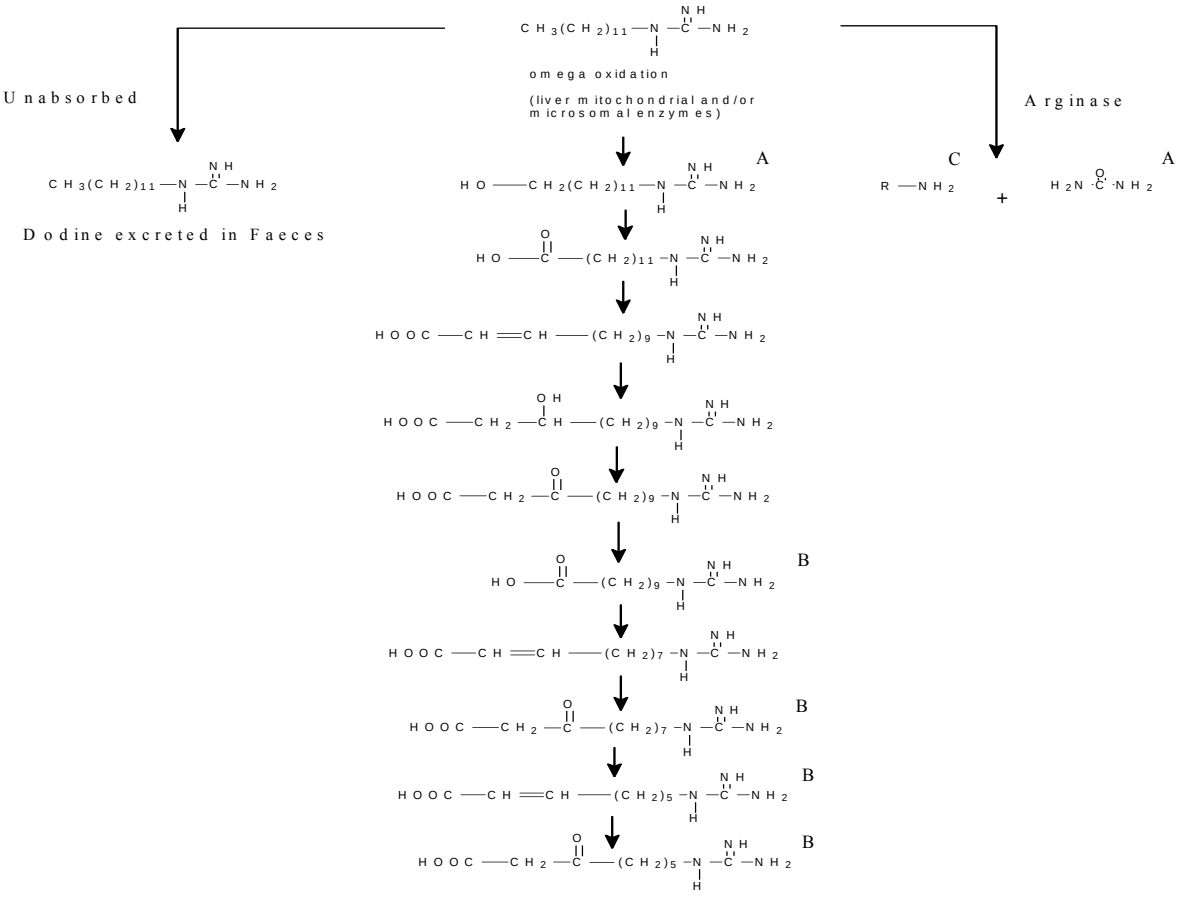
Animal metabolism

The meeting received information on the metabolism of dodine, following oral administration to a lactating goat. The metabolic fate of dodine in the lactating goat and rat are considered to be essentially similar. Dodine is extensively metabolized by both species, initially by omega-oxidation of the side chain to form a carboxylic acid, which is then subject to a series of "2-carbon" degradation cycles. This biotransformation is consistent with the beta-oxidation pathway, used by mammals to degrade medium- to long-chain fatty acids. Urea is also eliminated from the side chain. The presence of dodecylguanidine carboxylic acid, octylguanidine carboxylic acid, and hexylguanidine carboxylic acid in goat samples is consistent with the metabolic pathway proposed for dodine in the rat.

Rats

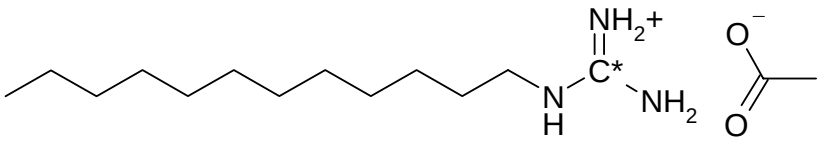
Absorption, distribution and excretion of dodine in rat was evaluated by the WHO panel of JMPR in 2000. Metabolism of dodine was considered extensive; less than 50% of [^{14}C]dodine was absorbed, biotransformed and excreted in urine and most of it was eliminated as metabolites. The proposed pathway for the metabolism of dodine in rats is presented in Figure 1.

Figure 1. Proposed pathway for metabolism of dodine in rats.



Goats

One study (Langford-Pollard, 1996) was conducted on a lactating goat, to investigate the distribution and excretion pattern following oral dosing of dodine at a nominal level of 10 ppm in the diet (rations of concentrates), equivalent to 21 mg dodine/day.



∗ position of radiolabel

[^{14}C]Dodine was administered daily by gavage in gelatine capsules, for five consecutive days, to a single lactating goat (British Saanen) at an actual dietary level of 12.8ppm. The goat was acclimatized for 7 days, prior to dosing, and the animal's health was checked daily for the duration of

the study. Urine and faeces were collected at 24-hour intervals after the first dose, until sacrifice. Cage washes were collected at each 24-hour collection period, immediately prior to dosing and after sacrifice. Milk was collected twice daily. Plasma was collected at: one hour prior to dosing; 2 hours after each daily dose; and 1, 2, 3, 4, 6, 8 and 12 hours after the last dose. The goat was sacrificed at approximately 23 hours after the final dose administration. Liver, fat, muscle, kidney and the gastro-intestinal tract were collected for analysis. The bile and rumen contents were also sampled. Measurements of total radioactivity were made in liquid samples by LSC and in solid samples following combustion of samples, by radio-assay. Details of the excretion and distribution pattern are given in the table 1.

Table 1. Excretion and retention of ^{14}C by a lactating goat during and after daily oral administration of [^{14}C]dodine for five consecutive days at a nominal dose level of 10 ppm (Langford-Pollard, 1996).

Sample material and time (hours after first dose)		Daily excretion [1/]	Cumulative excretion [2/]	Extractability (% matrix)	TRR (mg/kg dodine eq)
Urine	0-24	16.57	16.57	na	na
	24-48	44.79	30.68	na	na
	48-72	46.16	35.84	na	na
	72-96	37.30	36.20	na	na
	96-119	41.58	38.31 [3/]	na	na
Cagewash	0-119	-	1.69	na	na
Faeces	0-24	14.54	14.54	na	na
	24-48	21.73	18.13	na	na
	48-72	35.73	24.00	na	na
	72-96	43.28	28.82	na	na
	96-119	34.97	30.05	na	na
Omasum plus contents		-	1.16	na	na
Intestine plus contents		-	4.88	na	na
Rumen contents		-	9.52	na	na
Total GIT plus contents		-	15.56	na	na
Milk		-	0.05	100	0.014
Liver		-	0.22	90.0	0.168
Kidney		-	0.02	92.3	0.109
Fat		-	0.04	na	0.006-0.008
Muscle		-	0.32	100	0.015-0.020
Whole-blood		-	0.05	na	na
Bile		-	<0.1	na	na
Total recovery		-	86.31	na	na

GIT = gastro-intestinal tract.
na = not applicable.
[1/] Radioactivity excreted during the specified time period as a percentage of the daily dose.
[2/] Total radioactivity excreted up to and including the specified time period, as a percentage of the cumulative dose administered up to that time.
[3/] Includes 1.03% of the cumulative dose in urine in the bladder.

Overall recovery of radioactivity was 86% of the dose administered. Dodine was poorly absorbed: during the testing period, 38% and 30% of the administered dose was excreted in urine and faeces, respectively. Some radioactivity remained in the digestive tract and its contents at sacrifice (16%), although biliary excretion was evidently low (<0.1 % dose). Transfer of radioactivity into milk was low and accounted for 0.05% of the dose, total radioactive residues reaching a plateau of 0.01 mg/kg dodine equivalents in the milk during days 3-5 of administration (Table 2).

Less than 1% of the total dose administered remained in tissues and body fluids at sacrifice (Table 3). Radioactivity in the liver and kidney accounted for 0.2% (0.17mg/kg dodine equivalents) and 0.02% (0.11mg/kg dodine equivalents) of the administered dose. In tissues, the concentrations in muscle (0.02mg/kg dodine equivalents) and fat (0.006-0.008 mg/kg dodine equivalents) were very low. Concentrations similar to those in muscle were found in whole blood (0.02 mg/kg dodine equivalents). Following the final dose on day 5, the peak plasma concentration (0.16 mg/kg dodine equivalent) was observed at eight hours after dosing and had declined to 0.02 mg/kg dodine equivalent at sacrifice (23 hours after the final dose).

Table 2. Mean concentration of ^{14}C in milk (expressed as mg equivalent/l milk) from a lactating goat, dosed orally with [^{14}C]dodine at 10 ppm for five consecutive days (Langford-Pollard, 1996).

Time (hours after first dose)	Mean daily concentration in milk, mg/kg
0-24	0.005
24-48	0.007
48-72	0.012
72-96	0.014
96-119	0.014

Table 3. Concentrations of ^{14}C (expressed as dodine mg equivalent/kg) in tissues of a lactating goat, dosed orally with [^{14}C-dodine] at 10 ppm for five consecutive days (Langford-Pollard, 1996).

Tissue	Concentration (dodine equivalent, mg/kg)
Fat – omental	0.007
Fat - perirenal	0.006
Fat – subcutaneous	0.008
Kidney	0.109
Liver	0.168
Muscle –foreleg	0.020
Muscle-loin	0.015
Muscle -rump	0.016
Bile	0.041
Whole blood	0.015*

* Expressed as µg equivalents/ml.

Samples were frozen at below -15°C until analysis and initial chromatographic analysis of all tissues and excreta was completed within 12 weeks of sacrifice. To assess the stability of residues, extracts of liver and kidney were re-analyzed 18 weeks after sacrifice and the proportions of radioactive components were generally very similar to those obtained after 12 weeks.

The nature of the radioactive residues in faeces, milk, liver, kidney and muscle was investigated (Table 4), following extraction with organic solvent (methanol) and organic solvent/water mixtures. Additionally, the nature of the radioactive residues in urine was further investigated, following enzymic hydrolysis of conjugates (β-glucoronidase/sulfatase treatment of urine). Protease was used to extract additional radioactivity from in liver. Sub-samples of the post-extraction solids from liver, kidney and muscle, remaining after extraction, were analyzed by combustion. Characterization and quantification of extractable radioactive residues was by HPLC or TLC. Identification was by co-chromatography with reference standards, or by mass spectrometry for the faecal metabolite G10 and the urinary metabolites G3 and G5. Typical HPLC retention times and TLC Rf values for ^{14}C dodine and ^{14}C urea were provided.

Table 4. Characterization/identification of radioactive components in extracts of foreleg muscle, liver and kidneys from a lactating goat, following administration of [^{14}C]dodine for five consecutive days at nominal dose level of 10 ppm (Langford-Pollard, 1996).

Metabolite fraction	Foreleg muscle [1/]	liver [1/]	kidney [1/]
TRR (mg/kg)	0.02	0.17	0.109
Unchanged dodine	5.2 (0.0011)	2.4 (0.004)	2.9 (0.003)
G1(urea)	28.8 (0.006)	10.2 (0.017)	14.5 (0.016)
G2/G3	21.9 (0.004)	23.0 (0.039)	30.4 (0.033)
G4	2.2 (<0.001)	3.2 (0.005)	<1.8 (<0.002)
G5	26.9 (0.005)	17.1 (0.029)	21.5 (0.023)
G6	1.7 (<0.001)	1.6 (0.003)	<1.8 (<0.002)
G7	1.3 (<0.001)	2.1 (0.004)	1.9 (0.002)
G8	3.7 (0.001)	7.5 (0.013)	<1.8 (<0.002)
G9/G10 (not resolved)	3.1 (0.001)	9.1 (0.015) [3/]	12.3 (0.013) [4/]
Others [2/]	2.2	0.014 (8.4)	8.8 (0.010)
Non-chromatographed extracts	2.9	5.4 (0.009)	NS
Protease treatment		2.4 (0.004)	NS
Unextracted	<6.3 (<0.001)	7.5 (0.013)	7.6 (0.008)

[1/] With the exception of TRR (given as dodine equivalents in mg/kg), all values are given as % TRR with dodine equivalents in mg/kg in parenthesis.
[2/] Others included losses during chromatographic analysis due to diffuse or minor radioactive components which were below the limits of detection of 0.5%, ≤0.8% and ≤3.0% for foreleg muscle, liver and kidney, respectively.
[3/] On re-analysis, was resolved into two components G9 (0.009 mg/kg, 5.4%) and G10 (0.006 mg/kg, 3.8%).
[4/] On re-analysis, was resolved into two components G9 (0.011 mg/kg, 9.9%) and G10 (<0.003 mg/kg, <3.0%).
NS = no sample.

Efficiency of extraction was high, in the range 90-100 % for liver, kidney and muscle; unextracted residues accounted for 8% (0.01 mg/kg dodine equivalents) in liver, 7.6% (0.008 mg/kg dodine equivalents) in kidney and <6.3%(<0.001 mg/kg dodine equivalents) in muscle.

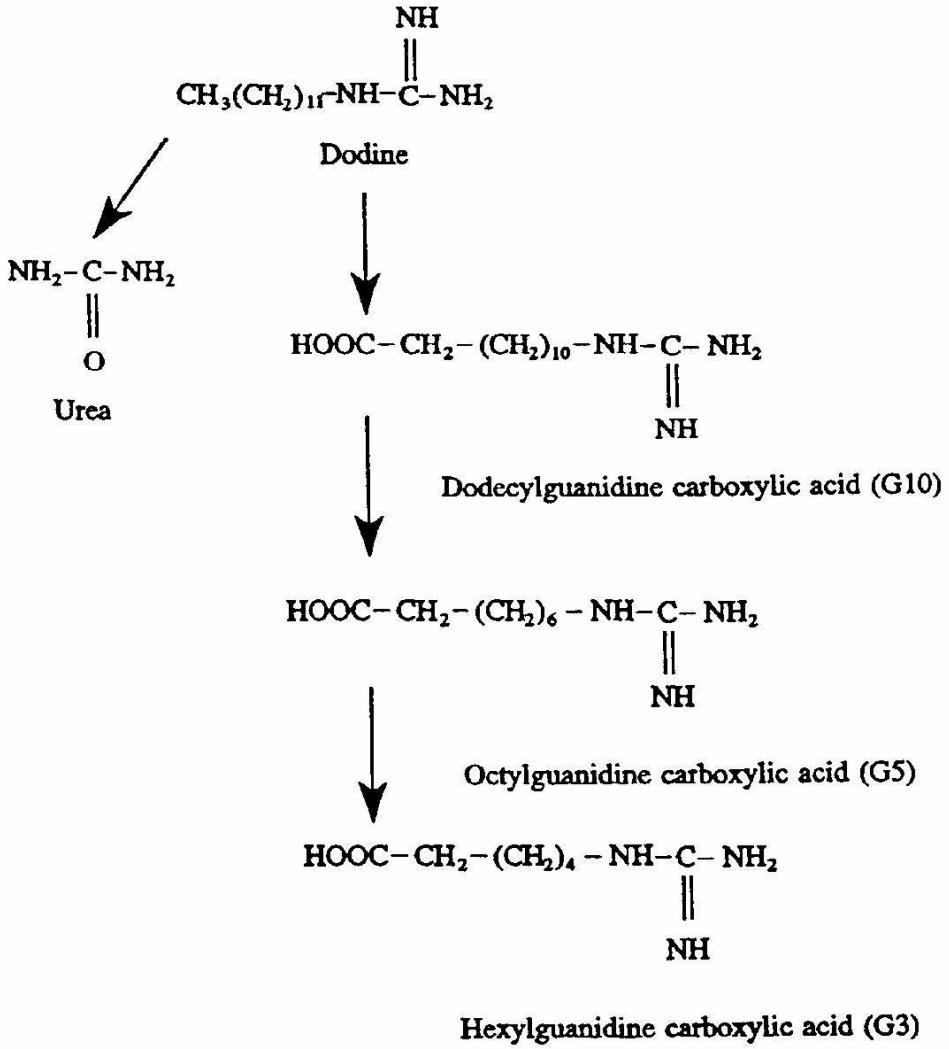
The major metabolites excreted in urine were identified as free hexylguanidine carboxylic acid (G3, 15.6% dose) and octylguanidine carboxylic acid (G5, 13% dose), as they were stable to enzyme hydrolysis. Unchanged [^{14}C]dodine was not detected in urine. Dodine (12% dose) was one of two major compounds in the faeces, the other was identified as dodecylguanidine carboxylic acid (G10, 8% dose).

In foreleg muscle, HPLC was used to characterize three major metabolite fractions: G1 and G5, accounting for 27 %(0.005 mg/kg dodine equivalents) and 29 % (0.006 mg/kg dodine equivalents), respectively; and G2/G3, which accounted for 21.9 % TRR (0.004 mg/kg dodine equivalents). Unchanged parent dodine accounted for only 5%TRR (0.001 mg/kg) in muscle.

From milk, 0.014 mg/kg was extracted with methanol (recovery based on measurement of radioactivity in the whole milk was 103.7%). Urea, a major metabolite which was identified by TLC, accounted for 57.4 % radioactivity (≤0.008 mg/kg dodine equivalents) in milk; whereas metabolites G3 and G5 were characterized but not quantified.

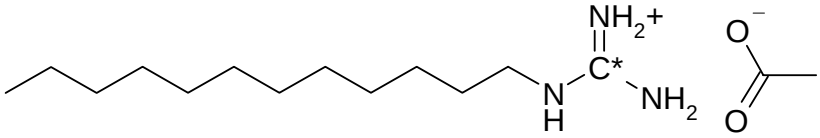
In liver, the major metabolites detected were G1, G2/G3, G5 and G9/G10, respectively accounting for 10.2% (0.02 mg/kg dodine equivalents), 23% (0.04 mg/kg dodine equivalents), 17% (0.03 mg/kg dodine equivalents) and 9.1% (0.02 mg/kg dodine equivalents). Unchanged parent dodine was a minor component, accounting for 2.4% TRR (0.004 mg/kg). In kidney, the metabolite profile was essentially similar, with dodine only a minor component of the radioactive residues, at 2.9% (0.003 mg/kg) and the different carboxylic acids being major components but none exceeding 0.05 mg/kg dodine equivalents. It was demonstrated that G9 and G10 were distinct metabolites in liver and kidney. The proposed pathways of biotransformation are shown in Figure 2.

Figure 2. Proposed routes of metabolism of dodine in the lactating goat.



Metabolism, distribution and expression of residues in plants

The meeting received information on the metabolism of dodine in apples, strawberries and pecan nuts. The studies aimed, firstly, to investigate the nature and quantity of the residues from dodine in the fruit and, secondly, to study the possible translocation of dodine in plants.



* position of radiolabel

Dodine parent was generally the major component of the residue in apples, strawberries and pecan nutmeat. Metabolism of dodine was slow and proceeded through oxidation, resulting in the formation of both urea and guanidine and, ultimately, of $^{14}CO_2$ and NH_3.

Apples

The metabolism of [^{14}C]dodine was investigated in field grown apple trees (cv. Red Delicious) in California (Mohseni *et al.,* 1992). The radio-labelled test substance was applied in a 65 WP formulation, diluted to 0.11 kg ai/hl and applied to run-off at each application. Three foliar applications were made; the first at bud break, the second at the immature fruit stage and the last at 7

days before final harvest of mature apples. Samples of apples were collected prior to both the second and third applications and at mature harvest, 7 days after the third application. Whole apples were surface-washed with water, then separated into peel and pulp. The samples were kept frozen at below -10°C, except for the water rinses, which were kept in a refrigerator at <6°C.

Determination of total radioactive residues in homogenized apple peel and pulp was by combustion, followed by liquid scintillation counting. Rinses were counted directly. Homogenized samples were extracted with acetonitrile/aqueous 1N HCl (50:50, v/v). Radioactive residues in the aqueous solutions were determined by direct LSC, whereas solids were dried and combusted prior to LSC. Characterization of residues was by TLC and HPLC.

The total radioactive residues (TRR) in immature apples (pulp + peel) collected 141 days after the first application, i.e. immediately before the second application, was <0.01 mg/kg dodine equivalents. A negligible amount of radioactivity was found in the rinse. At both second harvest (immediately before the third and final application) and at final mature harvest, whole apples contained higher levels, around 1.5 mg/kg. In both cases, 82-83% of the radioactive residues was in the apple peel, 5-7% in the pulp and 10-12% in the water rinses. The difference in distribution of radioactivity between peel and pulp at the second and third harvests and that of the first harvest probably reflected the fact that the first application was prior to the presence of fruits. Fruit at the first harvest would only have accumulated radiocarbon by translocation, which was evidently minimal.

Table 5. Distribution of radioactivity and residual [^{14}C]dodine in rinses and apple parts from field-grown apple trees (mg/kg fresh weight of whole apples, expressed as dodine equivalents) (Mohseni *et al.*, 1992).

Matrix	1st harvest [1/] mg/kg (% TRR)	2nd harvest [2/] mg/kg (% TRR)	3rd harvest [3/] maturity mg/kg (% TRR)
Apple rinse	0.0002 (2.0)	0.15 (10.5)	0.18 (12.0)
Apple peel	0.003 (33.7)	1.22 (83.0)	1.24 (82.3)
Apple pulp	0.006 (64.3)	0.096 (6.6)	0.09(5.7)
Total apple residues	0.0098	1.46	1.51

[1/] Harvested just before the 2nd application, 141 days after the 1st application: immature apples.
[2/] Harvested just before the 3rd application, 33 days after the 2nd application: immature apples.
[3/] Harvested seven days after the 3rd application, mature apples.

The efficiency of extraction was high, being 80% and 95% from apple pulp and apple peel, respectively, from the first harvest and >94% from the second and third harvest fruits. The rinse, the peel and the pulp from the first harvest immature fruits were not further analyzed, because the total residue levels were very low (<0.01 mg/kg in each case). Radio-chromatography (2-D TLC) of the apple rinses from the second and third harvests apples indicated a single radioactive component that co-chromatographed with dodine.

In apple pulp from the second harvest, analyzed by HPLC (Dionex PCX-500 cation exchange column, eluted with acidified acetonitrile/water), unchanged dodine was the major component, accounting for 72% of the TRR (0.085mg/kg). The remaining radioactivity was distributed among three minor components, at <0.05 mg/kg dodine equivalents, while a further unknown component was found at 0.017 mg/kg dodine equivalents. In apple pulp from mature fruits, dodine represented 81% (0.068mg/kg) of the TRR and minor components did not exceed 0.01mg/kg dodine equivalents.

In apple peel, unchanged dodine was the major component, accounting for 78% TRR (0.88 mg/kg) and 89% TRR (1.06 mg/kg) in immature and mature fruits, respectively. Of the minor components found in immature peel, one occurred at 0.07 mg/kg dodine equivalents, eight were between 0.01-0.05 mg/kg dodine equivalents and two were <0.01 mg/kg dodine equivalents. All minor components observed by HPLC were more polar than dodine but none eluted with the solvent front. In the peel from mature apple fruit, dodine and 25 of its metabolites were characterized. One of these (designated Metabolite A and tentatively identified by HPLC as the ^{14}C-guanidine moiety) was present at 0.017 mg/kg dodine equivalents but the remaining 24 metabolites were all <0.01 mg/kg dodine equivalents.

Table 6. Distribution of radioactivity as dodine and other components in apples treated with [^{14}C]dodine, at an application rate of 0.11 kg ai /hl (Mohseni *et al.*, 1992).

Matrix	Dodine	Other components		
	mg/kg (% of extracted TRR in the matrix)	> 0.05 mg/kg	0.01 mg/kg to 0.05 mg/kg	<0.01 mg/kg
2nd harvest [1/]				
Rinse	0.176	None	None	None
Apple pulp	0.085 (71.89)	None	1	2
Apple peel	0.884 (78.05)	1	8	2
3rd harvest [2/]				
Rinse	0.191	None	None	None
Apple pulp	0.068 (80.59)	None	None	4
Apple peel	1.055 (89.21)	None	1	24

[1/] Harvested just before 3rd application, 33 d after second application: immature apples.
[2/] Harvested 7 days after 3rd application: mature apples.

As part of the study, one designated branch on each of the ^{14}C-treated trees remained untreated throughout the study and was tightly covered during each application. Samples of leaves and apples taken from these branches at the last harvest were analyzed. Rinses of these apples and leaves showed very low levels of radioactivity (<0.001mg/kg dodine equivalents), showing that the branches were not contaminated during application. Combustion analysis of leaves from the third harvest showed residues of 0.023-0.052 mg/kg dodine equivalents but residues in apple peel and pulp were <0.01mg/kg dodine equivalents, showing that translocation to the apple fruit did not occur to any significant extent.

Strawberries

The metabolism of [^{14}C]dodine was investigated on outdoor, irrigated strawberries (cv. Selva) in California (Mohseni R. *et al*, 1993). The radio-labelled test substance was applied in a 65 WP formulation at a nominal application rate of 3.12 kg a.i./ha. Four foliar applications were made, spraying to run off. The first application was made to plants in early growth (foliage, flowers and any small berries present); the second was one month later, at the immature fruit stage; the third was 3 weeks later, when mature fruits had formed; and the last was 6 weeks later. Immature fruits were collected prior to the second application and mature fruits were harvested 14 days after the second, third and fourth applications. Further, in order to study the translocation of dodine, runners were protected from spray and harvested with the strawberry fruit.

Strawberries were surface-washed with water. Samples were kept frozen at <-10°C, prior to analysis, except for rinses, which were kept in a refrigerator at <6°C. Determination of total radioactive residues in homogenized rinsed strawberries was by combustion followed by liquid scintillation counting; rinses were counted directly.

Homogenized material was extracted with acetonitrile/aqueous 1N HCl (50:50, v/v). The extract of runners taken at the fourth sampling time was treated with concentrated hydrochloric acid (12M, 1.5ml). Radioactive residues in the extracts were determined by direct LSC, whereas residues were dried before combustion and quantification by LSC. Characterization was by 2-dimensional TLC and by HPLC; identification was by co-chromatography (TLC) using reference standards.

The TRRs in strawberry fruit collected 28 days after the first application and 14 days after the second, third and final applications, were 4.66 mg/kg, 6.97 mg/kg, 6.76 mg/kg and 4.28 mg/kg, respectively, as dodine equivalents, with >95% TRR in the strawberries and 0.3-5.3% TRR in the rinses (Table 7). TRRs (dodine equivalents) in the strawberry runners increased with time, ranging from 0.12 mg/kg in the first harvest runners to 0.84 mg/kg in the fourth harvest runners. As the runners were protected during each spray application, and prevented from coming into contact with the treated parts of the plant, these data indicate translocation of radioactive residues.

Table 7. Distribution of radioactivity and residual [^{14}C]dodine in outdoor strawberries (mg/kg fresh weight, expressed as dodine equivalents) in rinses and rinsed strawberries (Mohseni R. *et al*, 1993).

Matrix	1st harvest [1/] mg/kg (% TRR)	2nd harvest [2/] mg/kg (% TRR)	3rd harvest [3/] mg/kg (% TRR)	4th harvest [4/] mg/kg (% TRR)
Rinse	0.016 (0.34)	0.37 (5.27)	0.21 (3.15)	0.11 (2.54)
Strawberries	4.65 (99.66)	6.60 (94.73)	6.55 (96.85)	4.17 (97.46)
Total residue	4.66	6.97	6.76	4.28
Runners	0.12	0.41	0.33	0.84

[1/] Harvested 28 days after the 1st application of [^{14}C]dodine.
[2/] Harvested 14 days after the 2nd application of [^{14}C]dodine.
[3/] Harvested 14 days after the 3rd application of [^{14}C]dodine.
[4/] Harvested 14 days after the 4th application of [^{14}C]dodine.

Extraction efficiencies were >89% and unextracted ^{14}C residues were 0.9-3%. HPLC analysis of the first harvest strawberry rinse indicated 25 metabolites, each present at <0.01 mg/kg. In contrast with the first harvest rinse, the rinses of fruit harvested later contained dodine as the major component, corresponding to 55-77% of TRR. The remaining radioactivity was distributed between at least 9 minor components, which were <10.7 % TRR and in the range 0.01-0.03 mg/kg, dodine equivalents.

Extracts of the strawberries from the four harvests were analyzed by HPLC. In washed strawberries from the first, second, third, and fourth harvest extracts, dodine was the major component and accounted for 3.78 mg/kg (89.3% extracted radioactive residue, ERR), 5.89 mg/kg (89.4% ERR), 6.17 mg/kg (85.3% ERR), and 3.645 mg/kg (86.5% ERR), respectively (Table 8). The data were confirmed by TLC analysis. Isolation of a larger number of smaller fractions allowed some of the otherwise unresolved regions containing radiocarbon to be seen to be composed of many minor peaks. Low levels of urea and guanidine were verified by using ^{14}C-labelled reference standards.

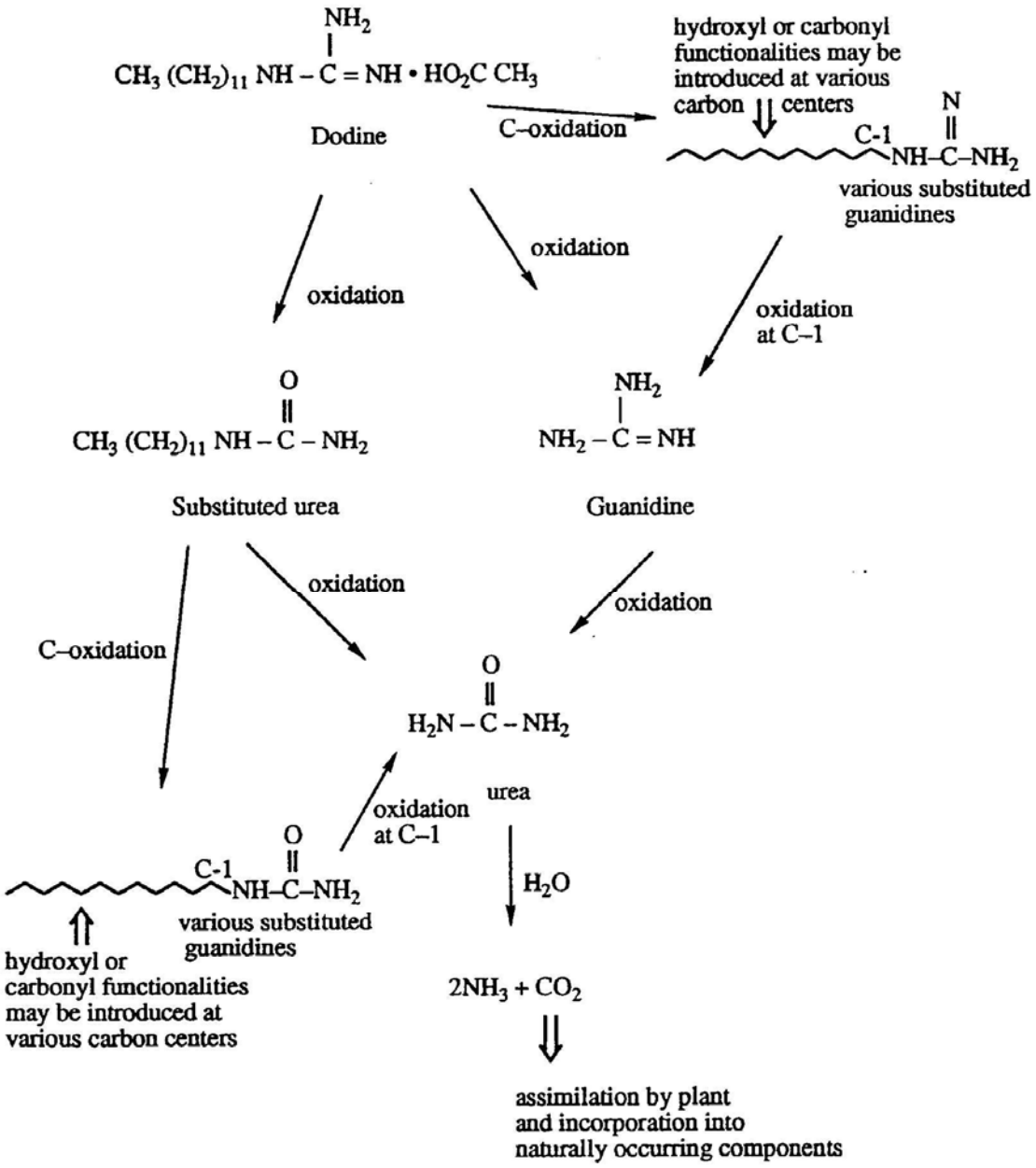
Table 8. Distribution of extracted radioactivity between dodine and other components, in rinses and in strawberries treated with [^{14}C]dodine (Mohseni R. *et al*, 1993).

Matrix	Dodine, mg/kg (% ERR)	Numbers of other components in concentration ranges		
		> 0.05 mg/kg	0.01 mg/kg to 0.05 mg/kg	<0.01 mg/kg
1st harvest				
Rinse	0 (0)	None	None	25
Strawberry	3.78 (89.28)	3	4	4
2nd harvest				
Rinse	0.28 (77.22)	None	3	6
Strawberry	5.89 (89.41)	5	9	1
3rd harvest				
Rinse	0.13 (61.86)	None	3	7
Strawberry	6.17 (85.33)	8 (none) [1/]	5 (8) [1/]	none (33) [1/]
4th harvest				
Rinse	0.06 (55.55)	None	2	7
Strawberry	3.65 (86.46)	2 (1) [1/]	9 (14) [1/]	4 (7) [1/]

[1/] The number of components in parentheses was obtained from radio-chromatograms with enhanced resolution, produced by collection of smaller fractions.

Fourth harvest runner samples contained 0.84 mg/kg dodine equivalents. They were extracted and analyzed. Dodine accounted for about 10% of the ERR and the only other region of radioactivity directly observable by TLC corresponded with urea, suggesting that this component was the major metabolite in runners and strawberries and that it was much more readily translocated than dodine. Dodine and its metabolites were stable for the duration of the study. The proposed biotransformation pathway is given in Figure 3.

Figure 3. Proposed metabolism pathway for dodine in strawberries.



Pecan nuts (tree nuts)

The metabolism of [^{14}C]dodine was investigated in field grown pecan nuts (cv. Wichita) in California (Baker *et al*, 1998). The radiolabelled test substance was applied in a 65 WP formulation, with a nominal spray concentration of 0.2kg ai/hl. Three foliar applications were made to three branches, spraying to run-off: the first application (18 June) occurred when many nut clusters were present; the second application (20 August) was to immature, but well developed, nuts; and the third application (08 October) was to mature nuts. In addition to harvest of mature nuts, two harvests of immature nuts were made by picking a few immature nuts, and surrounding foliage, immediately before the second and third applications. Nutmeat from mature nuts is the only raw agricultural commodity for pecans and analysis concentrated mainly on this commodity. Immature whole nuts, foliage samples and hulls were stored frozen. After air-drying to constant weight, the shells of mature nuts were cracked and the nutmeat removed. Nutmeat and shells were stored frozen.

Homogenized mature and immature nuts, and the post-extraction solids were combusted and counting by LSC (Table 9). Immature whole nuts were extracted by a series of solvents, including acetonitrile/1M HCl (1:1 v/v), then shaken, vortexed and sonicated before centrifugation. Mature nut meat was extracted using different solvents: hexane, methanol/0.1M HCl (9:1 v/v), 0.1M HCl, dichloromethane/methanol (9:1 v/v) and then, for the second sample only, 1M HCl and 1M Na OH. The combined hexane fraction was back extracted three times with acetonitrile/0.1 M HCL (9:1 v/v) in a separating tunnel. The volume of both phases was measured and aliquots were removed for assay by LSC. The methanol/0.1 M HCL extracts were combined and purified by solid phase extraction prior to HPLC and TLC analysis.

HPLC and TLC (1-D and 2-D) were used to characterize the radioactive residues in pecan extracts. The total radioactive residue (TRR) in immature pecans, harvested prior to the second application, was 2.15 mg/kg dodine equivalents. As developing hulls and shells were not removed from immature pecans prior to analysis, the sample included residues remaining on the surface of hulls following first application. Immature pecans (PHI 45 days) collected before the third application were not analyzed. The TRR of mature pecan nutmeat (shells removed) was equivalent to 0.11 mg/kg dodine equivalents.

Table 9. Total radioactive residues (mg/kg fresh weight, expressed as dodine equivalents) in pecan nuts after foliar application of [^{14}C]dodine (Baker *et al.*, 1998).

Matrix	1st harvest [1/], mg/kg (% TRR)	3rd harvest [2/], mg/kg (% TRR)
Immature nuts (including hulls and shells)	2.15 (100%)	Not analyzed
Mature nuts (nutmeat only)	Not analyzed	0.114 (100%)

[1/] Harvested just before the 2nd application: immature nuts, 60days after first application.
[2/] Harvested nine days after the 3rd application: mature nuts.

Efficiency of extraction for immature pecans was up to 89.5% (1.93 mg/kg dodine equivalents). No further work was done to increase extraction of radioactivity from immature pecans, because nutmeat from mature nuts is the edible commodity. Efficiency of extraction from mature pecans was slightly higher, 101.4-106.0 % (0.115 mg/kg to 0.121 mg/kg dodine equivalents), due to the combination of methods used.

Table 10. Extractability of total radiocarbon from [^{14}C]dodine treated mature pecan nutmeat (Baker *et al.*, 1998).

Fraction or extract	Dodine equivalents, mg/kg (% TRR)
Initial TRR	0.114 (100)
Hexane	0.026 (22.8)
Methanol/0.1M HCl (9:1, v/v)	0.074 (64.9)
0.1M HCl	0.005 (4.4)
Dichloromethane/methanol (9:1, v/v)	0.001 (0.9)
1M HCl	0.001 (0.9)
1M NaOH	0.002 (1.7)
Extract total	0.109 (95.6)
Post-extraction solids (PES)	0.010 (8.7)
Total	0.119 (104.3)

In immature nuts (2.15 mg/kg), dodine (0.98 mg/kg, 43.2% TRR) was partially metabolized to at least two more-polar metabolites (0.2 mg/kg dodine equivalents, 9.3 % TRR and 0.29mg/kg dodine equivalents, 13% TRR) and guanidine (0.33mg/kg dodine equivalents, 14.4% TRR). In mature nutmeat, the residue level detected was lower (0.114 mg/kg) and the main components were guanidine (0.041 mg/kg dodine equivalents, 36% TRR) and dodine (0.015 mg/kg, 13.2% TRR). Urea was not detected but it could account for the polar fraction (0.005 mg/kg, 4.4% TRR) unretained during SCX SPE fractionation. Partition experiments with hexane extracts of nutmeat, and saponification of extracts, confirmed that dodine, or closely related guanidine metabolites, were minor or absent from this fraction. ^{14}C was associated predominantly with the free fatty acid fraction (0.023 mg/kg dodine equivalents, 20.2% TRR). The proposed metabolic pathway in Figure 5 shows where radio-labelled $^{14}CO_2$, released from urea, could be incorporated into the fatty acid fraction.

Table 11. Identification and/or characterization of dodine metabolites in mature pecan nutmeat, from the metabolism study with ^{14}C-dodine (Baker *et al.*, 1998).

Extract	Metabolite	mg/kg (% of TRR)
Methanol/0.1M HCl (9:1)	Guanidine	0.041 (36%)
Methanol/0.1M HCl (9:1)	Dodine	0.015 (13.2%)
Methanol/0.1M HCl (9:1)	Neutral/non cationic	0.005 (4.4%)
Hexane	Free fatty acid fraction	0.023 (20.2%)
Total extracted		0.084 (73.8%)
Post-extraction solids (PES)		0.004 (3.9%)
Total		0.088 (77.7%)

Figure 4. Proposed metabolic scheme for conversion of [^{14}C]dodine to $^{14}CO_2$ in pecans.

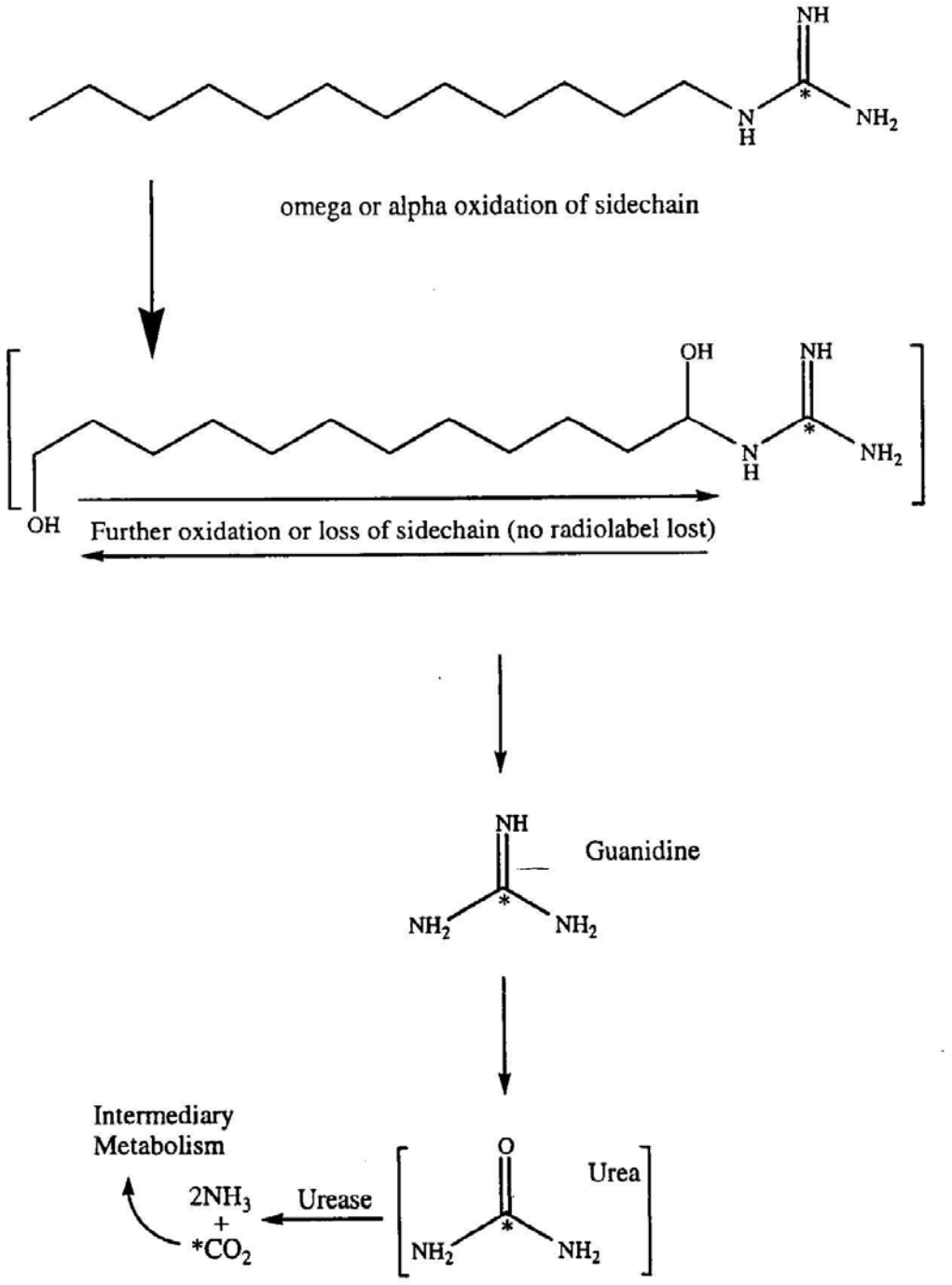
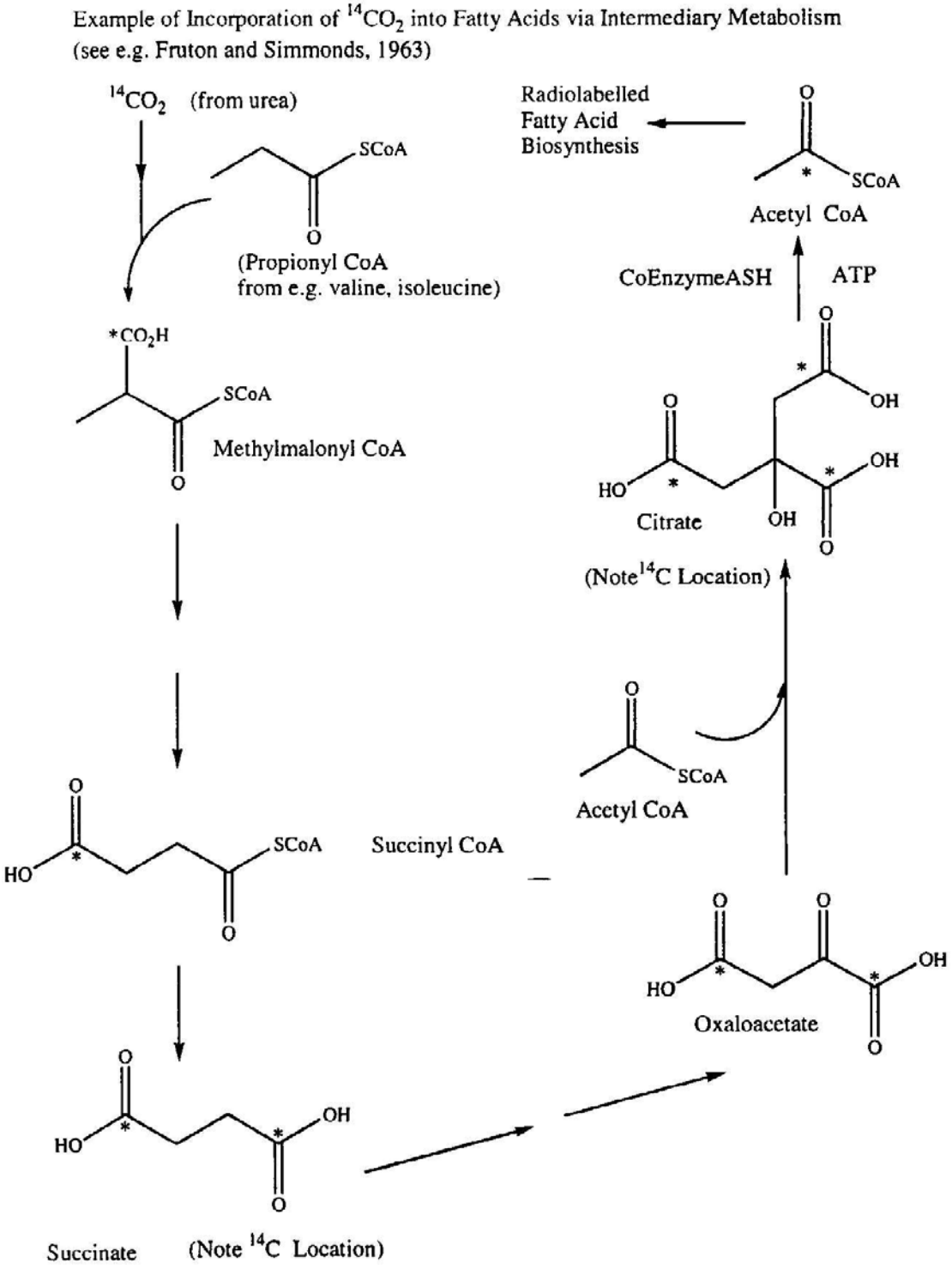


Figure 5. Proposed metabolic scheme for incorporation of $^{14}CO_2$ into radio-labelled free fatty acid fraction.

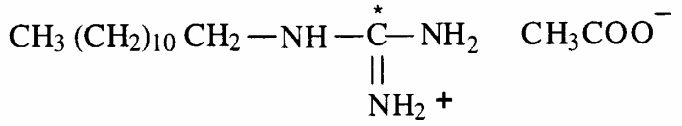


Environmental fate in soil

The meeting received information on the behaviour and fate of dodine during aerobic metabolism in a number of soils, on photodegradation on soil surfaces and on dissipation in the field.

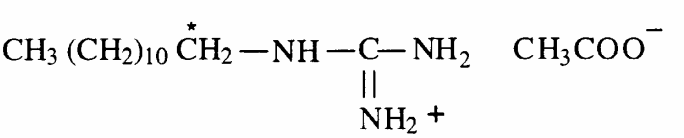
Aerobic soil metabolism

The fate and behaviour of dodine in soils was investigated using dodine labelled according to the study. Aerobic soil metabolism studies (Cooper *et al*, 1996, Lowden *et al*, 1997) and the soil photolysis study (Mislankar, 2001) were performed with ^{14}C-guanidine labelled dodine.



* indicates position of label

In addition, ^{14}C dodine labelled in the dodecyl moiety was also used in the second aerobic metabolism study (Lowden *et al*, 1997).



* indicates position of label

Two GLP studies were conducted in the laboratory, the first in two soils at 25°C (Cooper *et al*,. 1996) and the second in three soils at 20°C (Lowden *et al*, 1997).

The first study was conducted in two sandy loam soils, of USA and UK origins. The soil characteristics are summarized in Table 12. The metabolism of [^{14}C]dodine, applied at 4.4 mg dodine/kg dry soil (calculated dose rate of 3.36 kg dodine/ha with 0% foliar interception, 5cm of soil, 1.5 g/cm^3 bulk density), was followed for 100 days. The incubation was carried out aerobically, in the dark, at a temperature of 25°C ,with the soils at 75% of their 1/3 bar moisture holding capacity.

Table 12. Soils used to investigate degradation and metabolism of dodine under aerobic conditions (Cooper *et al*,. 1996).

Characteristic	Location 1: Essex, UK, Sandy loam	Location 2: Mississippi, USA, Sandy loam
pH (in water)	5.3	5.9
pH (in $CaCl_2$, 0.01 N)	4.6	-
Organic carbon	2.2%	0.6%
Bulk density (g/ml)	1.19	1.18
% moisture holding capacity (0.3 bar)	16%	17%
Microbial biomass (mg microbial carbon/kg soil)	366	29 (186)*

* recovered to 186 at the end of the study.

Recoveries of applied radioactivity were generally good throughout the study. The major metabolite detected was $^{14}CO_2$, which accounted for approximately 91% of the applied dose in the UK sandy loam and 92% in the US sandy loam, after 100 days. Bound residues remained at low levels, with a maximum of approximately 10% of the applied dose during the first 10 days and 3% at the end of the study. HPLC and TLC analysis showed that the non-volatile radiolabelled compounds detected in soil extracts were dodine and a group of 11 minor metabolites (named the 'M1 cluster"). In concentrated extracts, several other very minor metabolites were detected. A polar metabolite (M7) was detected in extracts from samples taken at the last two time-points. The combined metabolites were always <10% of the applied material and, at the end of the study accounted for less than 1%. The degradation rates of dodine (DT_{50} and DT_{90}) in those two soils under aerobic conditions was calculated using a KIM computer (one compartment model), as follows:

Soil origin and type	DT_{50} (days)	DT_{90} (days)
UK, sandy loam soil (soil 1)	9.5	32
USA, sandy loam soil (soil 2)	8.5	30

The second GLP aerobic study (Lowden *et al*, 1997) was conducted in three soils with [^{14}C]guanidine-labelled dodine and in one soil with [^{14}C]chain-labelled dodine. The study was conducted in 3 soils from UK, a sandy silt loam, a clay loam and a sand soil. The soil characteristics are summarized in the Table 13. The metabolism of [^{14}C]guanidine-labelled dodine, applied at a rate of 2.63 mg dodine/kg dry soil, equivalent to 1.97 kg dodine/ha (with 0% foliar interception, 5cm of soil, 1.5 g/cm^3 bulk density), was followed for 120 days. The incubation was carried out under aerobic conditions, in the dark at 20°C, with the soils at a moisture tension of pF 2.5. In addition, the metabolism of [^{14}C]chain-labelled dodine was followed in the clay loam, under similar conditions.

Table 13. Soils used to investigate degradation and metabolism of dodine under aerobic conditions (Lowden *et al*, 1997).

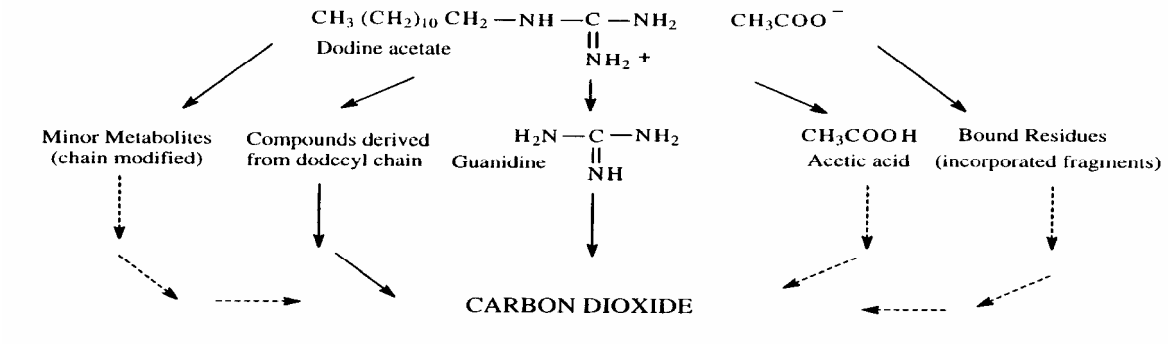
Characteristic	Location 3, Essex, UK Sandy silt loam	Location 4, Essex, UK Clay loam	Location 5, Suffolk, UK Sand
pH (in water)	6.6	7.4	6.7
pH (in $CaCl_2$, 0.01M)	6.0	7.0	6.3
pH (in KCl, 1M)	5.7	7.4	6.3
Organic carbon	1.2%	2.1%	2.3%
Organic matter	2.1%	3.6%	4.0%
% moisture content at pF value of 2.5	22.2%	33.7%	18.3%
Microbial biomass (mg microbial carbon/kg soil) at beginning (and end)	185 (107)	461 (268)	280 (288)

Recoveries of applied radioactivity were generally good throughout the study. In all experiments, dodine was rapidly degraded, with $^{14}CO_2$ as the major metabolite. The amount of extractable material declined rapidly, as the amount of radio-labelled compound in the soil decreased.

In the [^{14}C]guanidine-labelled dodine experiments, the levels of unextractable radioactive residues reached a peak within the first week after treatment and thereafter declined steadily. In the [^{14}C]chain-labelled dodine experiment, the unextractable radioactive residues remained at a similar level from the first sampling time until day 28, after which it decreased significantly. In all experiments, dodine was the major extractable compound throughout the study. By the end of the study, it accounted for less than 5% of the applied material, while all the metabolites combined accounted for less than 1.5%. The degradation rates of dodine (DT_{50} and DT_{90}) in the soils were calculated using the KIM computer and are summarized below and the proposed metabolic route for dodine in soils is given in Figure 5.

Label position and soil type	DT_{50} (days)	DT_{90} (days)
[^{14}C]guanidine-labelled dodine		
Sandy silt loam soil (soil 3)	4	16
Clay loam soil (soil 4)	3	11
Sand (soil 5)	4	15
^{14}C-chain labelled dodine		
Clay loam soil (soil 4)	4	12

Figure 5. Proposed routes of aerobic soil metabolism of dodine.



Field study

The dissipation of dodine, after application as a WP 65 formulation to bare ground plots simulating an orchard, was investigated at four different locations in the USA (California, Georgia, New Jersey and Washington) by Norris (1999). The soil characteristics are summarized in the Table 14.

Table 14. Soils used to investigate the degradation of dodine under field conditions (Norris, 1999).

Characteristic	Location 8, Washington, USA Sand (Quincy loamy fine sand)	Location 9, New Jersey, USA Loam (Penn)	Location 10, Georgia, USA (Dothan loamy sand)	Location 11, California, USA (Atwater loamy sand)
Climate, Summer Climate, Winter	Warm/dry Cool/dry	Warm/humid Cool/wet	Hot/humid Mild/wet	Hot/dry Cool/dry
Irrigation	Necessary	As needed	As needed	Necessary
USA textural analysis Sand Silt Clay	 89-93% 4-8% 3%	 29-55% 23-47% 20-26%	 65-87 % 7-12 % 3-26 %	 85-89 % 4-10 % 5-7 %
pH value (depth)	6.7 (15cm) 6.6 (30cm) 6.3 (45cm) 6.6 (60cm) 6.7 (75cm) 6.7 (90cm)	6.0 (15cm) 6.1 (30cm) 6.2 (45cm) 6.3 (60cm) 6.2 (75cm) 5.6 (90cm)	7.1-7.4 (15cm) 6.4-6.6 (30cm) 5.4-5.6 (45cm) 5.0 (60cm) 5.4 (75cm) 5.4-5.5 (90cm)	7.1 (15cm) 6.8 (30cm) 7.2 (45cm) 7.9 (60cm) 8.2 (75cm) 8.2 (90cm)
Organic Matter % (depth)	1.2 (15cm) 0.9 (30cm) 0.6 (45cm) 0.4 (60cm) 0.4 (75cm) 0.2 (90cm)	2.3 (15cm) 1.3 (30cm) 0.4 (45cm) 0.2 (60cm) 0.2 (75cm) 0.2 (90cm)	1.0-1.5 (15cm) 0.7-0.9 (30cm) 0.3-0.4 (45cm) 0.2-0.6 (60cm) 0.3-0.4 (75cm) 0.1-0.5 (90cm)	0.5 (15cm) 0.4 (30cm) 0.2 (45cm) 0.2 (60cm) 0.1 (75cm) 0.1 (90cm)
Cation exchange capacity (meq/100 g)	8.7 - 9.7	8.6 - 9.8	3.4 – 6.4	5.5-6.9
Bulk density (g/ml)	1.34 - 1.54	1.1 – 1.24	1.11 – 1.32	1.37-1.50
Field capacity (depth)	17.1 (15cm) 16.2 (30cm) 18.2 (45cm) 16.7 (60cm) 15.4 (75cm) 13.3 (90cm)	25.3 (15cm) 24.4 (30cm) 24.1 (45cm) 21.9 (60cm) 20.5 (75cm) 20.3 (90cm)	5.4-5.5 (15cm) 5.3-5.7 (30cm) 5.7-7.2 (45cm) 8.8-9.7 (60cm) 10.7-11.8 (75cm) 12.4-14.4 (90cm)	6.3 (15cm) 5.2 (30cm) 4.9 (45cm) 6.1 (60cm) 5.9 (75cm) 6.8 (90cm)

The degradation of dodine, following 6 applications each of 2.18 kg dodine/ha, with 7-day intervals between the applications, was followed for 1.5 years after the last treatment. Soils were irrigated to maintain at least the historical average rainfall for each site. Effective precipitation between sampling intervals was recorded, partly to verify that sufficient soil moisture was present to facilitate microbial degradation and partly to show that potential vertical mobility in the soil was also facilitated.

Soil samples were collected to a depth of 0.9 m in 0.15 m increments, frozen at the field site and sent to the laboratory for storage (1-17 months before analysis). A 12-month storage stability study showed that there were no appreciable losses of dodine during freezer storage. Since soil metabolism studies performed in the laboratory showed that the parent compound, dodine, dissipates without formation of significant quantities of metabolites, soil samples were analyzed for the presence of dodine residues, using GC-MSD after derivatization with hexafluoroacetylacetone (LOQ 0.01 mg/kg).

There were no significant residues (>0.01 mg/kg) of dodine below 15 cm in the soil profile at any location. In the four soils, residues declined rapidly during the first month following the last application, then dissipated more slowly. The data were evaluated as if the dissipation occurred in two phases. The determination of the half-life of dodine was based on least squares best fit exponential curves of the results after each application. DT_{50} and DT_{90} values were estimated to be as follows:

	Location 8, Washington, USA Sand (Quincy loamy fine sand)	Location 9, New Jersey, USA Loam (Penn)	Location 10, Georgia, USA (Dothan loamy sand)	Location 11, California, USA (Atwater loamy sand)
DT_{50} field	15 days	6 days	9 days	18 days
DT_{90} field	90 days	30 days	60 days	54 days

Soil photolysis

Mislankar (2001) studied the photodegradation of ^{14}C-guanidine-labelled dodine on soil in the laboratory. A sandy loam soil from California, USA, was used, which had characteristics as summarized in Table 15. Soil samples (20 g dry weight) were treated by dispensing a solution of the test substance over the surface at a rate of 4 mg/kg dry soil, corresponding to 3 kg ai/ha.

Table 15. Characteristics of a soil used to investigate photodegradation of dodine.

Characteristic	Location 7, California, USA, Sandy loam
sand	59.6 %
silt	29.2 %
clay	11.2 %
pH in water	6.2
pH in $CaCl_2$ 0.01M	5.8
pH in KCl 1.0N	5.4
Organic matter	0.44 %
Cation exchange capacity (meq/100 g)	3.44
Bulk density	1.58
WHC at ⅓ bar	7.46 %
WHC at 15 bar	2.45 %
WHC at saturation	15.57 %

Treated soil, in 6 x 3.5 cm rectangular steel containers, was exposed to simulated sunlight (λ >290 nm; Suntest CPS+ with Xenon lamp and appropriate filters) for periods 12 hours (followed by 12 hour periods of darkness) at 25 ± 1°C; the dark controls were incubated in the dark at 25 ± 1°C. Duplicate samples were taken from control and irradiated soil at 0 (start), 1, 3, 7, 14 and 30 days of exposure. The soil was extracted three times by shaking with 0.05 M KOH in 95:5 methanol/water and aliquots of the combined extracts were analyzed by LSC. In the case of samples taken at 3 ,7, 14 and 30 days, the third extraction was with 1%(v/v) concentrated hydrochloric acid in methanol and the extracts were combined and concentrated for HPLC-RAD analysis and confirmation of identity of parent compound by HPLC-MS.. The post-extraction solids from soil samples were combusted (Harvey Oxidiser) and radioactivity was determined by LSC.

Overall recovery of the applied radioactivity was in the range 97-105% from both irradiated and dark control samples. Over the period of 30 days, extractable radioactivity decreased from 101.7 to 83.3% in irradiated samples, and from 99.3 to 86.5% in dark control samples, and $^{14}CO_2$ production amounted to 14% and 12%, respectively. Unextractable residues in the soil were relatively constant, at approximately 4-5% in both cases. One metabolite fraction (metabolite 1) accounted for 10.1% of the applied radioactivity on day 1 in the irradiated sample. This fraction was shown to contain multiple components when re-analyzed under different HPLC conditions. The major metabolite was $^{14}CO_2$. The half-life of dodine, estimated assuming first-order kinetics, was 96 days and 130 days for the irradiated and dark control treatments, respectively.

METHODS OF RESIDUE ANALYSIS

Analytical methods

Method 45137, developed for the analysis of dodine in apples, plums and apple wet pomace, was validated by Pittman (1996). Dodine was extracted from fruit by homogenization with methanol. The extract was filtered, made to volume and an aliquot was cleaned-up by liquid-liquid partition (aqueous NaCl/dichloromethane). Dodine was then derivatized by refluxing for 2 hours with hexafluoroacetylacetone in 1-chlorobutane, to form 2-dodecylamino-4,6-bis(trifluoromethyl) pyrimidine. The solvent was evaporated and the residues dissolved in cyclohexane and determined by GC-MSD (quantification ion, *m/z* 244; qualifier ions, *m/z* 245 and 399). Dodine was determined as the , resulting from the reaction of dodine with hexafluoroacetylacetone. As in all analytical methods

for the determination of dodine residues, only the dodecylguanidinium cation was involved in the determination (determination as the acetate salt is effectively impossible and determination of the acetate anion is inappropriate) but the results were expressed in terms of the acetate, i.e. dodine.

Apple and plum samples were spiked at the LOQ (0.05 mg/kg), 5x LOQ and at the USA tolerance level of 5.0 mg/kg. Wet pomace was spiked at the LOQ (0.1 mg/kg), 5x LOQ and at the USA tolerance level of 5.0 mg/kg. Recoveries from all matrices at all levels were 72-93%, with RSD <12.5% (Table 16). For the ruggedness testing, apple wet pomace was fortified at 0.5 mg/kg and analyzed, with half the extracts being evaporated at 50°C, instead of 40°C. Recoveries were in the same range (71 and 73%).

To assess the efficiency of extraction of Method 45137, untreated control apple wet pomace and treated apple wet pomace, obtained from the metabolism study of [^{14}C]dodine in apples (Mohseni, *et al.*, 1992), were used. One control and three treated samples were analyzed by the method. The extracts were counted by liquid scintillation and the results converted to mg/kg, using the specific activity determined in the metabolism study. For the extraction only, the average value was 1.86 mg/kg whereas, for the entire method, the average value was 1.76 mg/kg. Dodine in the final extracts was determined by GC-MSD, using derivatized dodine standards, and the specific activity (5.4 mCi/mmol) was used to calculate the percentages of ^{12}C dodine and ^{14}C dodine. These data gave an average value of 2.15 mg/kg ^{14}C dodine. Samples extracted in the metabolism study gave an average value of 1.95 mg/kg by LSC, showing that the efficiencies of extraction and derivatization (assessed using procedural standards) were good.

Herzig (1996) conducted an independent laboratory confirmation of the method 45137 on apple wet pomace. Duplicate samples were spiked at 0, 1.0, 5.0, and 25 mg/kg and recoveries were 87-114% (average 97.11%).

Another validation of the analytical method 45137, for the determination of dodine residues in peach, pear, apple, cherry and plum samples (method AR 156-97) was conducted by Goller and Duchene (1998). Two minor modifications to the initial method 45137 were introduced (50 g anhydrous sodium sulfate was used to filter the dichloromethane phase, instead of 10 g, and evaporated extracts were reconstituted in 5ml toluene instead of 1 ml cyclohexane), otherwise the method was unchanged. The method was found to be specific in the tested matrices, with no interference observed at the retention time of the dodine derivative in the chromatograms of blank samples of peaches, pears, apples, cherries or plums. Linearity of detector response was demonstrated but no results or linearity curve were given. Individual and mean recoveries were acceptable, at 70-110 % with RSD <20%.

Table 16. Analytical recovery of spiked dodine from various substrates (Pittman, 1996; Herzig, 1996; Goller and Duchene, 1998).

Reference	Matrix	Fortification level (mg/kg)	Recovery (%)		RSD, (%)	n
			mean	SD		
Pittman, 1996.	Apples	0.05*	87.80	10.94	12.46	5
	Apples	0.25	79.92	8.80	11.01	5
	Apples	5.00	76.78	5.56	7.24	5
	Plums	0.05*	76.03	7.64	10.05	5
	Plums	0.25	71.63	4.65	6.49	5
	Plums	5.00	79.03	6.29	7.95	5
	Wet pomace	0.10*	92.18	12.16	13.19	5
	Wet pomace	0.50	92.54	13.11	14.16	5
	Wet pomace	5.00	88.73	6.08	6.28	5
Herzig, 1996	Wet pomace	1.00	96.00	87-105	nd	2
	Wet pomace	5.00	91.50	87-96	nd	2
	Wet pomace	25.00	102.00	90-114	nd	2

Goller and Duchene, 1998	Peaches	0.05	84.0	74-94	nd	2
		0.063	106.5	105-108	nd	2
		0.315	91.5	83-100	nd	2
		0.05-0.315	94	74-108	13	6
	Pears	0.05	86	76-96	nd	2
		0.063	102.5	102-103	nd	2
		0.315	81.5	76-87	nd	2
		0.05-0.315	90	76-103	12	6
	Apples	0.05	96	94-98	nd	2
		0.063	93.5	89-98	nd	2
		0.315	82	73-91	nd	2
		0.05-0.315	91	73-98	9.3	6
	Cherries	0.05	94	88-100	nd	2
		0.063	108	108-108	nd	2
		0.315	106	106-106	nd	2
		0.05-0.315	103	88-108	7.8	6
	Plums	0.05	93	88-98	nd	2
		0.063	102.5	100-105	nd	2
		0.315	110	110-110	nd	2
		0.05-0.315	102	88-110	8.4	6

nd = not determined.

Stability of residues in stored analytical samples

The meeting received information on the stability of dodine in various substrates. Dodine was considered stable up to 18 months in apples, cherries, peaches, apple juice and apple wet pomace, when stored in a freezer at -18°C or below.

Yang (1998) and Zenide (2001) examined the stability of dodine residues, using fortified samples (apple juice, apples, cherries) and treated samples (apples, wet pomace, peaches) obtained from several residue studies. Initial concentrations of dodine residues (either from field treatments or through fortification) were 0.1-1.7 mg/kg. In the first study, the initial residue level was about 1.7 mg/kg in apple and peach fruit, about 9 mg/kg in wet pomace, whereas apple juice was tested with a fortified residue of 0.5 mg/kg. In the second study, apples and cherries were fortified at 0.1 mg/kg. At each time point in the first study, one untreated control, one freshly fortified frozen sample and two stored samples were analyzed. In the second study, two untreated controls, one freshly fortified frozen sample and two stored samples were analyzed. In the two studies, the storage period for dodine was 18 months, with sampling intervals of 1, 3, 6, 9, 12, 15, 18 months in the first study and 3, 6, 12, 18 months in the second study. The method of analysis used was the validated method 45137, although slight modifications of the method are described in the respective reports.

In the first study, the freshly spiked recoveries of dodine were 63.1-109.7%, with averages of 87% for peaches, 92% for apple juice, 92% for apples and 70% for wet pomace. In the second study, average recoveries from freshly fortified apple and cherry samples were 76.6-110.4%, with averages of 95.1% from cherries 94.0% from apples. Residues measured in the stored samples are summarized in Table 17, each figure being the mean of the two analyses. The values are not corrected for the freshly fortified recovery values, nor for the control. For samples containing field-incurred residues (weathered samples), the concentration at day 0 is given as 100%.

Table 17. Residues (% remaining) of dodine in samples stored at ≤-18°C (Yang, 1998; Zenide, 2001).

Crop matrix		% remaining after storage period (months)							
		0	1	3	6	9	12	15	18
Weathered samples	Apples	100	130	98.2	105.4	110.8	106	106	96.7
	Apple wet pomace	100	104	90.5	91.2	85.1	92.7	85.4	81
	Peaches	100	91.5	104.8	92.3	83.5	76.5	98.17	116.2
Fortified samples	Apple juice, 0.5ppm	89	103	106	106	84	88	87	104
	Apples, 0.1ppm	100.7		101.3	100.4		83.8		84.9
	Cherries, 0.1 ppm	108.6		86.9	108.5		87.2		85.4

USE PATTERN

Dodine is the only active substance in the guanidine family. Tables 18 and 19 summarize current recommendations for the use of dodine, where data from supervised residue trials were submitted.

Table 18. Current recommendations for the use of dodine.

Crop	Disease	Timing of applications
Apple	Apple scab (*Venturia inaequalis*) and leaf spot (*Alternaria mali*)	From bud opening until 7-28 days before harvest (preferably 3-5 times max. per year to avoid resistance)
Cherry	Leaf spot (*Blumeriella jaapii = Coccomyces hiemalis*)	2 sprays from petal fall until 7-28 days before harvest followed by 2 sprays after harvest
	Peach leaf curl (*Taphrina deformans*)	1 spray in autumn (80% leaves on the ground) or at the end of winter (leaf bud swelling) + 2 sprays in spring (from bud opening up to petal fall).
Peach	Bacterial spot (*Xanthomonas pruni)*	1-2 sprays later in the season up to 15 days before harvest
Pear	Pear scab (*Venturia pyrina*) and leaf spot (*Alternaria sp.)*	From bud opening until 7-28 days before harvest (preferably 3-5 times max. per year to avoid resistance)

Table 19. Registered uses of dodine, according to the labels provided and information from the Netherlands and France.

Crop	Country	Form	Method	Application		Number (days/weeks between applications)	PHI, days
				Rate, kg ai/ha	Spray conc., kg ai/hl		
Apple	Algeria	WP 90 %	foliar	0.90	0.090	1-3x	
Apple	Australia	SC 400 g/l	foliar		0.032	6x	5
Apple	Austria	SC 450 g/l	foliar	-	0.045-0.063		14
Apple	Belgium	SC 400 g/l	foliar	0.60 [1]			28
Apple	Canada	WP 65%	foliar	1.46-2.1		(5-7 d)	7
Apple	Chile	WP 65%	foliar	-	0.04-0.08	(7 d)	
Apple	Chile	SC 400 g/l	foliar	-	0.04-0.08	(7 d)	
Apple	Czech	WP 65%	foliar	0.50-0.65	0.05-0.07	(10-14 d)	21
Apple	France	SC 400 g/l	foliar	0.7	0.07	4x (7-10 d)	28
Apple	Greece	WP 65%	foliar	-	0.04-0.07	2x	15
Apple	Hungary	SC 500 g/l	foliar	0.4-0.65	-		10
Apple	Italy	SC 400 g/l	foliar	-	0.03-0.06		10
Apple	Netherlands	SC 450 g/l	foliar	-	0.06	2-3x (5-7 d)	28
Apple	New Zealand	SC 400 g/l	foliar		0.016-0.03	(10-21 d)	14
Apple	Poland	WP 65%	foliar	0.65-1.5	-		14
Apple	Poland	SC 500 g/l	foliar	0.6-1.5	-		14
Apple	Portugal	WP 65%	foliar	-	0.09	(10-12 d)	15
Apple	Slovakia	WP 65%	foliar	0.56-0.84			21
Apple	Slovakia	SC 500 g/l	foliar	0.45-0.6	-		21
Apple	Spain	WP 65%	foliar	-	0.043-0.08		15
Apple	Switzerland	SC 410 g/l	foliar	0.78	0.05		28
Apple	Turkey	WP 65%	foliar		0.065		
Apple	UK	SC 400 g/l	foliar	0.7-1	0.03-0.045	(10-14 d)	
Apple	Uruguay	SC 500 g/l	foliar	0.4-1	0.03-0.08		10
Apple	USA	WP 65%	foliar**	0.75-2.2	-		7
Cherry	Canada	WP 65%	foliar	1.5	-	(7-10 d)	7
Cherry	Czech Rep.	WP 65%	foliar	0.49-0.65	0.05-0.07	(2-3 w)	21
Cherry	Hungary	SC 500 g/l	foliar	0.4-0.5	-		10
Cherry	Italy	SC 400 g/l	foliar	-	0.04		10
Cherry	Netherlands	SC 450 g/l	foliar	-	0.04	2-4x (7-14 d)	28
Cherry	Poland	WP 65%	foliar	0.98		2-3x (10-14 d)	14
Cherry	Portugal	WP 65%	foliar	-	0.05-0.07	(10-15 d)	
Cherry	Slovak Rep.	WP 65%	foliar	-	0.049		21
Cherry	Spain	WP 65%	foliar	-	0.05-0.08		15
Cherry*	Belgium	SC 400 g/l	foliar	-	0.04 [1/]	2-4x	28
Cherry*	Greece	WP 65%	foliar	-	0.05-0.07	1	15
Cherry*	USA	WP 65%	foliar	0.75-1.5	-	(7-10 d)	
Medlar	Algeria	WP 90 %	foliar	1.350	0.135	2	28
Medlar	Greece	WP 65 %	foliar		0.06-0.08	2	15
Medlar	Italy	SC 400 g/l	foliar		0.03-0.06		15

Crop	Country	Form	Method	Application		Number (days/weeks between applications)	PHI, days
				Rate, kg ai/ha	Spray conc., kg ai/hl		
Medlar	Portugal	WP 65%	foliar		0.09	2-3 w	15
Medlar	Spain	WP 65%	foliar		0.05-0.08		15
Peach	Czech Rep.	WP 65%	foliar	0.98-1.3	0.1-0.13		
Peach	France	SC 400 g/l	foliar	0.9	0.09		60 [2/]
Peach	Hungary	SC 500 g/l	foliar	1-1.3	-		10
Peach	Italy	SC 400 g/l	foliar	-	0.04-0.08		10
Peach	Poland	WP 65%	foliar	4.9			14
Peach	Poland	SC 500 g/l	foliar	4.9			14
Peach	Slovak Rep.	WP 65%	foliar	-	0.065-0.13		-
Peach	Slovak Rep.	SC 500 g/l	foliar	-	0.125		na
Peach	Spain	WP 65%	foliar	-	0.05-0.08		15
Peach	Uruguay	SC 500 g/l	floiar	1-1.25	0.04-0.1		15
Peach	USA	WP 65%	foliar	1.5-3		(7-10 d)	15
Pear	Algeria	WP 90 %	foliar	0.90	0.09	3x	-
Pear	Australia	SC 400 g/l	foliar		0.032-0.048	6x	5
Pear	Austria	SC 450 g/l	foliar	-	0.045-0.063		14
Pear	Belgium	SC 400 g/l	foliar	0.4-0.6 [1]		3-4x	28
Pear	Canada	WP 65 %	foliar	1.5-2.1	-	(5-7 d)	7
Pear	Chile	WP 65%	foliar	-	0.04-0.08	(7 d)	14
Pear	Chile	SC 400 g/l	foliar	-	0.04-0.08		14
Pear	France	SC 400 g/l	foliar	0.7	0.07	4x (7-10 d)	28
Pear	Greece	WP 65%	foliar	-	0.06-0.08	2x	15
Pear	Hungary	SC 500 g/l	foliar	0.4-0.65	-		10
Pear	Italy	SC 400 g/l	foliar	-	0.03-0.06		10
Pear	Netherlands	SC 450 g/l	foliar	-	0.06	2-3x (5-7 d)	28
Pear	New Zealand	SC 400 g/l	foliar		0.03-0.05	(7-10 d)	14
Pear	Poland	WP 65%	foliar	0.65-1.5	-		14
Pear	Poland	SC 500 g/l	foliar	0.6-1.5	-		14
Pear	Portugal	WP 65%	foliar	-	0.09		15
Pear	Slovakia	WP 65%	foliar	0.49-0.73			21
Pear	Spain	WP 65%	foliar	-	0.05-0.08		15
Pear	Switzerland	SC 410 g/l	foliar	0.78	0.05		28
Pear	Turkey	WP 65%	foliar	-	0.065		
Pear	UK	SC 400 g/l	foliar	0.7-1	0.03-0.045	10d-14d	
Pear	Uruguay	SC 500 g/l	foliar	0.4-1	0.03-0.08		10
Pear	USA	WP 65%	foliar**	1.5-2.25	-	6x (5-7 d)	7
Stone fruits	Spain	WP 65%	foliar	-	0.043-0.08		15
Stone fruits	Turkey	WP 65 %	foliar		0.065		

[1/] On "leaf wall" area basis.
[2/] Last treatment, end of flowering.
* Sour and sweet cherry.
**Ground or aerial application.

RESIDUES RESULTING FROM SUPERVISED TRIALS

The Meeting received information on supervised field trials for the following crops:

Pome fruit	Apples	Table 20
	Pears	Table 21
Stone fruit	Cherries	Table 22
	Peaches	Table 23
	Plums	Table 24

In all the supervised residue trials, dodine was determined using the validated method 45137, in which residues were determined by GC-MSD, with an LOQ of 0.05mg/kg. The trials were generally well documented, with full laboratory and field reports which included trial designs. Laboratory reports included method validation data, with batch recovery data from spiking at levels similar to those occurring in samples from the supervised trials, together with dates of analyses or duration of residue sample storage. Although the trials included control plots, no control data are recorded in the tables, except where residues in control samples exceeded the LOQ. Storage (in a

freezer) of samples, between sampling and analysis, was within the period of proven storage stability in each case.

Multiple data are recorded in the tables, below, in cases where the trial design included replicate plots which were treated with independently prepared spray dilutions. In the reverse decline studies, each sub-plot was considered to be an independent trial. Where multiple samples were taken from the same plot, the arithmetic mean value is reported. In some trials, residues were measured on samples taken immediately prior to the last application, as well as immediately afterwards (the "zero" day samples). Data from samples taken just before the last application are listed in the tables with one fewer application than those which received the final application and with a PHI equivalent to the interval between the penultimate and final applications. Residue values from the trials conducted according to maximum GAP were used for the estimation of maximum residue levels and these results are double underlined.

Pome fruit

Apples

Twenty GLP residue trials were conducted in Europe, all in France. Four conducted in 1997 were decline studies (Maestracci, 1998a), sixteen conducted in 1998 and 1999 were reverse decline studies (Baudet and Yslan, 1999a, Venet and Yslan, 2000a). Thirteen trials were conducted in the USA (Wargo, 1996a) over two growing seasons, 1995 and 1996 (one trial). Application was foliar in all the trials, using SC 400g/l in France and 65 WP in the USA.

In France, the trials plots were 12.5-84m^2. In the four decline studies conducted in 1997, 12 applications were made with an air-blast sprayer at 7-day intervals and samples were collected corresponding to nominal PHIs of 0, 7, 14 and 21 days. In the reverse decline trials, each sub-plot of each trial was considered as an independent trial. The intervals between the four first applications were 7 days but that between the fourth and the fifth applications was 7-60 days and harvest of mature fruit was at nominal PHIs of 14 days, 28 days, 45 days, 60 days, for the four sub-plots. An intermediate sampling point was also part of the design for the sub-plots with 45 and 60 days PHI. The samples at this intermediate point were, in most cases, immature fruit for the 60 days PHI sub-plots but to samples within two to three weeks of maturity in the 45 days PHI sub-plots.

In the USA, six applications were made to each plot, which were 180-361m^2. The intervals between the four first applications were 6-7 days. The two last applications were exactly 14 and 7 days before first harvest and the interval between the 4th and 5th applications varied from 66 to 151 days. Application equipment consisted of a air-blast sprayer, or a hand-lance sprayer in trial 950072, with application volumes of 916-950 l/ha.

Table 20. Dodine residues in apples resulting from supervised residue trials in France and USA (Maestracci, 1998a; Baudet and Yslan, 1999a; Venet and Yslan, 2000a; Wargo, 1996a).

APPLES Country, year, variety, report No.	Application				Commodity	PHI, days	Residue, mg/kg
	Form	no.	kg ai/hl, No. days [1/]	kg ai/hl			
France (N), Saulty, 1997 Golden Delicious Maestracci, 1998a, Study 97-528, 97528AM1	SC 400 g/l	12	0.68	0.11	Whole fruit	0 8 15 22	3.4 3.6 3.1 2.7
France (N) Tigy, 1997 Akane Maestracci, 1998a, Study 97-528, 975280R1	SC 400 g/l	12	0.68	0.07	Whole fruit	0 7 14 21	1.3 1.0 0.69 0.53
France (N), Souastre, 1998 Idared	SC 400 g/l	5	0.68 65 d	0.15 (3) to 0.18 (3)	Whole fruit	13	0.38
Baudet and Yslan, 1999a, Study 98-677, 98677AM1, reverse decline study	SC 400 g/l	5	0.68 49 d	0.15 (3) to 0.18 (3)	Whole fruit	29	0.39

APPLES Country, year, variety, report No.	Application				Commodity	PHI, days	Residue, mg/kg
	Form	no.	kg ai/hl, No. days [1/]	kg ai/hl			
Baudet and Yslan, 1999a, Study 98-677, 98677AM1, continued	SC 400 g/l	5	0.68 36 d	0.15 (3) to 0.18 (3)	Whole fruit	30 43	0.24 0.20
	SC 400 g/l	5	0.68 21 d	0.15 (3) to 0.18 (3)	Whole fruit	28 57	0.52 0.37
France (N), Mesnil-Domqueur, 1998 Jonagold	SC 400 g/l	5	0.68 64 d	0.12	Whole fruit	12	0.29
Baudet and Yslan, 1999a, Study 98-677, 98677AM2, reverse decline study	SC 400 g/l	5	0.68 49 d	0.12	Whole fruit	27	0.23
	SC 400 g/l	5	0.68 35 d	0.12	Whole fruit	29 41	0.26 0.22
	SC 400 g/l	5	0.68 21 d	0.12	Whole fruit	28 55	0.30 0.15
France (N), Sigloy, 1998 Golden Smoothee	SC 400 g/l	5	0.68 76 d	0.09	Whole fruit	14	0.16
Baudet and Yslan, 1999a, Study 98-677, 98677OR1, reverse decline study	SC 400 g/l	5	0.68 63 d	0.09	Whole fruit	27	0.14
	SC 400 g/l	5	0.68 48 d	0.09	Whole fruit	28 42	0.14 0.11
	SC 400 g/l	5	0.68 35 d	0.09	Whole fruit	28 55	0.26 0.19
France (N),Tigy, 1998 Idared	SC 400 g/l	5	0.68 76 d	0.1	Whole fruit	21	0.25
Baudet and Yslan, 1999a, Study 98-677, 98677OR2, reverse decline study	SC 400 g/l	5	0.68 63 d	0.1	Whole fruit	34	0.17
	SC 400 g/l	5	0.68 48 d	0.1	Whole fruit	28 49	0.12 0.12
	SC 400 g/l	5	0.68 35 d	0.1	Whole fruit	28 62	0.10 0.05
France (N), Saulty, 1999 Idared	SC 400 g/l	5	0.69 69 d	0.1 (1) 0.09 (4)	Whole fruit	15	0.30
Venet and Yslan, 2000a, Study 99-517, 99517AM1, reverse decline study	SC 400 g/l	5	0.69 55 d	0.1 (1) 0.09 (4)	Whole fruit	29	0.34
	SC 400 g/l	5	0.69 (1) 0.72 (1) 0.69 (3) 41 d	0.1 (1) 0.09 (4)	Whole fruit	28 43	0.19 0.21
	SC 400 g/l	5	0.69 28 d	0.1 (1) 0.09 (4)	Whole fruit	27 56	0.30 0.16
France (N), Mesnil-Domqueur 1999 Jonagold	SC 400 g/l	5	0.69 70 d	0.12	Whole fruit	15	0.08
Venet and Yslan, 2000a, Study 99-517, 99517AM2, reverse decline study	SC 400 g/l	5	0.69 56 d	0.12	Whole fruit	29	0.07
	SC 400 g/l	5	0.69 42 d	0.12	Whole fruit	28 43	0.11 0.06
	SC 400 g/l	5	0.69 29 d	0.12	Whole fruit	27 56	0.08 0.07
France (N), Sigloy, 1999 Golden Smoothee	SC 400 g/l	5	0.69 69 d	0.09	Whole fruit	12	0.09
Venet and Yslan, 2000a, Study 99-517, 995170R1, reverse decline study	SC 400 g/l	5	0.69 56 d	0.09	Whole fruit	26	0.14

APPLES Country, year, variety, report No.	Application				Commodity	PHI, days	Residue, mg/kg
	Form	no.	kg ai/hl, No. days [1/]	kg ai/hl			
Venet and Yslan, 2000a, Study 99-517, 995170R1, continued	SC 400 g/l	5	0.69 42 d	0.09	Whole fruit	28 40	0.07 0.1
	SC 400 g/l	5	0.69 28 d	0.09	Whole fruit	28 56	0.13 0.06
France (N) Celle les Condé, 1999 Douce Coet Venet and Yslan, 2000a, Study 99-517, 99517RS1, reverse decline study	SC 400 g/l	5	0.69 (2) 0.72 (1) 0.69 (2) 93 d	0.2	Whole fruit	14	0.12
	SC 400 g/l	5	0.69 (3) 0.74 (1) 0.69 (1) 69 d	0.2	Whole fruit	29	0.16
	SC 400 g/l	5	0.9 60 d	0.2	Whole fruit	28 42	0.12 0.083
	SC 400 g/l	5	0.9 40 d	0.2	Whole fruit	31 60	0.08 0.04
France (S), Vedene, 1997 Golden Delicious Maestracci, 1998a, Study 97-528, 97528AV1	SC 400 g/l	12	0.68	0.11	Whole fruit	0 7 14 21	1.3 0.54 0.70 0.64
France (S), Lugon et Ile du Carnet, 1997 Oregon Maestracci, 1998a, Study 97-528, 97528BX1 [2/]	SC 400 g/l	12	0.68	0.18	Whole fruit	0 7 14 21	2.9 1.8 0.67 0.73
France (S), Les Vigneres, 1998 Golden Delicious	SC 400 g/l	5	0.68 64 d	0.16	Whole fruit	12	0.28
Baudet and Yslan, 1999a, Study 98-677, 98677AV1, reverse decline study	SC 400 g/l	5	0.680 51 d	0.16	Whole fruit	25	0.31
	SC 400 g/l	5	0.680 36 d	0.16	Whole fruit	28 40	0.40 0.13
	SC 400 g/l	5	0.680 22 d	0.16	Whole fruit	29 54	0.36 <0.05
France (S), Saint Vincent de Paul, 1998 Golden Delicious	SC 400 g/l	5	0.68 64 d	0.15 (2) 0.20 (3)	Whole fruit	13	0.77
Baudet and Yslan, 1999a, Study 98-677, 98677BX1, reverse decline study	SC 400 g/l	5	0.68 49 d	0.15 (2) 0.20 (3)	Whole fruit	28	0.49
	SC 400 g/l	5	0.68 35 d	0.15 (2) 0.20 (3)	Whole fruit	29 42	0.19 0.21
	SC 400 g/l	5	0.68 21 d	0.15 (2) 0.20 (3)	Whole fruit	28 56	0.25 0.14
France (S), Seyssuel, 1998 Golden Delicious	SC 400 g/l	5	0.68 54 d	0.29	Whole fruit	14	0.45
Baudet and Yslan, 1999a, Study 98-677, 98677LY1, reverse decline study	SC 400 g/l	5	0.68 (1) 0.67 (1) 0.68 (3) 37 d	0.29 (1) 0.28 (1) 0.29 (2) 0.16 (1)	Whole fruit	31	0.59
	SC 400 g/l	5	0.68 (1) 0.67 (1) 0.68 (3) 27 d	0.29 (1) 0.28 (1) 0.29 (2) 0.16 (1)	Whole fruit	27 41	1.0 0.59

APPLES Country, year, variety, report No.	Application				Commodity	PHI, days	Residue, mg/kg
	Form	no.	kg ai/hl, No. days [1/]	kg ai/hl			
Baudet and Yslan, 1999a, Study 98-677, 98677LY1, reverse decline study, continued	SC 400 g/l	5	0.69 8 d	0.29 (1) 0.28 (1) 0.29 (2) 0.16 (1)	Whole fruit	29 60	1.2 0.49
France (S), Castelnaudary, 1998, Golden Delicious	SC 400 g/l	5	0.69 47 d	0.09	Whole fruit	14	0.8
Baudet and Yslan, 1999a Study 98-677, 98677TL1, reverse decline study	SC 400 g/l	5	0.69 35 d	0.09	Whole fruit	26	0.61
	SC 400 g/l	5	0.69 20 d	0.09	Whole fruit	27 41	0.25 0.31
	SC 400 g/l	5	0.69 5 d	0.09	Whole fruit	28 56	0.56 0.35
France (S), Robion, 1999 Granny Smith	SC 400 g/l	5	0.69 56 d	0.25	Whole fruit	14	0.11
Venet and Yslan, 2000a, Study 99-517, 99517AV1, reverse decline study	SC 400 g/l	5	0.69 41 d	0.25	Whole fruit	29	0.12
	SC 400 g/l	5	0.69 28 d	0.25	Whole fruit	29 43	0.16 0.08
	SC 400 g/l	5	0.68 13 d	0.25	Whole fruit	28 57	0.1 0.06
France (S), Saint Vincent de Paul, 1999 Golden Delicious	SC 400 g/l	5	0.6 7 d	0.08	Whole fruit	14	1.9
Venet and Yslan, 2000a, Study 99-517, 99517BX1, reverse decline study	SC 400 g/l	5	0.69 6 d	0.08	Whole fruit	28	0.87
	SC 400 g/l	5	0.69 7 d	0.08	Whole fruit	27 41	0.56 0.48
	SC 400 g/l	5	0.69 8 d	0.08	Whole fruit	27 55	0.75 0.30
France (S), Saint Didier sous Riverie, 1999 Golden Delicious	SC 400 g/l	5	0.69 56 d	0.11 (3) 0.1 (2)	Whole fruit	13	0.35
Venet and Yslan, 2000a, Study 99-517, 99517LY1, reverse decline study	SC 400 g/l	5	0.69 39 d	0.11 (3) 0.1 (2)	Whole fruit	28	0.17
	SC 400 g/l	5	0.69 30 d	0.11 (3) 0.1 (2)	Whole fruit	28 41	0.21 0.18
	SC 400 g/l	5	0.69 13 d	0.11 (3) 0.1 (2)	Whole fruit	28 56	0.42 0.12
France (S), Castelnaudary 1999 Variety not stated	SC 400 g/l	5	0.69 49 d	0.13	Whole fruit	13	0.57
Venet and Yslan, 2000a, Study 99-517, 99517TL1, reverse decline study	SC 400 g/l	5	0.69 35 d	0.13	Whole fruit	27	0.32
	SC 400 g/l	5	0.69 21 d	0.13	Whole fruit	28 41	0.23 0.21
	SC 400 g/l	5	0.69 7 d	0.13	Whole fruit	28 55	0.36 0.26
USA, New York, 1995 MacIntosh Wargo, 1996a, Study US95X01R 95-0069	WP, 65%	6	2.2	0.23	Whole fruit	7	1.32

APPLES Country, year, variety, report No.	Application				Commodity	PHI, days	Residue, mg/kg
	Form	no.	kg ai/hl, No. days [1/]	kg ai/hl			
USA, Pennsylvania, 1995 Empire Wargo, 1996a, Study US95X01R 95-0070	WP, 65%	6	2.1	0.43 0.38 (2) 0.36 0.49 0.40	Whole fruit	7	0.88
USA, Pennsylvania, 1995 Starkrimson, Red Delicious Wargo, 1996a, Study US95X01R 95-0071	WP, 65%	6	2.1	0.21 0.22 0.21 0.22 0.28 (2)	Whole fruit	7	1.55
USA, North-Carolina, 1995 Red Delicious Wargo, 1996a, Study US95X01R 95-0072	WP, 65%	6	2.1 2.2 (3) 2.1 (2)	0.12 (3) 0.1 0.12 (2)	Whole fruit	7	1.43
USA, Michigan, 1995 Macintosh Wargo, 1996a, Study US95X01R 95-0073	WP, 65%	6	2.2 (2) 2.2 2.2 (3)	0.31 0.33 0.32 0.33 0.32 (2)	Whole fruit	7	1.44
USA, Indiana, 1995 Red Stayman Wargo, 1996a, Study US95X01R 95-0074	WP, 65%	6	2.1 2.2(5)	0.23	Whole fruit	7	2.28
USA, California, 1995 Granny Smith Wargo, 1996a, Study US95X01R 95-0076	WP, 65%	6	2.2	0.1	Whole fruit	7	1.73
USA, Washington, 1995 Red Chief Wargo, 1996a, Study US95X01R 95-0077	WP, 65%	6	2.1 (4) 2.2 2.1	0.14 (5) 0.15	Whole fruit	7	2.01
USA, Washington, 1995 Red Delicious Wargo, 1996a, Study US95X01R 95-0078	WP, 65%	6	2.1 2.2 2.1 (2) 2.2 2.1	0.14 (5) 0.15	Whole fruit	7	2.35
USA, Oregon, 1995 Red Delicious Wargo, 1996a, Study US95X01R 95-0079	WP, 65%	6	2.1	0.18 0.19 (5)	Whole fruit	7	1.14
USA, Oregon, 1995 Red Delicious Wargo, 1996a, Study US95X01R 95-0080	WP, 65%	6	2.1	0.19 (5) 0.2	Whole fruit	7	1.03
USA, Arizona, 1996 Jonathan Wargo, 1996a, Study US95X01R 95-0322	WP, 65%	6	2.2 (3) 2.1 (1) 2.2 (2)	0.23 (4) 0.24 0.23	Whole fruit	7	1.85
USA, California, 1995 Golden Delicious Wargo, 1996a, Study US95X01R 8204-01	WP, 65%	6	2.1 (3) 2.2 2.1 2.2	0.15 (4) 0.07 (2)	Whole fruit	7	1.10

[1/] Interval between the two last applications for reverse decline studies.
[2/] Untreated samples contained dodine residues >LOQ at PHI 0, 7 and 14 d.

Pears

Data on 23 GLP residue trials were submitted: 14 were conducted in France in 1998 and 1999 as decline study trials (Baudet and Yslan, 1999b, Venet and Yslan, 2000b); 2 were conducted in Belgium in 2001 (Pigeon, 2002a); and 7 were conducted in the USA in 1995 (Wargo, 1996b). Foliar

applications from ground-based sprayers were made in all trials, using an SC 400g/l in France and Belgium and a WP 65 in the USA.

In France, 6 decline study trials were conducted in 1998, using plot sizes of 29.7-150m^2 and four foliar applications by air-blast sprayer at 14-day intervals. Samples were collected immediately before the last application, then at 0 (2 hours), 14, 28 and 41 days PHI (±2 days). Eight additional decline study trials were conducted in 1999, according to the same protocol.

In Belgium, 2 trials were performed in 2001 on 40m^2 plots, with a application rates of 0.766-0.896 kg dodine/ha, which is in accordance with the Belgian GAP of 900 g active ingredient/ha. Four foliar applications were made at 14-day intervals. An atomiser sprayer was used to apply about 200 l/ha leaf surface area (40 m^2 soil corresponded to 60 m^2 of leaf surface area). Samples were collected at 28 days PHI, at mature harvest.

In the USA, 7 supervised trials were conducted in 1995 (6) and 1996 (1). Six applications were made to plots of 281-713 m^2, using air-blast sprayers. The intervals between the first four applications were 6-7 days, with the two last applications being exactly 14 and 7 days before first harvest. The intervals between the fourth and penultimate applications were 60-110 days.

Table 21. Dodine residues in pears resulting from supervised residue trials in Belgium, France and the USA (Baudet and Yslan, 1999b; Venet and Yslan, 2000b; Pigeon, 2002a; Wargo, 1996b).

PEARS Country, year, variety, report No.	Application				Commodity	PHI, days	Residue, mg/kg
	Form	No.	kg ai/ha	kg ai/hl			
Belgium (N), Gembloux, 2001 Conference Pigeon, 2002a, Study 20238, 20238/1	SC, 400 g/l	4	0.87 0.77 0.79 0.90	0.26	Whole fruit	28	0.37
Belgium (N), Gembloux, 2001 Durondeau Pigeon, 2002a, Study 20238, 20238/2	SC, 400 g/l	4	0.79 0.85 (2) 0.74	0.26	Whole fruit	28	0.45
France (N), Mesnil-Domqueur, 1998 Conference Baudet and Yslan, 1999b, Study 98-678, 98678AM1	SC, 400 g/l	3 4	0.90 0.96 0.90 (2)	0.23	Whole fruit	14 0 14 26 41	1.5 2.1 2.0 1.3 0.78
France (N), Saulty, 1998, Conference Baudet and Yslan, 1999b, Study 98-678, 98678AM2	SC, 400 g/l	3 4	0.90	0.22 (2) 0.65 (2)	Whole fruit	13 0 13 26 41	1.2 2.8 1.0 0.61 0.57
France (N), Semoy, 1998, William Baudet and Yslan, 1999b, Study 98-678, 98678OR11	SC, 400 g/l	3 4	0.90s	0.14	Whole fruit	14 0 14 28 41	0.53 1.2 0.44 0.18 0.07
France (N), Semoy, 1998 Conference Baudet and Yslan, 1999b, Study 98-678, 98678OR2	SC, 400 g/l	3 4	0.90	0.1 0.13 (3)	Whole fruit	14 0 14 28 41	0.91 1.2 1.2 0.48 0.61
France (N), Saint Pryve, 1999 Passe Crassane Venet and Yslan, 2000b, Study 99-518, 99518OR1	SC, 400 g/l	3 4	0.91	0.09	Whole fruit	14 0 14 27 42	0.8 1.4 1.1 0.54 0.42
France (N), Sigloy, 1999 Williams Venet and Yslan, 2000b, Study 99-518, 99518OR2	SC, 400 g/l	3 4	0.1	0.13	Whole fruit	13 0 13 29 42	1.2 3.5 0.88 0.37 0.27

PEARS Country, year, variety, report No.	Application				Commodity	PHI, days	Residue, mg/kg
	Form	No.	kg ai/ha	kg ai/hl			
France (S), Simandre 1998 Alexandrine Baudet and Yslan, 1999b, Study 98-678, 98678AV1	SC, 400 g/l	3 4	0.90	0.23	Whole fruit	28 0 14 28 43	0.48 1.6 0.67 0.6 0.46
France (S), Cabannes, 1998 Williams Baudet and Yslan, 1999b, Study 98-678, 98678LY1	SC, 400 g/l	3 4	0.90	0.24	Whole fruit	13 0 13 27	0.76 2.4 1.0 0.54
France (S), Cabannes, 1999 Alexandrine Venet and Yslan, 2000b, Study 99-518, 99518AV1	SC, 400 g/l	3 4	0.91	0.23	Whole fruit	14 0 14 28 43	1.0 1.1 1.7 0.40 0.12
France (S), Eyragues, 1999 Guyot Venet and Yslan, 2000b, Study 99-518, 99518AV2	SC, 400 g/l	3 4	0.91	0.21	Whole fruit	15 0 14 28 46	0.8 2.8 0.68 0.29 0.11
France (S), Saint Didier sous Riverie, 1999 Williams Venet and Yslan, 2000b, Study 99-518, 99518LY1	SC, 400 g/l	3 4	0.91	0.14	Whole fruit	14 0 14 28 41	0.32 1.9 0.43 0.25 0.13
France (S), Marcilly, 1999 Params Venet and Yslan, 2000b, Study 99-518, 999518LY2	SC, 400 g/l	3 4	0.91	0.12	Whole fruit	15 0 15 28 43	0.59 1.9 0.88 0.31 0.25
France (S), Villeneuve du Pareage, 1999 Conference Venet and Yslan, 2000b, Study 99-518, 99518TL1	SC, 400 g/l	3 4	0.91	0.11	Whole fruit	13 0 12 26 40	0.5 1.7 0.42 0.26 0.18
France (S), Bazus, 1999 Comice Venet and Yslan, 2000b, Study 99-518, 99518TL2	SC, 400 g/l	3 4	0.91	0.18	Whole fruit	17 0 14 28 37	0.49 0.52 0.22 0.16 0.11
USA (New York), 1995 Bartlett Wargo, 1996b, Study US95X03R, 95-0087	WP, 65%	6	2.2	0.31	Whole fruit	7	2.43
USA (California), 1995 Shenseikie Wargo, 1996b, Study US95X03R, 95-0088	WP, 65%	6	2.2	0.12 (5) 0.13	Whole fruit	7	0.50
USA (California), 1995 Bach Wargo, 1996b, Study US95X03R, 95-0089	WP, 65%	6	2.2	0.12	Whole fruit	5	1.71
USA (Washington), 1995 Bartlett Wargo, 1996b, Study US95X03R, 95-0090	WP, 65%	6	2.1 (4) 2.2 (2)	0.13 0.12 0.13 (4)	Whole fruit	7	1.74
USA (Washington), 1995 Deanjo Wargo, 1996b, Study US95X03R, 95-0091	WP, 65%	6	2.1 (4) 2.2 2.1	0.16 0.15 0.16 (3)	Whole fruit	7	1.82
USA (Oregon), 1995 Bartlett Wargo, 1996b, Study US95X03R, 95-0092	WP, 65%	6	2.1 (4) 2.2 2.1	0.22 (4) 0.23 (2)	Whole fruit	7	1.68
USA (California), 1996 Variety no stated Wargo, 1996b, Study US95X03R, 2207-01	WP, 65%	6	2.1 (2) 2.2 (2) 2.1 (2)	0.16 (3) 0.15 0.14 (2)	Whole fruit	7	1.94

Stone fruits

Cherries

Twenty-two GLP residue trials were conducted, 16 in France during the four growing seasons 1997, 1998, 1999 and 2001, (Maestracci, 1998b, 1998d and 1998e; Baudet and Yslan, 1999c and 1999d; Venet and Yslan, 2000c and 2000d; Pigeon, 2002b), and 6 trials in the USA during 1995 (Wargo, 1996c). Foliar applications were made in all trials, using a SC 400g/l in France and a 65 WP in the USA.

In France, the 16 supervised residue trials included seven decline studies and the treated plot sizes were 36-320 m^2. The first application was made at early flowering stage, the second at least seven days later at the end of flowering and the third three weeks after the second application. The intervals between the first and second applications, and the second and third applications, were 11-28 days and 14-22 days, respectively.

In the USA, six supervised residue trials were conducted in 1995, with 6 applications made by air-blast sprayers to plot sizes of 178-1070 m^2. The PHI was nominally 7 days in all cases. The intervals between applications were 6 ± 1 days, except between applications 4 and 5, with the 5th application being made at PHI 14 days, in all cases. The interval between the 5th and 6th applications varied from 5 to 30 days.

Table 22**.** Dodine residues in cherries resulting from supervised residue trials in France and the USA (Maestracci, 1998b, 1998d and 1998e; Baudet and Yslan, 1999c and 1999d; Venet and Yslan, 2000c and 2000d; Pigeon, 2002b; Wargo, 1996c).

CHERRIES Country, year, variety, report No.	Application				Commodity	PHI, days	Residue, mg/kg
	Form	No.	kg ai/ha	kg ai/hl			
France (N), Coulange-la-Vineuse, 1997 Starking Maestracci, 1998b, Study 97-547, 97547DJ1	SC 400 g/l	3	0.8	0.27	Whole fruit	0 7 14 54	4.5 1.3 0.70 0.05
France (N), Jussy, 1997 Sunburst Maestracci, 1998b, Study 97-547, 97547DJ2	SC 400 g/l	3	0.91 0.8 (2)	0.27	Whole fruit	0 7 14 54	2.8 0.35 0.27 0.05
France (N), Coulange-la-Vineuse, 1997 Starking Maestracci, 1998d, Study 97-549, 97549DJ1	SC 400 g/l	3	0.8	0.27	Whole fruit	54	<0.05
France (N), Jussy, 1997 Starking Maestracci, 1998d, Study 97-549, 97549DJ2	SC 400 g/l	3	0.8	0.27	Whole fruit	54	0.06
France (N), Coulange la Vineuse, 1998 Sunburst Baudet and Yslan, 1999c, Study 98-510, 98510DJ	SC 400 g/l	3	0.8	0.37	Flesh	40	<0.05
France (N), Jussy, 1998 Sunburst Baudet and Yslan, 1999d, Study 98-511, 98511DJ	SC 400 g/l	3	0.8	0.32	Whole fruit Whole fruit Flesh	0 6 40	1.78 1.10 <0.05
France (N), Jussy, 1999 Sunburst Venet and Yslan, 2000c, Study 99-514, 99514DJ	SC 400 g/l	3	0.81	0.32	Whole fruit Whole fruit Whole fruit Flesh	0 7 16 45	1.78 1.2 0.7 0.06
France (N), Jussy 2001 Marmotte Pigeon, 2002b, Study 20253	SC 400 g/l	3	0.82 0.8(2)	0.08	Whole fruit	13	0.14

CHERRIES Country, year, variety, report No.	Application				Commodity	PHI, days	Residue, mg/kg
	Form	No.	kg ai/ha	kg ai/hl			
France (S), Les Chères, 1997 Bigarreau Van Maestracci, 1998b, Study 97-547, 97547PAD1	SC 400 g/l	3	0.82 0.81 0.82	0.2	Whole fruit	0 6 13 42	1.0 1.1 0.77 0.07
France (S), Les Chères, 1997 L'Empereur Maestracci, 1998e, Study 97-550, 97550PAD1	SC 400 g/l	3	0.82 0.81 (2)	0.2	Whole fruit	32	0.08
France (S), Les Chères 1997 Geant Hedelfingen Maestracci, 1998e, Study 97-550, 97550PAD2	SC 400 g/l	3	0.82 (2) 0.81	0.2	Whole fruit	44	<0.05
France (S), Pernes les Fontaines, 1998 Burlat Baudet & Yslan, 1999c, Study 98-510, 98510AV1	SC 400 g/l	3	0.8	0.32	Flesh	21	0.15
France (S), Meilhan sur Garonne, 1998 Sunburst Baudet & Yslan, 1999d, Study 98-511, 98511DJ1	SC 400 g/l	3	0.8	0.27	Whole fruit Flesh	0 7 14 28	1.98 0.96 0.46 0.09
France (S), Belcastel, 1999 Stark Venet and Yslan, 2000c, Study 99-514, 99514TL1	SC 400 g/l	3	0.81	0.14	Whole fruit Flesh	0 7 12 42	2.16 0.70 0.56 0.04
France (S), Villeneuve du Paréage, 1999 Burlat Hâtive Venet and Yslan, 2000d, Study 99515, 99514TL1	SC 400 g/l	3	0.81	0.17	Flesh	38	0.04
France (S), Murs, 2000 Sumit Pigeon, 2002b, Study 20253, 01FARCHPO8	SC 400 g/l	3	0.77 0.8 0.79	0.08	Whole fruit	14	0.14
USA, Michigan, 1995 Cavalier Wargo, 1996c, Study US95X0R2, 95-0081	WP, 65%	6	1.46 (3) 1.45 (2) 1.46 (2)	0.21 (2) 0.22 (3) 0.21	Whole fruit	7	0.34
USA, Michigan, 1995 Sam's Wargo, 1996c, Study US95X0R2, 95-0082	WP, 65%	6	1.45 1.47 1.46 (4)	0.19 0.17 0.18 0.17 (3)	Whole fruit	7	1.15
USA, California, 1995 Burk Wargo, 1996c, Study US95X0R2, 95-0083	WP, 65%	6	1.46 (3) 1.45 (3)	0.08	Whole fruit	8	2.11
USA, California, 1995 Ruby Wargo, 1996c, Study US95X0R2, 95-0084	WP, 65%	6	1.46 (2) 1.45 (2) 1.49 1.46	0.07	Whole fruit	7	1.08
USA, Washington, 1995 Bing Wargo, 1996c, Study US95X0R2, 95-0085	WP, 65%	6	1.4	0.11	Whole fruit	7	1.40
USA, Oregon, 1995 Lambert Wargo, 1996c, Study US95X0R2, 95-0086	WP, 65%	6	1.4	0.14 0.15 (4) 0.14	Whole fruit	7	1.27

Peaches

Seventeen GLP supervised residue trials were conducted, 9 in the USA during 1995 (Wargo, 1996d) and 8 in France during 1997 and 1998, of which three were decline studies (Maestracci, 1998f and 1998g; Baudet and Yslan, 1999e and 1999f). Foliar applications were made in all trials, using a 400 g/l SC in France and a 65 WP in the USA.

In France, the 8 supervised residue trials were treated with 5 applications of 0.90 kg ai/ha. According to the proposed French GAP, the last treatment should be made at the end of flowering.

In the USA, the 9 supervised residue trials were treated with a nominal rate of 1.5 kg a.i/ha at each of the five applications, except in two of the trials, where the two first applications were made at 2.9 kg a.i./ha. The higher dose rate is only permitted for early applications, up to blossoming, and these have no impact on residues at harvest. The two last treatments were applied 25 and 15 days before harvest (except in one trial where harvest was at PHI 8 days). Application equipment consisted of air-blast sprayers at all sites, except for the trial in NC, where a hand-lance sprayer was used. Application volumes were 468-2834 l/ha and plot sizes were 111-1505 m^2.

Table 23. Dodine residues in peaches resulting from supervised residue trials in France and the USA (Wargo, 1996d; Maestracci, 1998f and 1998g; Baudet and Yslan, 1999e and 1999f).

PEACHES	Application				Commodity	PHI,	Residue,
Country, year, variety, report No.	Form	No.	kg ai/ha	kg ai/hl		days	mg/kg
France (S), Meynes, 1997 Snow Queen Maestracci, 1998f, Study 97-512, 97512AV1	SC 400 g/l	5	0.9	0.38	Whole fruit Flesh Whole fruit	64 79 95	<u><0.05</u> <0.05 <0.05
France (S), Bouloc,1997 Maycrest Maestracci, 1998f, Study 97-512, 97512TL	SC 400 g/l	5	0.9	0.1	Whole fruit Flesh Whole fruit	58 71 80	0.06 <u>0.07</u> <0.05
France (S), Barbentane, 1997 Silver King Maestracci, 1998g, Study 97-513, 97513AV1	SC 400 g/l	5	0.9	0.2	Flesh	87	<0.05
France (S), Meynes, 1997 Snow Queen Maestracci, 1998g, Study 97-513, 97513AV1	SC 400 g/l	5	0.9	0.27	Flesh	75	<u><0.05</u>
France (S),Millery 1998 Redwing Baudet & Yslan, 1999e, Study 98-530, 98530LY1	SC 400 g/l	5	0.9	0.36	Flesh	106	<0.05
France (S), Charly 1998 Barbara Baudet & Yslan, 1999e, Study 98-530, 98530LY2	SC 400 g/l	5	0.9	0.28 0.25 (4)	Flesh	93	<0.05
France (S), Ste Bazeille1998 Daisy Baudet & Yslan, 1999f, Study 98-531, 98531BX1	SC 400 g/l	5	0.9	0.2	Flesh	57 85 105	<u>0.053</u> <0.05 <0.05
France (S), Bouloc ,1998 Maycrest Baudet & Yslan, 1999f, Study 98-531, 98531TL1	SC 400 g/l	5	0.9	0.09	Flesh	76	<u><0.05</u>
USA, New York, 1995 Red Haven/Glo Haven Wargo, 1996d, Study US95X06R, 95-0100	WP, 65%	5	1.47 (2) 1.48 1.47 1.46	0.31	Whole fruit	15	<u>0.68</u>
USA, Georgia, 1995 June Prince Wargo, 1996d, Study US95X06R, 95-0101	WP, 65%	5	1.46 1.54 1.5(3)	0.31 0.3 (5)	Whole fruit	15	<u>0.46</u>
USA, South Carolina, 1995 Winblo Wargo, 1996d, Study US95X06R, 95-0102	WP, 65%	5	1.45 1.46 1.44 1.5 1.46	0.16(4) 0.15	Whole fruit	15	<u>0.77</u>
USA, North Carolina, 1995 Madison Wargo, 1996d, Study US95X06R, 95-0103	WP, 65%	5	1.47 1.44 1.48 1.47 1.48	0.08	Whole fruit	15	<u>0.48</u>
USA, Michigan, 1995 PF 16 Wargo, 1996d, Study US95X06R, 95-0104	WP, 65%	5	1.48 1.46(2) 1.45 1.46	0.21	Whole fruit	15	<u>1.27</u>

PEACHES Country, year, variety, report No.	Application				Commodity	PHI, days	Residue, mg/kg
	Form	No.	kg ai/ha	kg ai/hl			
USA, Oklahoma , 1995 Hales Best Wargo, 1996d, Study US95X06R, 95-0105	WP, 65%	5	1.52 1.4 1.54 1.44 1.46	0.05 0.06 0.08 0.06(2)	Whole fruit	11	3.71
USA, California, 1995 Starnes Wargo, 1996d, Study US95X06R, 95-0106	WP, 65%	5	3.1 2.9 1.46 (3)	0.16 0.15 0.07 0.08 (2)	Whole fruit	15	2.50
USA, California, 1995 Ryan Sun Wargo, 1996d, Study US95X06R, 95-0107	WP, 65%	5	2.94 2.9 1.46 (3)	0.16 (2) 0.08 (3)	Whole fruit	14	1.65
USA, California, 1995 Fay Alberta Wargo, 1996d, Study US95X06R, 95-010	WP, 65%	5	2.91 2.94 1.46 1.47 1.46	0.16 (2) 0.08 (3)	Whole fruit	15	1.77

Plums

Six supervised trials were conducted in the USA in 1995, using treated plots of 348-664 m^2 (Wargo, 1996e). Using a WP 65 formulation, 6 applications were made to each plot; the two last applications were made 14 and 7 days before the first harvest, with an interval of 7 ± 1 days between them. The nominal application rate was 1.560 kg ai/ha, using an air-blast sprayer with an average spray volume of 1562 l/ha. The first application was at petal fall, or early post-petal fall, and the last one was made to mature fruit.

The overall mean residue level was 0.80 mg/kg, with a range 0.36-1.69 mg/kg, at mature harvest, each value representing the mean of two samples from each treated plot).

Table 24**.** Dodine residues in plums resulting from supervised residue trials in the USA (Wargo 1996e).

PLUMS country, year	Application				Commodity	PHI, days	Residue, mg/kg
	Form	No.	kg ai/ha	kg ai/hl			
USA Michigan), 1995 Stanley Wargo, 1996e, Study US95X04R, 95-0093	WP, 65%	6	1.46 (4) 1.45 1.46	0.23 (2) 0.24 (2) 0.23 0.24	Whole fruit	7	1.55
USA (California), 1995 Angelino Wargo, 1996e, Study US95X04R, 95-0094	WP, 65%	6	1.47 1.46 (5)	0.08	Whole fruit	7	0.55
USA (California), 1995 Angelino Wargo, 1996e, Study US95X04R, 95-0095	WP, 65%	6	1.44 1.46 (5)	0.08	Whole fruit	7	0.68
USA (California), 1995 Howard Sun Wargo, 1996e, Study US95X04R, 95-0096	WP, 65%	6	1.46	0.08	Whole fruit	7	0.49
USA (California), 1995 Angelino Wargo, 1996e, Study US95X04R, 95-0097	WP, 65%	6	1.5	0.08	Whole fruit	7	1.05
USA (Oregon), 1995 Italian Wargo, 1996e, Study US95X04R, 95-0098	WP, 65%	6	1.44 1.43 (5)	0.11 0.12 0.11 (4)	Whole fruit	7	0.37

FATE OF RESIDUES IN STORAGE AND PROCESSING

A GLP Study on the magnitude of residues of dodine in/on apple processed fractions, obtained from apples that had been treated in the field (NY State, USA) with Syllit 65W, was conducted by Wargo, (1996f). Dodine was applied 6 times at a nominal exaggerated rate of 7.3 kg ai /ha by foliar spraying and apples were collected 7 days after the last application. Duplicate, unwashed whole apple samples were frozen to provide the whole fruit samples. Other samples were processed the day after, into

fresh unclarified juice and wet pomace, using procedures which closely simulated commercial practice. Duplicate samples of each product were collected, frozen immediately at <-18°C, then stored in the freezer for approximately 14 months before analysis. Dodine residues were determined in the processed fractions using the method validated by Pittman (1996), which had an LOQ of 0.05mg/kg (Table 25).

Table 25. Mean residue levels of dodine in apple processed fractions, following field treatment of apples with Syllit 65 WP (Wargo, 1996f).

Trial	Form	Rate, kg a.i/ha	PHI	Matrix	Mean residue (mg/kg)	Processing factor
USA, New York, 1995	WP 65	6 x 7.3	7 days	Whole fruit	1.52	
				Unclarified juice	0.13	0.09
				Wet pomace	7.77	5.11

Dodine levels in the untreated control samples were below the LOQ of 0.05 mg/kg. The mean recovery of dodine from fortified untreated control samples of apple processed fractions was 80.9 ± 9.6% (n = 2) from whole apples, 106.25 ± 13.95% (n = 2) from unclarified juice and 94.4% (n = 1) from wet pomace. Treated apple samples showed a mean residue value of 1.67 mg/kg in the whole apples, 0.13 mg/kg in the juice and 7.77 mg/kg in the wet pomace. These results show that the residue is effectively concentrated in the wet pomace (processing factor of 5.11) with very little dodine in the juice (processing factor of 0.09).

RESIDUES IN ANIMAL COMMODITIES

No studies were submitted to the meeting.

RESIDUES IN SUCCEEDING CROPS

Not needed because there are no successional crops.

NATIONAL MAXIMUM RESIDUE LIMITS

Table 26. National MRLs.

Region or country	Commodity	MRL, mg/kg	Residue definition
EU	Pome fruit (apples, pears, others) Stone fruit (peaches, cherries, plums, others) Others	1.0 1.0 0.2	Dodine (Dir. 88/298 EEC)
Australia	Pome fruit Stone fruit	5.0 5.0	Dodine
Canada	Apples, Pears Cherries (sour/sweet) Strawberry	5.0 2.0 5.0	Dodine
USA	Apples, Pears, Cherries (sour/sweet), Peaches, Strawberries Pecans, Walnuts Spinach Meat, Milk	5.0 0.3 12.0 0.0	Dodine

APPRAISAL

Dodine, 1-dodecylguanidinium acetate (dodecylguanidine monoacetate), is a fungicide and bactericide registered for foliar use on pome fruits, stone fruits including cherries, and nuts including walnuts.

Dodine is the only active substance from the guanidine family, which was first evaluated in 1974 for toxicology and residues by the JMPR and subsequently in 1976 and 1977. The latest toxicology review was in 2000. It was listed under the Periodic Review Programme at the 30th Session of the CCPR (ALINORM 99/24) for review by the 2001 JMPR but was re-scheduled for 2003.

The 2000 JMPR allocated an acceptable daily intake for humans of 0-0.1 mg/kg bw and an acute reference dose of 0.2 mg/kg bw.

The 1977 JMPR considered that a feeding study with large animals, to determine whether feeding apple pomace and grape pomace would contribute residues to meat and milk, was still desirable.

The manufacturer supplied information on identity, methods of analysis, use pattern, metabolism in plants and farm animals, residue trials on apples, pears, cherries, peaches and plums, storage stability in analytical samples, effects of processing on residues and fate in the environment.

In addition, information on GAP was provided by the governments of France and The Netherlands.

Dodine is currently formulated as wettable powders, suspension concentrates and water dispersible granules. It is a slightly yellow fine powder with low solubility in water (<1g/l) and organic solvents. Dodine is not considered fat-soluble, as its log P_{ow} is 0.96.

Animal metabolism

The metabolism of radiolabelled dodine was investigated in rats and a lactating goat. The metabolic pathway in both rats and goat suggests that dodine is extensively metabolized by both species by initially forming a carboxylic acid chain with the elimination of urea and a subsequent series of 2-carbon degradation cycles, consistent with the beta-oxidation pathway used by mammals to degrade medium to long chain fatty acids.

Metabolism by rats was reviewed by the 2000 JMPR. Cumulative excretion in urine and faeces was reported as being above 90% of the dose. Absorbed dodine was extensively metabolized in rats. Four metabolites were seen in urine: hydroxydodecylguanidine, the main metabolite, urea, and two unidentified metabolites which appeared to be a mixture of carboxylic acid products arising from oxidation of the alkane side chain.

In a lactating goat dosed orally for five consecutive days with [^{14}C]dodine at the mean equivalent dietary level of 12.8 ppm by gelatin capsule, dodine was extensively metabolized. A total of 68% of the dose was excreted, in urine (38%), faeces (30%) and milk (0.05%). Less than 1% of the dose remained in the tissues. Dodine was a minor component in all edible tissues and no parent compound was present in milk. In the dosed goat, ^{14}C levels were much higher in kidney and liver (0.168 mg/kg and 0.109 mg/kg as dodine) than in muscle or fat (0.02 mg/kg-0.008 mg/kg as dodine). Hexylguanidine carboxylic acid, octylguanidine carboxylic acid and dodecylguanidine carboxylic acid were identified but none exceeded 0.001 mg/kg dodine equivalents in the foreleg muscle or 0.05 mg/kg in the liver and kidney; urea was present in all edible tissues and milk (from <0.01 mg/kg dodine equivalents in milk and muscle to <0.017 mg/kg in liver and kidney).

Plant metabolism

Plant metabolism studies on apples, strawberries and pecan trees were reported. In apples and strawberries, the parent compound was the main component of the residue; metabolism appeared to be more active in nuts with dodine and guanidine being the main residues found in kernels. In apples much of the residue remained in the peel. The metabolism of dodine was found to be essentially similar among the plants tested. Degradation of dodine in fruits is a relatively slow process, occurring by successive oxidation and hydrolysis to CO_2 and ammonia; guanidine and urea are intermediate degradation products.

After three foliar applications of [^{14}C]dodine to field grown apple trees at a rate of 0.108 kg ai/hl each, radioactive residues at mature harvest (7 days after the third application) were mainly located in the apple peel (82.3% of the TRR). Dodine accounted for 72 to 89% of the TRR extracted from apple peel and pulp. Several minor metabolite fractions were observed, all below 0.01 mg/kg except one compound tentatively identified as guanidine, found at 0.017 mg/kg dodine equivalents.

After four foliar applications of [^{14}C]guanidine dodine to strawberries at 3.12 kg ai/ha, radioactive residues in mature fruit harvested 14 days after the third and fourth applications represented 4.3 to 6.8 mg/kg dodine equivalents. Unchanged dodine accounted for >85% of the TRR in washed strawberries. Several metabolite fractions were observed, all below 0.01 mg/kg dodine

equivalents except one at 0.05 mg/kg. No major metabolite was found, although urea and guanidine were identified as possible metabolites. In rinses (2.5% of the TRR), the parent was also the major component of the residue. No degradation product occurred at >0.01 mg/kg dodine equivalents.

After three foliar applications of [^{14}C]dodine to pecan trees during the growing season at 0.2 kg ai/hl, a low level of the applied dodine reached the kernels. Kernels isolated from mature pecans contained 0.114 mg/kg radioactive residues, including guanidine (0.041 mg/kg expressed as dodine, 36% of the TRR) and dodine (0.015 mg/kg, 13.2% of the TRR). Some 20% of the TRR (0.023 mg/kg dodine equivalents) was associated with the free fatty acid fraction.

Most of the parent compound underwent extensive metabolism to guanidine, followed by subsequent metabolism to $^{14}CO_2$ and NH_3. Carbon dioxide was assimilated into the metabolic pool. The very high proportion of lipid in the kernels is consistent with incorporation of $^{14}CO_2$ into the fatty acid fraction.

Immature pecans (including shells and hulls) harvested before the second application (60 days after the first) contained 2.152 mg/kg TRR, with dodine (0.976 mg/kg, 43.2% of the TRR) and guanidine (0.326 mg/kg dodine equivalents, 14.4% of the TRR) being the main compounds. Two unidentified metabolites, putative oxidation products of dodine, accounted for 0.2 mg/kg dodine equivalents (9.3% of the TRR) and 0.288 mg/kg dodine equivalents (13% of the TRR).

Environmental fate

Soil

The Meeting received information on the degradation of dodine under aerobic conditions in a number of soils, on soil photolysis and on field dissipation.

Aerobic soil degradation of dodine was rapid; the calculated half-lives ranged from 3 to 10 days in the tested soils. This degradation ultimately resulted in the formation of carbon dioxide without the formation of any other significant degradation products or persistent unextractable residues.

Field experiments confirmed that dodine is not a persistent compound and had a rather short half-life of 6-18 days at four locations; it did not move down the soil profile. Dodine did not undergo significant photolysis on soil surfaces.

It was suggested that the degradation of dodine in the environment is mainly microbial.

Analytical methods

The Meeting received a descriptionof analytical method 45137 and validation data for dodine in fruit crops. The method is based on GC with mass-selective detection (MSD) and achieved an LOQ of 0.05 mg/kg in apples, plums, peaches, pears and cherries, and 0.1 mg/kg in wet apple pomace.

Dodine was extracted from the fruit by homogenization with methanol and the solution was filtered and made to volume. An aliquot was cleaned up by liquid-liquid partition and the dodine was derivatizated by refluxing for two hours with hexafluoroacetylacetone in 1-chlorobutane. The solvent was evaporated and the extracts were dissolved in cyclohexane, for GC-MSD.

Apple wet pomace samples from the metabolism study with [^{14}C]dodine were extracted and analyzed by method 45137, giving an average value of 2.15 mg/kg. The average value obtained by LSC, after re-extraction by the 45137 technique, was 1.95 mg/kg, which is close to the value obtained by method 45137.

Stability of pesticides in stored analytical samples

The Meeting received information on the stability of dodine in various substrates at freezer temperatures. In the two studies conducted to examine the stability of dodine residues under deep freezer storage conditions, no significant degradation of dodine was observed in any of the substrates analyzed, for the duration of the study. The Meeting concluded that dodine was stable up to 18 months in apple, cherry, peach, apple juice and wet apple pomace samples when stored frozen.

Residue definition

Dodine was the main identified component (in samples containing ≥0.05 mg/kg) detected in edible portions in plant metabolism studies, representing 80.6% of the extracted TRR in apple pulp, 86.5% of the extracted radioactivity of washed strawberries and 13.2% of the TRR in mature pecan kernels. No major metabolite was identified except in pecan kernels, where guanidine represented 36% of the TRR but only 0.041 mg/kg.

In the metabolism study on a lactating goat dosed orally, dodine represented less than 1% of the TRR in edible tissues and was not identified in milk. The major metabolites of dodine identified in tissues and milk, resulting from beta-oxidation, were hexylguanidine carboxylic acid, octylguanidine carboxylic acid and dodecylguanidine carboxylic acid, each representing less than 0.05 mg/kg dodine equivalents.

The Meeting concluded that dodine residues, both for compliance with MRLs and for the estimation of dietary intakes, should be defined as dodine.

The definition applies to both plant and animal commodities.

Results of supervised trials

Supervised trials of the foliar application of WP and SC formulations to apples, pears, peaches, cherries and plums were reported from Europe (Belgium and France) and the USA.

In all supervised trials reported from France on pears, residues were measured on fruit taken just before the last application as well as just after it. The first residue expressed as a percentage of the second provided an indication of the contribution of previous applications to the final residue in the case of multiple applications. The average carryover of 48% (range 16%-91%) suggested that the number of applications may have an influence on the final residue at harvest. Decline studies on both apples and pears suggested that dodine has an average half-life of about 20 days after multiple applications. It was therefore considered that 2 applications would be likely to produce a higher residue level than one application and would provide reliable information for estimating residue levels.

Trials were not reported on strawberries or grapes, for which CXLs exist at 5 mg/kg for both commodities. The Meeting agreed to recommend withdrawal of these CXLs.

Apples. Field data were reported from France and the USA.

GAP for use of SC formulations in France is 0.7 kg ai/ha with a PHI of 28 days, with a maximum of four applications. Seventeen supervised residue trials in France complied with the French PHI and application rate but would probably have produced lower residues than expected as the interval between the penultimate and last applications was generally longer than intended. The residues at mature harvest were 0.07, 0.12, 0.14 (2), 0.16, 0.17 (2), 0.23, 0.25, 0.31, 0.32, 0.34, 0.39, 0.49, 0.59, 0.61, 0.87 mg/kg.

GAP for the WP formulation in the USA specifies foliar application of 0.75 to 2.2 kg ai/ha with a PHI of 7 days, with no information on the maximum number of applications. Thirteen trials in the USA complied with US GAP; the residues were 0.88, 1.03, 1.10, 1.14, 1.32, 1.43, 1.44, 1.55, 1.73, 1.85, 2.01, 2.28 and 2.35 mg/kg.

The Meeting decided to use only the US trials in the evaluation, because the two populations of results were considered to be different.

Pears. Field data were reported from Belgium, France and the USA.

GAP for France is the same as for apples. Fourteen supervised trials in France matched French GAP. The residues in rank order were 0.16, 0.18, 0.25, 0.26, 0.29, 0.31, 0.37, 0.40, 0.61, 0.54 (2), 0.6, 0.61 and 1.3 mg/kg.

GAP for use of SC formulations in Belgium is 1 kg ai/ha, with three or four applications. Two Belgian trials supported the Belgian use pattern and the residues were 0.37 and 0.45 mg/kg.

GAP for use of the WP formulation in the USA is for foliar application at 1.5-2.25 kg ai/ha with a PHI of 7 days. Seven trials in the USA accorded with US GAP. The residues in rank order were 0.50, 1.68, 1.71, 1.74, 1.82, 1.94 and 2.43 mg/kg.

The Meeting decided to use only the USA trials in the evaluation because the results from Europe and the USA were considered to be from different populations, with higher residues in the US trials.

As the use patterns of dodine on pears and apples were considered similar in terms of PHIs and dose rates, the Meeting agreed to combine the results from the US trials for estimating a maximum residue level for pome fruits.

The combined residues in the 20 trials were (median underlined) 0.50, 0.88, 1.03, 1.10, 1.14, 1.32, 1.43, 1.44, 1.55, 1.68, 1.71, 1.73, 1.74, 1.82, 1.85, 1.94, 2.01, 2.28, 2.35 and 2.43 mg/kg.

The Meeting agreed to recommend the withdrawal of the existing separate CXLs of 5 mg/kg for apples and pears and made a new recommendation for pome fruits of 5 mg/kg, and estimated an STMR of 1.70 mg/kg and an HR of 2.43 mg/kg.

Cherries. Field trials were reported from France. Dodine is not registered in France for use on cherries. Two of the French trials could be evaluated against Spanish GAP (0.05-0.08 kg/hl, 15 days PHI, no information on the maximum number of applications allowed), for foliar applications of the SC formulation. The results were 0.14 (2) mg/kg.

Dodine is registered in the USA at a dose rate of 0.75-1.5 kg for foliar applications but no current PHI was provided. GAP for use of a WP formulation in Canada is 1.5 kg/ha by foliar application and a PHI of 7 days but no information was provided on the maximum number of applications. The six US trials were evaluated against Canadian GAP. The results in rank order (median underlined) were 0.34, 1.08, 1.15, 1.27, 1.4 and 2.11 mg/kg.

The Meeting decided to use the results of US trials in the evaluation and agreed to recommend withdrawal of the current CXL of 2 mg/kg for cherries to be replaced by 3 mg/kg, and estimated an STMR and an HR of 1.21 mg/kg and 2.11 mg/kg, respectively, both expressed on the whole fruit as no information was available on the edible portion.

Peaches and nectarines. Field trials on peaches were reported from France and the USA.

Five of the 7 supervised residue trials reported from France complied with the current French GAP of 0.9 kg ai/ha by foliar application of an SC formulation with a 60-day PHI (last treatment at the end of flowering). The resultant residues were <0.05 mg/kg in whole fruit and <0.05(2), 0.05 and 0.07 mg/kg in pulp.

Nine supervised trials reported from the USA complied with the current US GAP of 1.5-3 kg ai/ha by foliar application with a WP formulation and a PHI of 15 days. The results in rank order (median underlined) were 0.46, 0.48, 0.68, 0.77, 1.27, 1.65, 1.77, 2.50 and 3.71 mg/kg.

The results from the US trials were evaluated. The Meeting confirmed the previous recommendation for an MRL of 5 mg/kg, now a CXL, and estimated an STMR of 1.27 mg/kg and an HR of 3.71 mg/kg (both expressed on whole fruit as no information was available on the edible portion).

The Meeting agreed to extrapolate the recommendations to nectarines, as current GAP for peaches applies to nectarines in the USA.

Plums. Field trials were reported from the USA. Dodine is not registered for use on plums in the USA, so the trials could not be evaluated.

Processing

One processing study was reported from the USA on apples. The residues in processed fractions from treated apples were determined after six foliar applications to apple trees, each at the nominal rate of 7.3 kg ai/ha. Samples taken at 7 days PHI were processed the next day into fresh unclarified juice and wet pomace using procedures closely simulating commercial practices.

Dodine in the processed fractions was determined by the current validated method and the results showed that the residue was concentrated in the wet pomace (processing factor of 5.11) with very little found in the juice (processing factor 0.09).

These processing factors were applied to the STMR of the raw commodity, to estimate STMR-Ps of 8.69 mg/kg and 0.15 mg/kg in wet apple pomace and apple juice, respectively.

Farm animal dietary burden

The Meeting estimated the dietary burden of dodine residues in farm animals on the basis of the feeding stuffs listed in appendix IX of the FAO manual.

Wet apple pomace might be used as feed for diary and beef cattle. As this is a processed commodity, the STMR-P estimated by the Meeting was used for the estimation of both the maximum and the median farm animal dietary burdens (Table 27).

Table 27. Farm animal dietary burden estimates.

Commodity	STMR/ STMR-P (mg/kg)	Group	Dry matter %	Residue on dry basis, mg/kg	% of diet		Residue contribution mg/kg	
					Beef cattle	Dairy cattle	Beef cattle	Dairy cattle
Apple pomace, wet	8.69	AB	40	21.8	40	20	8.7	4.4
						Total:	8.7	4.4

The estimated dietary burdens of dodine for animal commodity MRL and STMR estimations (residue levels in animal feed expressed on dry weight) are: beef cattle 8.7 ppm, dairy cattle 4.4 ppm.

Farm Animal feeding studies

No animal feeding study was provided. However, in the metabolism study on a lactating goat dosed orally for five consecutive days with a calculated mean daily dose of 12.8 ppm and slaughtered approximately 23 h after the last dose (the plasma peak was reached 8 h after the last dose), dodine was not considered fat-soluble. The Meeting therefore expected that on the basis of the current calculated dietary burdens, residues of dodine would be low in the edible tissues, organs and milk of beef or dairy cattle ingesting 8.7 ppm or 4.4 ppm dodine, respectively.

Animal commodity maximum residue levels

In the absence of an animal feeding study and a method of analysis for dodine residues in animal products, the Meeting did not estimate a maximum residue level or an STMR for animal products.

FURTHER WORK OR INFORMATION

Desirable

1. A method for determination of residues of dodine in animal products.
2. A farm animal feeding study.

RECOMMENDATIONS

On the basis of the data from supervised trials, the Meeting concluded that the residue levels listed in Table 28 are suitable for establishing maximum residue limits and for IEDI assessment.

Definition of the residue for compliance with MRLs and for estimation of dietary intake: *dodine*.

Table 28. Summary of recommendations.

Codex Classification Number	Commodity	MRL, mg/kg		STMR or STMR-P, mg/kg	HR or HR-P, mg/kg
		New	Previous		
FP 0226	Apples	W	5		
JF 0226	Apple juice			0.15	
FS 0013	Cherries	3	2	1.21	2.11
FB 0269	Grapes	W	5		
FS 0245	Nectarines	5		1.27	3.71
FS 0247	Peaches	5	5	1.27	3.71
FP 0230	Pears	W	5		
FP 0009	Pome fruits	5		1.70	2.43
FB 0275	Strawberries	W	5		

DIETARY RISK ASSESSMENT

Long term intake

The International Estimated Daily Intakes (IEDIs) of dodine, based on the STMRs estimated by the Meeting for pome fruits (apples and pears), peaches, nectarines and cherries, and on the STMR-P for apple juice, were 0-2% of the maximum ADI of 0.1 mg/kg bw/day (JMPR 2000) for the five GEMS/Food regional diets (Table 29).

The Meeting concluded that the intake of residues of dodine, resulting from the uses considered by the JMPR, was unlikely to present a public health concern.

Table 29. Assessment of risk from the long-term dietary intake of residues of dodine (ADI = 0-0.1 mg/kg bw/day).

Code	Commodity	MRL mg/kg*	STMR or STMR-P mg/kg*	Diets: g/person/day. Intake = daily intake: µg/person									
				Mid-East		Far-East		African		Latin American		European	
				diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
JF 0226	Apple juice	-	0.15	4.5	0.7	0	0.0	0	0.0	0.3	0.0	3.8	0.6
FS 0013	Cherries	-	1.21	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.0	3.6
FS 0245	Nectarines	-	1.27	1.3	1.6	0.3	0.3	0.0	0.0	0.4	0.5	6.3	7.9
FS 0247	Peaches	-	1.27	1.3	1.6	0.3	0.3	0.0	0.0	0.4	0.5	6.3	7.9
FP 0009	Pome fruits	-	1.70	10.8	18.4	7.5	12.8	0.3	0.5	6.5	11.1	51.3	87.2
Total intake (µg/person)=					22.2		13.4		0.5		12.1		107.3
Bodyweight per region (kg bw) =					60		55		60		60		60
ADI (µg/person)=					6000		5500		6000		6000		6000
%ADI=					0.4		0.2		0.0		0.2		1.8
Rounded %ADI=					0		0		0		0		2

Short term intake

The International Estimated Short-Term Intakes (IESTIs) for dodine were calculated for commodities for which STMRs o*r* HRs were estimated by current Meeting. On the basis of the acute reference dose of 0.2 mg/kg bw allocated in 2000, the estimated intakes based on the HRs estimated by the Meeting for apples, pears, peaches, nectarines and cherries were 6-30% of the acute RfD for the general population (Table 30) and 20-80% of that for children up to 6 years (Table 31).

The Meeting concluded that the short-term intake of residues of dodine, resulting from the uses considered by the JMPR, was unlikely to present a public health concern.

Table 30. Assessment of risk to the general population from the short-term dietary intake of residues of dodine (acute RfD = 0.2 mg/kg bw or 200 µg/kg bw).

Codex Code	Commodity	STMR or STMR-P, mg/kg	HR or HR-P, mg/kg	Large portion diet			Unit wt, g	Country	Unit wt, edible portion, g	Variability factor	Case	IESTI, µg/kg bw/day	% acute RfD, rounded
				Country	Body wt (kg)	Large portion g/person							
FP 0226	Apples	-	2.43	USA	65.0	1348	138	USA	127	3	2a	59.89	30
JF 0226	Apple juice	0.15		-	-	-	-	-	-	-	-	-	-
FS 0013	Cherries	-	2.11	FRA	62.3	375	12	UNK	10	-	1	12.70	6
FS 0245	Nectarines	-	3.71	USA	65.0	590	136	USA	125	3	2a	47.97	20
FS 0247	Peaches	-	3.71	SAF	55.7	685	98	USA	85	3	2a	56.99	30
FP 0230	Pears	-	2.43	USA	65.0	693	166	USA	151	3	2a	37.20	20

Table 31. Assessment of risk to children up to 6 years old from the short-term dietary intake of residues of dodine (acute RfD = 0.2 mg/kg bw or 200 µg/kg bw).

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P, mg/kg	Large portion diet			Unit wt, g	Country	Unit wt, edible portion, g	Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body wt (kg)	Large portion, g/person							
FP 0226	Apples	-	2.43	USA	15.0	679	138	USA	127	3	2a	151.09	80
JF 0226	Apple juice	0.15	0.22	-	-	ND	-	-	-	-	-	-	-
FS 0013	Cherries	-	2.11	FRA	17.8	297	12	UNK	10	-	1	35.17	20
FS 0245	Nectarines	-	3.71	AUS	19.0	302	136	USA	125	3	2a	107.85	50
FS 0247	Peaches	-	3.71	AUS	19.0	315	98	USA	85	3	2a	94.90	50
FP 0230	Pears	-	2.43	UNK	14.5	279	166	USA	151	3	2a	97.38	50

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