### **THIABENDAZOLE (65)**

### **EXPLANATION**

Thiabendazole was evaluated by the Joint Meeting in 1970, 1971, 1972, 1975, 1977, 1979, and 1981. MRLs were recommended for apple, banana, cereal grains, citrus fruits, edible offals, meat, milks, bulb onions, pear, potato, strawberry, sugar beet, sugar beet leaves, molasses and dried pulp, and tomato, and have now been adopted as CXLs. JECFA reviewed thiabendazole in 1992 and recommended MRLs of 0.1 mg/kg for all edible tissues of cattle, goats, sheep and pigs as well as for milk of cows and goats. The compound is now reviewed under the CCPR periodic review programme on the basis of a submission by the basic manufacturer and information provided by Codex member countries.

### **IDENTITY**

ISO common name:thiabendazoleChemical nameIUPAC:CA:2-(thiazol-4-yl)benzimidazole; 2-(1,3-thiazol-4-yl)benzimidazoleCAS No:148-79-8Synonyms:Bovizole, Eprofil, Equizole, Lombristop, Mertect, Mintezol,<br/>Minzolum, Nemapan, Omnizole, Polival, Thiaben, Thibenzole

Structural formula:



Molecular formula:	C <sub>10</sub> H <sub>7</sub> N <sub>3</sub> S
Molecular weight:	201.26

## Physical and chemical properties

Pure active ingredient

Vapour pressure:	4 x 10 <sup>-9</sup> mm Hg (Torr) at 25 <sup>o</sup> C
Melting point:	304-305 °C
Octanol/water	
Partition coefficient:	log P <sub>OW</sub> = 2.2 (pH 5); 2.4 (pH 9)
Solubility, mg/ml:	water 38 at pH 2; 0.03 at pH >5
	methanol 8.7
	acetone 2.9
	ethyl acetate 2.1

Hydrolysis:	stable to strong acids and bases
Photolysis:	decomposes to benzimidazole and benzimidazole-2-
	carboxamide in strong UV light (half-life = 29 h in water)
Chelation:	forms stable complexes with a number of metals including
	iron. It does not bind calcium.

Technical material

Purity:	≥98% w/w	
Melting range	296-303 <sup>o</sup> C	
Stability:	stable to acid or base hydrolysis and heat; unstable in	strong UV light

### Formulations

Thiabendazole is marketed in the following formulations: SC: 1 g/l, 50 g/l, 100 g/l. 220 g/l, 300 g/l, 450 g/l, 485 g/l SL: 220 g/l TC: 985 g/kg WP: 400 g/kg, 600 g/kg, 900 g/kg WG: 890 g/kg In combinations: 100 g/l+300 g tecnazene/l SL 300 g/l +100 g imazalil/l SC

## METABOLISM AND ENVIRONMENTAL FATE

### Farm animal metabolism

Three <u>lactating goats</u> (*Capra hircus*, ~1 year old, 45-60 kg each, healthy) were dosed with single gelatine capsules containing 120 mg and 564  $\mu$ Ci of [<sup>14</sup>C]thiabendazole daily for 7 consecutive days. Two goats served as controls. The goats were slaughtered on the 8th day, within 24 hours after the final dosing. Milk was collected twice daily and tissue samples after slaughter (Chukwudebe *et al.*, 1994; Halls *et al.*, 1991b). An average of 74% of the administered dose was accounted for at the end of the study in the excreta (urine + faeces), tissues and milk. Nearly all the recovered radioactivity was in the urine (69%) and faeces (28%). The total residues in the excreta, tissues and milk are shown in Table 1.

The proposed metabolic pathways in goats are shown in Figure 1. As in previous studies (Rosenblum, 1965; Rosenblum *et al.*, 1964) the tissue residues consisted of low levels of unmetabolized thiabendazole, unconjugated 5-hydroxythiabendazole, and benzimidazole at maximum concentrations of 0.2, 0.12 and 0.08 mg/kg as thiabendazole respectively, all in the liver. The residues in milk reached a plateau (1.13 mg/kg) on the 3rd day, with a maximum concentration of 1.24 mg/kg on day 5. The major individual residue (about 39% or 0.4 mg/kg) in milk was the *O*-sulfate conjugate of 5-hydroxythiabendazole. No other individual residue was detectable (i.e. [0.5% of the total radioactivity). Earlier fractionation studies in animal substrates (Rosenblum, 1965, Rosenblum *et al.*, 1964) indicated that the unidentified residues were mainly products arising from extensive degradation of thiabendazole followed by incorporation into proteins (20-60%), lipids (12-14%) and polysaccharides (~1%). In the urine the residues consisted of unconjugated 5-hydroxythiabendazole (~0.4 mg/kg) and its *O*-sulfate conjugate (~9.5 mg/kg. The residues in faeces consisted of unconjugated 5-hydroxythiabendazole (~0.4 mg/kg), together with lower levels of benzimidazole (~0.4 mg/kg) and unmetabolized thiabendazole (~0.3 mg/kg).

Sample	Total radioactive residues, mg/kg as thiabendazole					
	Average of 3 goats	Minimum	Maximum			
Urine <sup>2</sup>	40.2					
Faeces <sup>2</sup>	24.3					
Liver	4.8	3.7	6.2			
Kidney	1.4	1.3	1.5			
Milk	$1.0^{4}$	0.49 <sup>3</sup>	1.24 <sup>3</sup>			
Gall bladder contents	0.85	0.37	1.49			
Heart	0.22	0.19	0.24			
Blood	0.19	0.17	0.21			
Muscles <sup>5</sup>	0.10	0.08	0.12			
Fat <sup>6</sup>	0.03	0.01	0.05			

Table 1. Distribution of thiabendazole residues in the urine, milk, faeces and tissues of goats<sup>1</sup>.

<sup>1</sup>Total residues in tissues were determined ~24 hr after end of dosing;

<sup>2</sup>Daily average of total residues

<sup>3</sup>Average from 3 treated goats. The minimum and maximum values were observed during the 1st and 5th day of feeding

<sup>4</sup>Average of 7 days

<sup>5</sup>Composite of semimembranosus, triceps and longissimus dorsi muscles 1:1:1 w:w:w.

<sup>6</sup>Composite of perirenal and omental fat 1:1 w:w

Five groups of four <u>laying hens</u> (*Gallus domesticus*, ~26 weeks old, 1-2 kg each, healthy) were dosed orally with single gelatine capsules, each containing 3.19 mg and ~25.2  $\mu$ Ci of [<sup>14</sup>C]thiabendazole, daily for 10 consecutive days with one control for each group. Eggs and excreta were collected twice and once daily respectively. The hens were slaughtered and tissue samples collected for analysis on the 11th day, within 24 hours after the final dosing (Chukwudebe *et al.*, 1994; Halls *et al.*, 1991a). Concentrations of the total residues in the excreta, eggs and tissues are shown in Table 2. The total residues in the excreta and eggs were determined daily.

An average of 96.6% of the total administered dose was recovered, 99.6% of which was found in the excreta. Cumulatively, the total residues found in the tissues and eggs accounted for about 0.4%, or less, of the administered <sup>14</sup>C. The total residues in eggs reached a plateau of about 0.1 mg/kg as thiabendazole by day 2 and remained at about that level throughout the next 8 days of dosing.

The residues in the excreta consisted of 3.4 mg/kg of unconjugated and 4.4 mg/kg of conjugated 5-hydroxythiabendazole. The residues in the tissues and eggs were qualitatively similar and consisted mostly of unconjugated 5-hydroxythiabendazole, unmetabolized thiabendazole, and benzimidazole at maximum concentrations of 0.4, 0.11 and 0.12 mg/kg thiabendazole equivalents respectively, all in the kidneys.

None of these residues are likely to persist in the tissues or eggs in view of the low concentrations present and their rapid elimination. The proposed metabolic pathways in poultry are the same as in goats, and are also shown in Figure 1.



Figure 1. Proposed metabolic pathways of thiabendazole in dairy goats and laying hens.

These results are consistent with those reported previously in the literature on the metabolism of thiabendazole in sheep, cattle, dogs, pigs and humans. The oral administration of thiabendazole to sheep (Tocco *et al.*, 1964), cattle, goats (Tocco *et al.*, 1965), dogs and humans (Tocco *et al.*, 1966) resulted in rapid absorption from the gastrointestinal tract. The time taken to achieve peak plasma levels varied with species and ranged from about 1 hour after dosing in dogs and humans to 7 hours in sheep, goats and cattle. In dogs, goats and cattle approximately 82% of the dose was excreted in the urine and faeces within the first 72 hours. Excretion in humans was more rapid, with approximately 80% being found in the urine within the first 24 hours. In all the species studied, hydroxylation of the benzimidazole ring to form 5-hydroxythiabendazole and subsequent conjugation to the glucuronide and sulfate were the major metabolic steps. These conjugates accounted for 70- 95% of the urinary metabolites in sheep, goats and pigs, 23% in dogs and 38% in humans. At peak plasma levels, which occurred about 6 h after dosing with 50 mg/kg of either [<sup>14</sup>C] or [<sup>35</sup>S]thiabendazole, the total radioactive residues retained in lamb tissues were relatively low (e.g. 2 mg/kg in muscle). By 5 days residues were undetectable (<0.06 mg/kg) in nearly all of the lamb tissues (Tocco *et al.*, 1964). The

total radioactive residues in calf, pig and goat tissues were also low by 24 h after dosing (e.g. 0.90 mg/kg in goat small intestines) and very low ( $\leq 0.08$  mg/kg) in most of the tissues by 17 days (Tocco *et al.*, 1965). This rapid excretion in the urine and faeces, predominant metabolism via hydroxylation at the 5-position followed by glucuronidation or sulfation and low residue retention by the tissues has been confirmed by various investigators (e.g. Delatour and Parish, 1986; Lanusse and Prichard, 1993; McKellar and Scott, 1990; Prichard *et al.*, 1981; Rosenblum, 1977; Weir and Bogan, 1985).

Sample	Total radioactive residues, mg/kg as thiabendazole					
	Average <sup>1</sup>	Maximum <sup>2</sup>				
Excreta <sup>3</sup>	26.1 <sup>3</sup>					
Liver	1.5	1.39	1.6			
Kidney	1.2	1.17	1.25			
Gizzard	0.3	0.25	0.34			
Heart	0.3	0.31	0.34			
Egg	0.1	0.13	0.18			
Muscle, breast	0.07	0.06	0.76			
Muscle, thigh	0.09	0.08	0.11			
$\operatorname{Fat}^4$	0.02	0.013	0.022			

Table 2. Distribution of thiabendazole residues in hen excreta, eggs and tissues.

<sup>1</sup>Averaged from 20 treated chickens

<sup>2</sup>Minima and maxima of average residues in the 4 chickens of each of the 5 groups

<sup>3</sup>Average of 10 days

<sup>4</sup>Composite from different parts of the body

#### Plant metabolism

The fate of [*phenyl*-<sup>14</sup>C]thiabendazole was studied in wheat, soya beans and sugar beet treated at maximum recommended rates (Halls and Sanson, 1991a-c; Van den Heuvel *et al.*, 1996). The results are shown in Tables 3 and 4, and the proposed metabolic pathways are shown in Figure 2.

<u>Wheat</u>. Actively growing wheat plants, at the 2-3 tiller stage, were sprayed once with  $[{}^{14}C]$ thiabendazole at a rate of about 0.80 kg ai/ha, representing the maximum recommended rate for wheat. Immature samples (foliage, forage and haylage) were taken after 2 hours, 7 days and 37 days respectively. At about 63 days after treatment, mature plants were harvested for samples of grain and straw. After extractions with acid, base and enzyme preparations, the extractable residues were characterized by a combination of GC-MS, reverse-phase HPLC and TLC.

The percentage of unextractable residue increased from about 1.8 in immature foliage to 16.8 in mature straw. Fractionation of the unextracted residues from straw by tissue solubilization followed by enzymatic and chemical hydrolyses demonstrated that most of the <sup>14</sup>C was distributed throughout several natural product fractions, including soluble polysaccharides, proteins, pectins, lignins and cellulose, but the level in any individual chromatographic fraction was less than 0.05 mg/kg as thiabendazole.

These results are consistent with findings from residue trials on wheat with unlabelled thiabendazole (Justin, 1985a,b, 1986) in which wheat seeds were treated with thiabendazole at rates up to 70% above the recommended maximum (1.4 g ai/litre of seeds) before planting. The growing wheat crops were also sprayed with thiabendazole at the maximum recommended field use rate (0.8 kg ai/ha) about 6-8 weeks before harvest. No thiabendazole (<0.05 mg/kg) was found in the grain harvested from the treated wheat.

<u>Soya beans</u>. The aerial portions of actively growing soya bean crops at the stage between late flowering and early pod set were sprayed twice, at a 14-day interval, with [<sup>14</sup>C]thiabendazole at a combined rate of about 0.68 kg ai/ha, the maximum recommended rate on soya beans. Samples of foliage and forage were taken at intervals of 2 hours and 27 days after treatment and mature plants were harvested to provide seeds and straw about 78 days after the first spray. The extractable residues were characterized as above (Halls and Sanson, 1991b; Van den Heuvel *et al.*, 1996).

Plant,	<sup>14</sup> C, % of TRR					
Fraction	Time after treatment & type of sample					
Wheat	2 hours foliage 7 days forage 37 days haylage 63 days					
	-	· -	• • •	Straw	grain	
Organo-extractable	97.2	79.3	46.3	60.1	41.5	
Thiabendazole	97.2	79.3	36.8	33.1	23.2	
Polars	$ND^1$	0	3.2	19.1	18.3	
Water-soluble	1.1	6.8	39.3	23.1	13.7	
Polars	0	0	19.9	14.4	0	
Benzimidazole related	0	0	23.1	33.5	18.3	
Unextractable (tissue-associated)	1.8	14.0	11.7	16.8	17.5	
Soya beans	2 hours foliage	27 day forage		78	78-day	
				straw	Seeds	
Organo-extractable	93.3	60.8		47.3	63.2	
TBZ	93.3	60.6		43.6	42.9	
Polar	0	0		0	0	
Aqueous soluble	1.4	35.5		41.4	33.3	
Polar	0	1.4		7.3	0	
BNZ-related	0	1.4		7.3	0	
Unextractable (tissue associated)	5.4	3.8		11.2	1.0	
Sugar beet	2 hours tops	56	days	90	days	
		tops	roots	tops	Roots	
Organo-extractable	91.1	54.1	56.4	28.5	29.0	
TBZ	91.0	52.2	55.6	27.1	25.8	
Polar	0	<1	0	0	0	
Aqueous soluble	2.1	39.2	43.3	60.4	65.0	
Polar	0	11.5	6.8	14.1	10.8	
BNZ related	0	11.5	6.8	14.1	10.8	
Unextractable (tissue associated)	6.9	6.8	0.2	11.0	6.0	

Table 3. Distribution and characterization of <sup>14</sup>C-labelled thiabendazole residues in plants (percentage of total radioactive residues).

<sup>1</sup>Not determined

<u>Sugar beet</u>. Actively growing sugar beet plants were sprayed five times, at 14-day intervals, with  $[{}^{14}C]$ thiabendazole at a total application rate of 2.015 kg ai/ha, the maximum recommended rate for sugar beet. Immature treated and control tops and roots were taken at about 2 hours after the first and at last (56 days) treatments. At about 90 days after the initial treatment (35 days after the fifth and final treatment) mature plants were harvested and tops and roots were sampled. All samples were characterized by HPLC (Halls and Sanson, 1991c; Van den Heuvel *et al.*, 1996).

Crop, Sample	Appli	cation	DAT <sup>2</sup>	Residues, mg/kg <sup>1</sup>			
	kg ai/ha	No.		Total	TBZ <sup>3</sup>	$BNZ^4$	Unextractable <sup>5</sup>
WHEAT	0.8	1					
Immature Foliage			0 (2 h)	67.46	65.57	< 0.05	1.21
Immature Forage			7	41.20	32.67	< 0.05	5.77
Immature Haylage			37	21.93	8.07	5.06	2.57
Straw			63	22.36	6.40	7.49	3.76
Grain			63	0.12	< 0.05	< 0.05	< 0.05
SOYA BEANS	0.34	2					
Immature Foliage			0 (2 h)	14.32	13.36	< 0.05	0.77
Immature Forage			27	25.45	15.12	0.36	0.97
Straw			78	10.15	4.22	0.74	1.14
Seed			78	0.88	0.38	< 0.05	< 0.05
SUGAR BEET	0.40	5					
Immature Tops			0 (2 h)	10.13	9.22	< 0.05	0.70
Immature Tops			56	24.66	12.87	2.84	1.68
Immature Roots			56	0.86	0.48	0.06	< 0.05
Mature Tops			90	10.01	2.43	1.41	1.10
Mature Roots			90	0.40	0.10	< 0.05	< 0.05

Table 4. Thiabendazole residues in plants following foliar applications of [<sup>14</sup>C]thiabendazole.

<sup>1</sup>Thiabendazole equivalents

<sup>2</sup>Days after first treatment

<sup>3</sup>Thiabendazole

<sup>4</sup>Sum of conjugated and unconjugated benzimidazole

<sup>5</sup>With KOH/MeOH reflux

The residue distributions in wheat, soya beans and sugar beet agree with other results showing the predominant movement of thiabendazole through plant axoplasm (Aharonson and Ben-Aziz, 1973; Allam *et al.*, 1969; Ben-Aziz and Aharonson, 1974; Chatrath *et al.*, 1972; Erwin *et al.*, 1968, 1970, 1971; Gray and Sinclair, 1971; Hide and Cayley, 1977; Lyda and Burnett, 1970; Wang *et al.*, 1971). This axoplasmic movement results in measurable levels of thiabendazole residues in shoot tissues (stems, leaves, straw) and relatively less in storage tissues (grain, seeds, roots).

<u>Seed potatoes</u>. The uptake, distribution and metabolism of thiabendazole by King Edward seed potatoes were examined under post-harvest storage conditions by Tisdale and Lord (1973). The potatoes were briefly immersed in solutions of  $[{}^{14}C]$ thiabendazole (~9.94 µCi/mg) at concentrations of 50, 100, 200 and 500 mg/l. Skin and tissue sections were subsequently processed and analysed. Metabolism and penetration were also studied by applying a pH 3 solution of  $[{}^{14}C]$ thiabendazole (196 mg/l) to cylindrical glass rings anchored to the surface of washed tubers by a thin layer of grease for periods of 5 and 60 minutes. The tubers were sectioned and autoradiographed at intervals of 2, 10, 21, 45, 75 and 120 days after treatment. The remaining tubers were subjected to multiple extractions with acidified methanol or sodium acetate-HCl buffer, followed by centrifugation and neutralisation of the supernatant solutions with base. The residues were partitioned into ethyl acetate, back-extracted into acid and then characterized by a combination of TLC, LSC, UV spectrometry and mass spectrometry.

Potato tubers absorbed thiabendazole from aqueous solutions at all pH levels examined (2-9) within 5 minutes. Thiabendazole penetrated only about 2 mm into the tubers in 2 weeks and a little further after 12 weeks. Autoradiography demonstrated that most of the thiabendazole (~96%) remained in the outer skin of the tubers; this is consistent with the high partition coefficient of

thiabendazole between skins and water (27.7) and the coefficient of only 1.0 between the underlying tissues and water. The sorption of residues to the tubers was directly proportional to the concentration of applied thiabendazole; at the highest applied concentration of 500 mg/l  $\geq$ 96% of thiabendazole in the tubers remained sorbed to the outer skin with negligible movement into the fleshy internal tissues. Even after 120 days of post-harvest storage only one radioactive component was detected, accounting for over 80% of applied [<sup>14</sup>C]thiabendazole. The mass spectral characteristics of this radioactive component (M<sup>+</sup> 201; base peak 174, (M-HCN)<sup>+,</sup> were identical to those of an authentic thiabendazole standard and demonstrated that the only residue in the potato tuber was thiabendazole.

Figure 2. Fate of thiabendazole in plants following foliar applications.



Sugar conjugate(s) of benzimidazole

Post-harvest applications of [<sup>14</sup>C]thiabendazole to stored potatoes did not result in detectable metabolic transformations (Tisdale and Lord, 1973). The major residual component was parent thiabendazole; benzimidazole was not detected ([0.05 mg/kg). Over 90% of the residue was confined to the potato skins and none was detected in the fleshy inner tissues. This is consistent with the results of other post-harvest studies with unlabelled thiabendazole (Briggs, 1981; Cayley *et al.*, 1979; Eckert, 1970; Friar and Reynolds, 1991; Griffith and Hide, 1976; Hide and Cayley, 1977, 1983, 1989; Justin and Johnson, 1993; Lentza-Rizos, 1986). No evidence of thiabendazole metabolism was found even after 4 months storage under conditions favourable for metabolism. Even with adhering soil on the surface of stored tubers, the stability of thiabendazole in soil indicates that the only residual product will be thiabendazole itself (Daly and Williams, 1990, 1991).

In another study with unlabelled thiabendazole, over 90% of the thiabendazole residue, determined by bioassay, was found in the outer peel of post-harvest-treated pears, with negligible penetration into the inner fruit (Ben-Arie, 1975).

<u>Oranges</u>. The uptake, distribution and fate of [C]thiabendazole (specific activity ~0.4  $\mu$ Ci/mg;  $\geq$ 99% pure) in oranges under typical post-harvest storage conditions were examined in Valencia oranges (Rosenblum and Meriwether, 1970). Oranges were treated in a 1-litre cylinder with 0.1% [<sup>14</sup>C]thiabendazole as an aqueous wettable powder suspension. The treated oranges were shaken free of excess liquid, allowed to air-dry for 2 hours and stored under simulated commercial conditions for 28 days at temperatures of  $10 \pm 1^{\circ}$ C and  $21 \pm 1^{\circ}$ C. At specified intervals, samples were separated into whole peel, inner peel and fleshy pulp. The uptake and distribution of <sup>14</sup>C in these separate fractions were determined by oxidative combustion, LSC and reverse isotope dilution assay.

Irrespective of storage duration and temperature, radioactivity was taken up by the treated oranges; virtually all (~95%) of the <sup>14</sup>C was sorbed to the peel and none penetrated into the fleshy inner pulp. Assays of the orange samples over the 28-day storage period demonstrated that about 95% of the radioactivity consisted of parent thiabendazole itself in spite of the duration and conditions (28 days, 21°C) being favourable for metabolism.

<u>Rotational crops</u>. Thiabendazole products are used mainly for post-harvest treatments (e.g. on stored potatoes, citrus, pome fruits and bananas) where outdoor applications to agricultural soil are not involved. There are, however, some uses of thiabendazole (e.g. as cereal seed dressing, pre-plant treatment of seed potatoes and limited foliar applications) from which relatively low residues could remain in soil and potentially be transferred to rotational crops. A confined accumulation study with [<sup>14</sup>C]thiabendazole applied to soil at the maximum anticipated use rates was therefore conducted on rotational crops (Halls and Sanson, 1992). The study represents a worst-case situation for the uptake of residues that might be encountered during these relatively minor commercial uses of thiabendazole. Three outdoor plots of 235 x 82.5 cm containing sandy loam soil were sprayed with [<sup>14</sup>C]thiabendazole once, or twice two weeks apart, at a total application rate of 2.15 kg ai/ha. The rotational crops were planted at different times after the last spray treatment, to represent the scenarios of crop failure or premature sowing (planting 30 days after the 2nd application) and normal agronomic practice (planting after 120 and 320 days, i.e. about 6 months and one year).

Three representative crops, wheat (small grain), turnips (root crop) and lettuce (leafy vegetable) were planted in each plot. At culturally and agronomically appropriate harvest intervals, the crops were sampled for the determination of total residues. Quantitatively significant components of the residues ( $\geq$ 10% of the total in the sample) were also characterized. Immediately after the last thiabendazole treatments, and at appropriate harvest intervals during the study, soil cores (0 to 30 cm depth) were taken for the determination of total residues. The total residues in the soil and crop samples were quantified by oxidative combustion followed by LSC. Residues were characterized, after acid, base or enzymatic hydrolytic extractions, by a combination of GC-MS, reverse-phase HPLC and TLC radiochromatographic analyses.

Residue levels in the top 15-cm layers of the three plots were about 0.8-1.1 mg/kg and were quantitatively consistent with a total thiabendazole application rate of 2.15 kg ai/ha (Table 5). In general, no significant residues ([0.1 mg/kg) were detected below the 15-cm soil depth. The results demonstrate that neither thiabendazole nor any of its soil degradation products has the propensity to leach into ground water. About 75-94% of the total soil residue was extractable and most of it (~63-94%) was thiabendazole (Table 6.). This picture agrees with the results of previous studies of the degradation of thiabendazole in soil (Daly and Williams, 1990, 1991).

The major components of the rotational crop residues were thiabendazole and benzimidazole and its sugar conjugate(s). Lower levels of 5-hydroxythiabendazole (maximum 25-30% of the thiabendazole residue) were also observed in some plant samples. Since 5-hydroxythiabendazole is produced by degradation in soil but not in plants, it is reasonable to conclude that the 5-hydroxythiabendazole was soil-generated and subsequently taken up by the crops through axoplasmic mechanisms in the same way as thiabendazole (e.g. Gray and Sinclair, 1971; Wang *et al.*, 1971). In addition to thiabendazole, benzimidazole, 5-hydroxythiabendazole and the unextractable residues, other radioactive components were observed in the HPLC radiochromatograms of various crop extracts, but all were individually at levels below 0.05 mg/kg.

Sample	Total residue, mg/kg as thiabendazole	Extractable, % of total	Thiabendazole, % of total
Plot A planted after 30 days			
2 h after treatment	0.79	93.8	93.8
137 days after treatment	0.98	75.3	69.6
Plot B planted after 120 days			
2 h after treatment	1.07	89.0	89.0
223 days after treatment	0.76	88.6	86.9
Plot C planted after 320 days			
2 h after treatment	0.95		
398 days after treatment	0.95	78.1	63.2

Table 5. Residues of thiabendazole in soil plots planted with rotational crops.

Table 6. Nature of the residues in rotated crops grown in thiabendazole treated soil.

Sample	DAT <sup>1</sup>	Residues, mg/kg as thiabendazole						
		Total	Thiabendazole	Total benzimidazole <sup>2</sup>	5-OH- TBZ <sup>3</sup>	Unextractable		
IMMATURE LETTUCE								
30-Day Plot	75	0.37	0.07	0.05	< 0.05	0.05		
120-Day Plot	153	0.66	0.23	0.15	0.05	0.09		
320-day Plot	357	1.56	0.29	0.81	0.10	0.16		
MATURE LETTUCE								
30-Day Plot	95	0.66	0.23	0.03	< 0.05	0.12		
120-Day Plot	174	0.27	0.05	0.09	< 0.05	< 0.05		
320-Day Plot	372	0.51	0.08	0.32	< 0.05	< 0.05		
IMMATURE TURNIP TOP	S							
30-Day Plot	56	0.10	0.04	< 0.05	< 0.05	< 0.05		
120-Day Plot	153	0.85	0.42	0.22	< 0.05	< 0.05		
320-Day Plot	357	0.34	0.05	0.12	< 0.05	< 0.05		
MATURE TURNIP TOPS								
30-Day Plot	95	0.63	0.22	0.09	< 0.05	0.07		
120-Day Plot	180	0.77	0.32	0.05	< 0.05	0.05		
320-Day Plot	398	1.05	0.11	0.43	0.05	0.06		
MATURE TURNIP ROOTS	MATURE TURNIP ROOTS							
30-Day Plot	95	0.15	0.08	< 0.05	< 0.05	< 0.05		
120-Day Plot	180	0.16	0.09	< 0.05	< 0.05	< 0.05		
320-Day Plot	398	0.15	0.11	< 0.05	< 0.05	< 0.05		

Sample	DAT <sup>1</sup>	Residues, mg/kg as thiabendazole				
		Total	Thiabendazole	Total benzimidazole <sup>2</sup>	5-OH- TBZ <sup>3</sup>	Unextractable
IMMATURE WHEAT FOL	IAGE					
30-Day Plot	56	0.56	0.13	0.07	0.05	0.11
120-Day Plot	153	2.29	0.66	0.49	0.18	0.25
320-Day Plot	357	1.23	0.58	0.31	< 0.05	0.11
Wheat Straw						
30-Day Plot	137	6.79	2.52	2.12	0.15	0.07
120-Day Plot	223	2.61	0.89	0.80	< 0.05	< 0.05
320-Day Plot	408	10.25	2.55	2.49	0.70	0.49
WHEAT HULLS						
30-Day Plot	137	4.65	2.42	0.57	< 0.05	< 0.05
120-Day Plot	223	1.13	0.64	< 0.05	< 0.05	0.08
320-Day Plot	408	6.58	2.01	1.87	< 0.05	0.14
WHEAT GRAIN						
30-Day Plot	137	0.09	0.05	< 0.05	< 0.05	< 0.05
120-Day Plot	223	0.05	< 0.05	< 0.05	< 0.05	< 0.05
320-Day Plot	408	0.18	0.09	< 0.05	< 0.05	< 0.05

<sup>1</sup>Days after final treatment with [<sup>14</sup>C]thiabendazole

<sup>2</sup>Sum of conjugated and unconjugated benzimidazole

<sup>3</sup>5-hydroxythiabendazole

#### **Environmental fate in soil**

<u>Degradation</u>. The fate of thiabendazole in microbially active sandy loam soil was studied under aerobic conditions at  $25 \pm 1^{\circ}$ C (Daly and Williams, 1991). Thiabendazole was degraded with an aerobic half-life approximating 737 days, consistent with results from a similar study by Aharonson and Kafkafi (1975). Degradation products consisted of low levels of benzimidazole (<2.5%) and 5-hydroxythiabendazole (<0.5%). The proposed degradation pathways are shown in Figure 3. Unextractable radiocarbon increased slowly during the study, ranging from 1.24% at day 0 to 20.20% at day 120. This increase, despite the use of hydrolytic extractants such as HCl and KOH, is consistent with the strong binding of thiabendazole to soil (Aharonson and Kafkafi, 1975; Cayley and Lord, 1980; Dykes, 1989). Volatile material, 96% of which was <sup>14</sup>CO<sub>2</sub>, also increased slowly, attaining its highest level after 12 months and accounting for 5.8% of the applied radioactivity. These results indicate that thiabendazole, despite its relative stability in soil, would eventually be mineralized to CO<sub>2</sub>.

Thiabendazole was stable in soil (half-life >737 days) under anaerobic conditions (Daly and Williams, 1990), but its levels in soil decreased during the preliminary aerobic phase of the study, before the attainment of anaerobic conditions, with a calculated half-life of about 211 days. Unextractable residues and <sup>14</sup>CO<sub>2</sub> attained levels of 5.8 and 0.8% respectively of the applied radioactivity. The only degradation product detected was benzimidazole at a maximum of 5.9%, formed mainly during the preliminary aerobic phase of the study.

<u>Photolysis</u>. The degradation of [<sup>14</sup>C]thiabendazole on sandy loam soil exposed to artificial sunlight was studied at  $25 \pm 2.5$ °C (Dykes and Kabler, 1990). Thiabendazole was found to be photolytically stable with a calculated half-life of 933 days. Recoveries of <sup>14</sup>C from exposed and unexposed soil

samples averaged about 98 and 104% respectively, and nearly all of this radioactivity (90-100%) was due to  $[{}^{14}C]$  thiabendazole; no other residue was found.

<u>Mobility</u>. To quantify the sorption of [<sup>14</sup>C]thiabendazole to soil, batch equilibrium studies were conducted with silt loam, clay, sandy loam and sandy soils (Dykes, 1989). The adsorption  $K_{OC}$  values ranged from 1,104 to 22,467, indicating that thiabendazole binds very tightly to soil, and desorption was correspondingly low with  $K_{OC}$  values from about 1,336 to 18,325. On the basis of the high  $K_{OC}$  values (>1,000) thiabendazole is considered to be immobile in soil.

Results from soil column leaching studies conducted by the WARF Institute (1976) also demonstrated that thiabendazole is immobile in soil under simulated conditions of either rapid (gravity-controlled) or slow (1.25 cm/day for 45 days) leaching. In another leaching study (Aharonson and Kafkafi, 1975), it was further demonstrated that thiabendazole is practically immobile in soil even under conditions simulating the passage of 1,000 mm of rain water through a soil column.

Results from leaching studies with aged residues (WARF Institute, 1978) demonstrated that both aerobically and photolytically aged thiabendazole residues are immobile in soil. In these studies, with about 10 physico-chemically different soils more than 98% of the recovered radioactive residues remained in the top 2.5-cm layer of the soils. The results of these batch equilibrium and leaching studies show that thiabendazole residues can be classified as being immobile in soil under both laboratory and field conditions. Pesticides that are immobile in soil are considered unlikely to leach into groundwater or travel in run-off water into streams and lakes (Kenaga, 1980).





## Environmental fate in water

<u>Photolysis</u>. [<sup>14</sup>C]Thiabendazole was shown to be degraded rapidly in water when exposed to artificial sunlight, with a half-life of approximately 29 hours (Flynn, 1994). The degradation resulted in the

formation of benzimidazole-2-carboxamide (~10%), a polar fraction (8.6%) and benzimidazole (~6%). These residues were confirmed by MS. A minor degradation product with HPLC retention properties consistent with benzimidazolecarboxylic acid was also present in trace amounts. These products are not likely to have significant biological activities (Stone *et al.*, 1965; Delatour and Parish, 1986). It can therefore be concluded that thiabendazole is degraded rapidly in the aquatic environment to non-toxic products: the only potential residue of concern to which non-target aquatic species might be exposed is the parent thiabendazole.

## METHODS OF RESIDUE ANALYSIS

## **Analytical methods**

The methods used for the quantification of thiabendazole and its metabolites in plant and animal commodities were validated by spiking the untreated commodity with known levels of thiabendazole and metabolites before solvent extraction. The limit of determination (LOD) is defined as the lowest fortification level that yields acceptable recoveries (>70%) of the analyte with a chromatographic signal to noise (S/N) level >10. The limit of detection is defined as the lowest concentration of analyte that can be detected with an S/N level >3.

## Bananas, whole and pulp

Liquid chromatography. Extraction with ethyl acetate is followed by concentration and purification on a cation exchange solid-phase extraction (SPE) column. The purified extract is analysed for thiabendazole by liquid chromatography on a cation exchange column eluted with acetonitrile/phosphate buffer (30:70, pH 4) with fluorescence detection (excitation 305 nm, emission 380 nm). Recoveries of thiabendazole averaged 93% for whole bananas fortified with thiabendazole at 0.05-10 mg/kg and 95% for pulp fortified at 0.01-2 mg/kg, with an LOD and limit of detection in whole bananas of 0.05 and <0.01 mg/kg (Arenas & Johnson, 1994a).

<u>Spectrofluorimetry</u>. Extraction with ethyl acetate is followed by purification by a series of acid/base partitions. The purified extract in 0.1N HCl is analysed for thiabendazole by spectrofluorimetry. Recoveries were >85%, with an LOD and limit of detection in whole bananas of 0.05 and 0.01 mg/kg (Justin & Johnson, 1993a).

## Chicory (Endive)

<u>Spectrofluorimetry</u>. An aqueous slurry of the sample homogenate is extracted with ethyl acetate and the extract purified by a series of acid/base partitions. The thiabendazole in the final 0.1N HCl solution is determined by fluorescence spectrofluorimetry with an excitation wavelength of 305 nm and an emission wavelength of 360 nm. The limit of detection is 0.005 mg/kg. (Johnson, 1994b).

## Citrus fruit and by-products

<u>Liquid chromatography</u>. The method is identical to that for bananas. Recoveries of thiabendazole averaged 96% for citrus fortified at 0.05-20 mg/kg. The LOD and limit of detection were 0.05 and <0.01 mg/kg respectively (Arenas *et al.*, 1996).

<u>Spectrofluorimetry</u>. The method is the same as for chicory. The limit of detection is 0.02 mg/kg for whole citrus fruit, 0.1 mg/kg for citrus oil, 0.02 mg/kg for citrus juice, 0.1 mg/kg for molasses and 0.3 mg/kg for dried citrus pulp (Justin & Johnson, 1992a,b).

## Mushrooms

<u>Spectrofluorimetry</u>. As for chicory. The LOD and limit of detection for whole mushrooms are 0.1 and 0.05 mg/kg (Justin & Johnson, 1992c).

## Pome fruit and by-products

<u>Liquid chromatography</u>. The homogenized sample is extracted with ethyl acetate after the addition of sodium sulfate and the crude extract is filtered. The filtrate is extracted with 0.1N HCl, the pH adjusted to 8, and the thiabendazole partitioned into ethyl acetate. The ethyl acetate is evaporated to dryness, the residue is dissolved in methanol, and the solution analysed by liquid chromatography on a C18 column eluted with methanol/water (60:40) containing 0.3% ammonia. The limit of detection is 0.05 mg/kg (Johnson, 1994a).

<u>Spectrofluorimetry</u>. As for chicory. The LOD is 0.05 mg/kg for whole fruit, 0.03 mg/kg for juice and 0.5 mg/kg for dried pomace. The limit of detection is 0.01 mg/kg for juice and 0.2 mg/kg for dried pomace (Justin & Johnson, 1992d,e).

## Potato tubers

Liquid chromatography. The method is the same as that for chicory except that the buffer is 25:75 acetonitrile/phosphate, pH 3.4. Recoveries of thiabendazole averaged 100% for whole white potatoes at 0.05-20 mg/kg and 94% for sweet potatoes fortified at 0.005-0.1 mg/kg. The LODs were 0.05 and 0.005 mg/kg respectively. The limit of detection was 0.0025 mg/kg (Arenas *et al.*, 1995).

<u>Spectrofluorimetry</u>. An aqueous slurry of the sample homogenate is hydrolysed on a steam bath with sulfuric and hydrochloric acids and the resulting mixture is digested overnight with diastase. The mixture is extracted with ethyl acetate and determination completed as with chicory. Recoveries of thiabendazole exceeded 85%. The LOD was 0.05 mg/kg for whole potatoes and 0.025 mg/kg for potato flakes, with limits of detection of 0.02 and 0.01 mg/kg respectively (Justin, 1993b).

## Cereal seed, straw and processed commodities - wheat

Liquid chromatography, thiabendazole. The grain, straw or processed commodity is extracted with methanol and the residue remaining after filtration is extracted again with hot methanol/KOH. The extract is purified by a series of acid/base liquid-liquid partitions. The final solution is analysed by liquid chromatography on a C-18 column eluted with methanol/water (40:60) containing 0.1% ammonium acetate. Detection is by fluorescence (excitation 300 nm; emission 350 nm). Recoveries averaged 89% over the fortification range 0.05-2 mg/kg. The LOD was 0.05 mg/kg and the limit of detection 0.02 mg/kg. (Armstrong & Norton, 1993b).

Liquid chromatography, free and conjugated benzimidazole. The grain, straw or processed commodity is extracted with methanol and the residue remaining after filtration is extracted again with hot methanol/KOH. Concentrated HCl is added and the filtered solution is concentrated under vacuum. Beta-glucosidase is added to the residue, the pH adjusted to 5 and the solution incubated for two hours at 37°C. The solution is acidified and extracted with ethyl acetate. The aqueous solution is adjusted to pH 9, extracted 3 times with ethyl acetate and the combined extracts are evaporated to dryness. The residue is analysed for benzimidazole by liquid chromatography on a C-18 column eluted with methanol/water (25:75) containing 0.1% ammonium acetate. Detection is by fluorescence (excitation 260 nm; emission 300 nm). Recoveries averaged 84% over the fortification range 0.1-2 mg/kg, with an LOD of 0.1 and a limit of detection of 0.05 mg/kg (Fieser & Johnson, 1994a).

## Fruits and vegetables

<u>Liquid chromatography</u>. The crop is homogenised with aqueous HCl, the filtrate adjusted to pH 8, the thiabendazole partitioned into ethyl acetate and the ethyl acetate evaporated to dryness. The residue is dissolved in methanol and the solution analysed by liquid chromatography on a C-18 column eluted with methanol/phosphate buffer (65:35), pH 8. Detection is by fluorescence. Recoveries of thiabendazole were >80%, with a limit of detection of 0.01 mg/kg (Johnson, 1994c).

## <u>Soil</u>

<u>Liquid chromatography</u>. The method is used for the determination of thiabendazole and benzimidazole. The soil sample is extracted with methanolic KOH, then with dimethylformamide in HCl. The solution is extracted with ethyl acetate, the extract purified by a series of acid/base liquid-liquid partitions and the ethyl acetate evaporated to dryness. The residue is dissolved in aqueous acid and the solution is analysed by liquid chromatography, eluting with methanol/water (60:40) containing 0.1% ammonium acetate. Detection is by fluorescence (excitation 300 nm, emission 350 nm). Recoveries of thiabendazole and benzimidazole averaged 87% and 92% respectively at 0.01-1 mg/kg. The LOD was 0.01 mg/kg and the limit of detection 0.005 mg/kg (Fieser & Jacobson, 1994).

## Water

<u>Liquid chromatography</u>. The method is used for the determination of thiabendazole in drinking water. The sample is passed through an "EMPORE" C-18 disk and the adsorbed thiabendazole is eluted with acetonitrile. The solution is analysed for thiabendazole by reverse-phase HPLC with fluorescence detection. The LOD is 0.0001 mg/kg (Johnson, 1996).

## Feed

<u>Liquid chromatography</u>. The feed sample is extracted with methanol and the solution analysed for thiabendazole by liquid chromatography on a cation exchange column eluted with acetonitrile/phosphate buffer (25:75) at pH 3.4. Detection is by fluorescence (excitation 305 nm; emission 380 nm). Recoveries were >95%. The limit of detection is 5 mg/kg. (Cobin, 1994)

## Animal tissues

<u>Liquid chromatography</u>. Thiabendazole and the animal metabolites 5-hydroxythiabendazole (5-OH-TBZ) and benzimidazole are released from the tissue by digesting with 6N HCl at 90-95°C for 24 hours. The solution is adjusted to pH 8, extracted with ethyl acetate and the extract purified on a cation exchange solid-phase extraction column. Quantification is by liquid chromatography on a cation exchange column eluted with acetonitrile/phosphate buffer (25:75) at pH 3.0-3.4 with fluorescence detection. Recoveries were >85%, with LODs and limits of detection of 0.1 and 0.005 mg/kg for each analyte (Arenas & Johnson, 1994b).

<u>Spectrofluorimetry</u>. The tissue is homogenised with phosphate buffer, pH 4.5, then incubated overnight with glusulase at 37°C. The solution is adjusted to pH 6.5, extracted with ethyl acetate and the extract purified by a series of acid/base partitions. Thiabendazole and 5-OH-TBZ are determined by fluorescence (thiabendazole, excitation 305 nm, emission 360 nm; 5-OH-TBZ, excitation 340, emission 420 nm). Recoveries were >85%, with LODs and limit of detection of 0.1 and 0.05 mg/kg respectively (Justin, 1990c).

## Milk

<u>Liquid chromatography</u>. The sample containing residues of thiabendazole, 5-hydroxy thiabendazole, and its sulfate conjugate is heated with concentrated HCl for four hours at 85-90°C. The cooled solution is adjusted to pH 8, extracted with ethyl acetate and the extract purified on a cation exchange solid-phase extraction column. The solution is analysed for thiabendazole and 5-OH-TBZ by liquid chromatography on a cation exchange column eluted with acetonitrile/phosphate buffer (20:80) at pH 3.8, with fluorescence detection. Recoveries were >85%, with an LOD and limit of detection of 0.05 and 0.005 mg/kg respectively (Arenas & Johnson, 1995).

<u>Spectrofluorimetry</u>. The method is the same as that for animal tissues. Recoveries were >80%, with an LOD and limit of detection of 0.05 and 0.02 mg/kg respectively (Justin, 1990c).

## Eggs

<u>Liquid chromatography</u>. The method is the same as for tissues. Recoveries were >85%. The LOD was 0.05 mg/kg and the limit of detection was 0.01 mg/kg for each analyte (Arenas & Johnson, 1994c).

<u>Spectrofluorimetry</u>. As for tissues. Recoveries were >85%, with an LOD and limit of detection of 0.1 and 0.05 mg/kg respectively (Justin, 1990b).

## Stability of pesticide residues in stored analytical samples

The stability of residues was tested in apples, apple juice, apple pomace, bananas, citrus, mushrooms, potatoes, wheat, milk, eggs, and chicken liver, muscle and kidney. The homogenised samples were fortified with known amounts of residues and stored in sealed high-density polyethylene bottles in the dark at  $-20 \pm 10^{\circ}$ C. The residues measured at various intervals after fortification are shown in Table 7.

## **Definition of the residue**

On the evidence of the 5 studies carried out with labelled thiabendazole and other related studies using unlabelled material the only detectable residue ( $\geq 0.05 \text{ mg/kg}$ ) in edible crop commodities is likely to be thiabendazole.

The animal metabolism studies and transfer studies with cows and poultry indicate that thiabendazole and 5-hydroxythiabendazole are the main residue components in meat and eggs, while the sulfate conjugate of 5-hydroxythiabendazole is the main component in milk.

The Meeting concluded that the following residue definitions are appropriate.

## For compliance with MRLs

For plant products: thiabendazole. For animal products: sum of thiabendazole and 5-hydroxythiabendazole.

## For estimations of dietary intake

For plant products: thiabendazole. For animal products: sum of thiabendazole, 5-hydroxythiabendazole and its sulfate conjugate.

Table 7. Stability of thiabendazole and metabolites in stored analytical samples.

Sample		Resi	dues, mg/kg, af	Residues, mg/kg, after storage periods, months									
	0	1	2	3	6	9	12						
	TBZ	TBZ	TBZ	TBZ	TBZ	TBZ	TBZ						
Apple, whole	0.093			0.084		0.093		Norton,					
Apple juice	0.083			0.097		0.094		1992c					
Dried pomace	0.85			0.84		0.77		1					
Banana, whole	0.49	0.49	0.48	0.48				Norton, 1993					
Banana pulp	0.097	0.097	0.097	0.096									
Citrus, whole	0.42		l 	0.47		0.48		Norton,					
Citrus oil	2.0		l	1.9		2.1		1992a					
Molasses	1.8		l 	1.8		1.8							
Dried peel	1.9		 	2.0	<u> </u>	1.7							
	0	3	6	9	12	27	28						
	TBZ	TBZ	TBZ	TBZ	TBZ	TBZ	TBZ						
Mushroom	0.0175	0.024	0.02					Johnson,					
	0.094	0.10	0.089		0.097		0.097	1995					
	47.2	50.1	51.7		50.6		49.9						
Potato, whole	0.20	0.20				0.22		Norton,					
Potato peel	0.54	0.52				0.47		1995c					
	0	1	3	6	12	18	23						
	TBZ /BNZ	TBZ/	TBZ/BNZ	TBZ/BNZ	TBZ/BNZ	TBZ/	TBZ/BNZ						
		BNZ	l			BNZ							
Wheat grain	0.22/0.21		0.20/0.18	0.21/0.20		0.21/0.1 9	0.19/0.18	Armstrong and					
Wheat bran	0.22/0.18	0.20/0.20	0.20/0.18	0.18/0.18	0.18/0.19	0.20/0.1		Norton, 1993b					
Wheat flour	0.20/0.19	0.19/0.21	0.17/0.21	0.19/0.20	0.19/0.19	0.18/0.2							
Wheat straw	0.17/0.21	0.19/0.16	0.20/0.14	0.26/0.14	0.22/0.18	0.19/0.2	0.20/0.19						
		0				2							
	TBZ	5-OH- TBZ	5-NaSO <sub>4</sub> - TBZ	TBZ	5-OH- TBZ	5-Nas	so <sub>4</sub> -tbz						
Milk	0.38	0.30	0.14	0.36	0.34	(	0.16	Arenas,1994a					
Egg yolk	0.084	0.47		0.095	0.47			Dahmen, 1990					
Egg white	0.086	0.48		0.094	0.49			1					
Chicken liver	0.42	0.38	i	0.44	0.33			Arenas, 1994b					
Chicken muscle	0.43	0.42		0.45	0.40								
Beef kidney	0.44	0.37		0.46	0.34			-					

TBZ: thiabendazole

BNZ: benzimidazole 5-OH-TBZ: 5-hydroxythiabendazole 5-NaSO<sub>4</sub>-TBZ: sulfate conjugate of 5-hydroxythiabendazole

# **USE PATTERNS**

The major registered or approved uses of thiabendazole on food crops are shown in Tables 8 and 9.

Crop	Country				
•		Form., concn.	Method	g ai/100 l	Rate (ai)
Apples, pears	Argentina	SC, 450 G/L	Spray	50-90	0.90 g /t
11 / 1	Australia	SC, 900G/KG	Dip	100	
	Canada	SC, 450 G/L	Dip, drench	45	
	France	SC, 450 G/L	Spray	45;	
		SC. 450 G/L	Dip	225	
	Italy	SC, 450 G/L	Dip	45 - 110	
	Mexico	WP, 600 G/KG	Dip, drench	200-850	
	Netherlands	SC. 450 G/L	Sprav	135 <sup>a</sup>	
	South Africa	SC. 450 G/L	Dip	100	
	Spain	SL, 220 G/L	Dip	110 - 130	
	USA	SC. 450 G/L	Dip. sprav	61	
Avocado	South Africa	SC, 450 G/L	Dip	135	
Bananas	Argentina	SC, 450 G/L	Dip	20-40	
Dununus	Australia	SC, 900G/KG	Dip	20-40	
	Brazil	SC, 485 G/L	Dip. sprav	20-45	
	Colombia	SC. 450 G/L	Dip. spray	20-45	
	Continuity	SL, 220 G/L	Dip, spray	20-40	
	Costa Rica	SL, 220 G/L	Dip. spray	20-40	
		SC, 450 G/L	Dip, spray	20-40	
	Ecuador	SL. 220 G/L	Dip. sprav	20-40	
	France	SL, 220 G/L	Dip. spray	45	
	French Antilles	SC, 450 G/L	Dip. spray	22-45	
	Guatemala	SC, 450 G/L	Dip. spray	20-40	
		SL, 220 G/L	Dip, spray	20-40	
	Honduras	SC. 450 G/L	Dip. sprav	20-40	
		SL, 220 G/L	Dip, spray	20-40	
	Israel	SC, 450 G/L	Dip, spray	60	
	Mexico	WP, 600 G/KG	Dip, spray	40-80	
	Nicaragua	SC, 450 G/L	Dip, spray	20-40	
	C C	SL, 220 G/L	Dip, spray	20-40	
	Panama	SC, 450 G/L	Dip, spray	20-40	
		SL, 220 G/L	Dip, spray	20-40	
	South Africa	SC, 450 G/L	Dip	20	
	USA	SC, 50 G/L	Dip	20	
		TC, 985 G/KG	Dip	20	
		SC, 450 G/L	Dip, spray	20	
Cabbages	Germany	SC, 450 G/L	Spray	68	0.034 g/100 kg
Carrots	USA	SC, 450 G/L	Dip	560	
Celery	Israel	SC, 450 G/L	Dip	200	
Citrus fruit	Argentina	SC, 450 G/L	Dip, spray	50-500	
	Australia	SC, 900G/KG	Dip	100	
	Brazil	SC, 485 G/L	Dip, spray	50-500	
	Columbia	SC, 450 G/L	Spray	45-90	
	Israel	SC, 450 G/L	Dip	110	
	Mexico	WP, 600 G/KG	Drench, spray	150-180	
	South Africa	TC, 985 G/KG	Dip	400	
		SC, 450 G/L	Dip	100-200	
	Spain	SL, 220 G/L	Dip	130-220	
	USA	SC, 500 G/L	Spray	100	
		TC, 985 G/KG	Spray	100-500	0.88-2.5 g/t
Endive	France	SC, 450 G/L	Dip	100-135	
	Germany	SC, 450 G/L	Dip	100-135	

Table 8. Major approved post-harvest and pre-planting uses of thiabendazole.

Crop	Country		APP	LICATION	
		Form., concn.	Method	g ai/100 l	Rate (ai)
Papayas	USA	TC, 985 G/KG	Spray	100-200	2.0 g/t
Potatoes	Argentina	SC, 450 G/L	Spray	2100	42 g/t
	Australia	SC, 450 G/L	Spray	2250	45 g/t
	Canada	SC, 450 G/L	Spray	2100	42 g/t
	Columbia	SC, 450 G/L	Dip	180	
		SC, 450 G/L	Spray	225	4.5 g/t
	France	SC, 450 G/L	Spray	3150	63 g/t
	Germany	SC, 450 G/L	Spray	3150	63 g/t
	Italy	SC, 450 G/L	Spray	2000-4000	40 g/t
	Mexico	WP, 600 G/KG	Spray	5000	50-100 g/t
	Netherlands	SC, 209 G/L	Spray		30 g/t, PHI 60 days
		DP, 20 G/KG	Dusting		30 g/t, PHI 90 days
	New Zealand	SC, 450 G/L	Spray	2115	42 g/t
	South Africa	SC, 450 G/L	Spray	160-315	6.4 –12.8 g/t
			Dip	200	
(ware potatoes)	UK	SC, 450 G/L	Spray		40 g/t
		SL, 100 G/L	Spray		40 g/t
		SL, 220 G/L	Spray		44 g/t
	USA	SC, 450 G/L	Spray, dip	139	5.6 g/t
Potato seed roots	Argentina	SC, 450 G/L	Dip	180	
	USA	SC, 450 G/L	Dip	375	
Soya beans (seed)	Brazil	SC, 485 G/L	Spray		10-20 g/100 kg
(Pre-plant)	Mexico	WP, 600 G/KG	Spray	50-100	50-200 g/100 kg
Squash	Mexico	WP, 600 G/KG	Spray	150-250	
Wheat (seed)	Italy	SC, 450 G/L	Spray	120	120 g/100 kg
(Pre-plant)	Mexico	WP, 600 G/KG	Spray	100-300	100-300 g/100 kg
	USA	SC, 300 G/L	Spray	30000	67-200 g/100 kg

Table 9. Major approved pre-harvest uses of thiabendazole.

Crop	Country		Application		PHI,
	-	Form., concn.	kg ai/ha	g ai/100 l	days
Apples, pears	Argentina	SC, 450 g/l	0.45-0.90	<u> </u>	0
	Italy	SC, 450 g/l		60	15
	Mexico	WP, 600 g/kg	0.50-1.0	500-1000	
	Japan	WP, 75 g/kg		7.5	14
	Spain	SC, 450 g/l	0.45-0.90	45	30
	Spain	WP, 600 g/kg	0.42-0.84		
Asparagus	ŪK	LS, 220 g/l	Dip, high vol. drench	100	180
Avocados	Mexico	WP, 600 g/kg	0.50-0.75	500-750	15
Bananas	Spain	SC, 450 g/l	0.45		15
	Spain	WP, 600 g/kg	0.42		15
Broccoli	Spain	SC, 450 g/l	0.45 - 0.90	68-90	7
	Spain	WP, 600 g/kg	0.30-0.85	45-85	7
Celery	Israel	SC, 450 g/l	0.40		3
	Spain	SC, 450 g/l	0.45 - 0.90	68-90	7
	Spain	WP, 600 g/kg	0.30-0.85	45-85	7
Cherries	Spain	SC, 450 g/l	0.36	45-68	15
	Spain	WP, 600 g/kg	0.42-0.44	1	
Citrus fruit	Japan	WP, 600 g/kg	1	50	1
	Mexico	WP, 600 g/kg	0.5-1.0	150-180	0
Cucumbers	Spain	SC, 450 g/l	0.45 - 0.90	68-90	3
Garlic	Italy	SC, 450 g/l	1.4 g ai/kg	135	1
Grapes	Mexico	WP, 600 g/kg	0.50-1.0	500-1000	1
Î.	Japan	WP, 75 g/kg		30	45
Green beans	Spain	SC, 450 g/l	0.45 - 0.90	68-90	3
	Spain	WP, 600 g/kg	0.30-0.85	45-85	3

Crop	Country		Application		PHI,
_	-	Form., concn.	kg ai/ha	g ai/100 l	days
Lettuce	Spain	SC, 450 g/l	0.45-0.90	68-90	7
	Spain	WP, 600 g/kg	0.30-0.85	45-85	7
Mangoes	Mexico	WP, 600 g/kg	0.50-0.70	500-700	15
Melons	Spain	SC, 450 g/l	0.45-0.90	68-90	3
Mushrooms	Australia	SC, 450 g/l	225 g ai/kg moss		
	Japan	WP, 600 g/kg		60	
	Japan	SL, 100 g/l		50-100	
	South Africa	SC, 450 g/l	120-150 g ai/80 m <sup>2</sup>	120-150	
	UK	WP, 600 g/kg		69	1
	USA	SC, 450 g/l	265 g ai/93 m <sup>2</sup>		0.5
Onions	Italy	SC, 450 g/l	1.4 g ai/kg	135	
	UK	SC, 450 g/l	0.293		
Peppers	Spain	SC, 450 g/l	0.45 - 0.90	68-90	3
		WP, 600 g/kg	0.30-0.85	45-85	3
Potatoes (seed)	Argentina	SC, 450 g/l	1.2		
	Italy	SC, 450 g/l		180	
	Mexico	WP, 600 g/kg		2000-3000	
	South Africa	SC, 450 g/l	dip	200-400	
			spray	1000-2000	
Potatoes (foliar)	Mexico	WP, 600 g/kg	0.50-1.0	500-1000	
Soya beans	Argentina	SC, 450 g/l	0.22-0.32		21
	Mexico	WP, 600 g/kg	0.35-0.70	350-700	
	UK	SC, 450 g/l	0.225-0.315		
Strawberries	Netherlands	FT, 120 g/kg	43 g ai/m <sup>2</sup>		3 <sup>a</sup>
	Spain	SC, 450 g/l	0.45-0.90	68-90	3
	Spain	WP, 600 g/kg	0.30-0.85	45-85	3
Tomatoes	Netherlands	FT, 120 g/kg	43 g ai/m <sup>2</sup>		3 <sup>a</sup>
	Spain	SC, 450 g/l	0.45-0.90	68-90	3
	Spain	WP, 600 g/kg	0.30-0.85	45-85	3
Vines	Spain	SC, 450 g/l	0.68-0.90	90	7
		WP, 600 g/kg		90-135	7
Rice	Mexico	WP, 600 g/kg	0.50-0.75	500-750	10
Wheat (foliar)	Argentina	SC, 450 g/l	0.22-0.32		14
	USA	WG, 890 g/kg	0.52-0.78	1600	

<sup>a</sup> Indoor use

## **RESIDUES RESULTING FROM SUPERVISED TRIALS**

Residue data from supervised trials with thiabendazole on apples, bananas, chicory, citrus, mushrooms, pears, potatoes, strawberries, tomatoes and wheat are shown in Tables 10 to 17.

Table 10. Residues from post-harvest application to citrus

- Table 11. Residues from pre- and post-harvest application to apples and pears
- Table 12. Residues from pre-harvest applications to strawberries
- Table 13. Residues from post-harvest application to bananas
- Table 14. Residues from pre-harvest applications to tomatoes
- Table 15. Residues from post-harvest application to chicory
- Table 16. Residues from post-harvest application to potatoes

Table 17. Residues from pre-harvest irrigation and direct spray application to mushrooms

<u>Citrus fruits</u>. Post-harvest trials were conducted in the USA (8) and Spain (10) from 1990 to 1994 on oranges, lemons, grapefruit and tangerines. In the Spanish trials oranges were treated with single post-harvest drench applications of 66 or 110 g ai/hl. The US trials were with initial post-harvest dips at

100 or 500 g ai/hl followed by mist applications in wax at 350 or 500 g ai/hl. Benzimidazole residues were not detectable (<0.01 mg/kg). Samples were stored frozen and analysed within nine months of treatment.

Table 10. Residues of thiabendazole in or on whole unwashed citrus fruits from post-harvest applications of SC, SL, WP or TC formulations of thiabendazole in supervised trials.

Fruit,				Applicat	ion		Residues, mg/kg	Remarks	Ref.
Country, Variety	Year,	Form.	kg ai/ha	kg ai/hl	l/t	Туре			
Orange		FMC 555,		0.50		dip	<u>1.8, 1.8</u>	$(2/1)^1$	Norton, 1995b
USA, 1990		Mertect				(3 min)			
Navel		Fungicide	12	0.50	2.4	plus spray			
Orange		FMC 555,		0.50		dip	1.2, 1.2	(2/1)	
USA, 1991		Mertect				(3 min)			
Valencia		Fungicide	12	0.50	2.4	plus spray			
Grapefruit		FMC 555,		0.50		dip	2.9, 2.9	(2/1)	
USÂ, 1991		Mertect				(3 min)			
		Fungicide	12	0.50	2.4	plus spray			
Lemon		FMC 555,		0.50		dip	5.1, 5.4	(2/1)	
USA, 1991		Mertect				(3 min)			
		Fungicide	12	0.50	2.4	plus spray			
Orange		FMC 555,		0.10		dip	4.4, 4.8, 4.7,	(3/2)	
USA, 1994		Mertect				(3  min)	4.4, 4.4, 4.6		
Navel		Fungicide	8.4	0.35	2.4	plus spray			
Orange		FMC 555,		0.10		dip	3.0, 3.1, 3.0,	(3/2)	
USA, 1994		Mertect				(3  min)	2.8, 2.7, 2.7		
Hamlin		Fungicide	8.4	0.35	2.4	plus spray	, ,		
Tangerine		FMC 555,		0.10		dip	3.9, 3.5, 3.3,	(3/2)	
USĂ, 1994		Mertect				(3  min)	3.1, 3.5, 3.4		
Sunburst		Fungicide	8.4	0.35	2.4	plus spray			
Grapefruit		FMC 555,		0.10		dip	3.0, 2.8, 2.5,	(3/2)	
USÂ, 1994		Mertect				(3  min)	3.6, 3.8, 3.5		
Marsh		Fungicide	8.4	0.35	2.4	plus spray	, ,		
Orange		Tecto 20S		0.066		drench	<0.1, 0.89, 0.81	(1/3) 8 DAT	Tecnidex,
Spain,	1990			0.11			< 0.1, 1.1, 1.1	(1/3) 8-11 DAT	1992a <sup>2</sup>
Clementing	de						, , , ,		
nules									
Spain, 199	1	Tecto 20S		0.066		drench	1.3. 3.9.	(1/2) 28-42 DAT	
Clementing	de			0.11			1.2. 8.5	(1/2) 28-42 DAT	
fina							, ,		
Spain, 199	1	Tecto 20S		0.11		drench	1.7. 2.5	(1/2) 40 DAT	
Clementina	L						,		
Hernandina	i								
Spain, 1990	)	Tecto 20S	1	0.066	1	drench	0.72, 0.69, 0.79	(1/3) 10-12 DAT	
Navel	-			0.11			0.64, 0.68, 0.68	(1/3) 10-12 DAT	
Spain, 199	1	Tecto 20S	1	0.066	1	drench	3.5.0.69.0.98	(1/3) 20-20 DAT	
Navel				0.11			3.8, 0.52, 2.7	(1/3 20-29 DAT	

<sup>1</sup>Number of analyses per sample/number of samples analysed

<sup>2</sup>Summary reports only

DAT: days after last treatment

<u>Pome fruits</u>. Post-harvest residue trials were conducted in the USA and Spain in 1990-1991 on apples and pears. An initial post-harvest dip at 60 g ai/hl was followed by a mist application in wax at 200 mg ai/hl 30 days after cold storage in ten US trials. Five trials were also conducted in Spain at 110 g ai/hl. Samples were stored frozen and analysed within nine months of treatment.

Four pre-harvest residue trials were conducted in Japan on apples and pears with WP formulations of thiabendazole (600 g ai/kg). Nine sprays at 30 g ai/hl, 1.8 kg ai/ha, were applied to apples and five at 30 g ai/hl, 1.2 kg ai/ha, to pears. Samples were analysed after PHIs of 7, 14 and 21 days.

Table 11. Residues of thiabendazole in or on whole apples and pears from applications of SC, SL, TC and WP formulations of thiabendazole in supervised trials.

Fruit, country,		Applic	cation			Residues, mg/kg	Remarks <sup>1</sup>	Reference
year	Form.	kg ai/ha	kg ai/hl	l/t	Туре			
Apple Golden USA, 1990	Mertect 340F & Mertect Fungicide	8.4	0.060 0.20	4.2	Dip plus spray	3.0, 2.7	(2/1)	Norton , 1992c
Red Delicious						3.0, 3.4	(2/1)	
Red Delicious						3.1, 3.4	(2/1)	
Non Delicious						3.2, 3.2	(2/1)	
Non Delicious						3.2, 3.4	(2/1)	
Apple <sup>2</sup> Golden Spain, 1991	Tecto 20S		0.11		Drench	1.8, <u>2.1</u> 1.9, <u>2.2</u>	DAT 32 DAT 61	Tecnidex, 1992b
-						1.8, <u>1.9</u>	DAT 147	
Apple <sup>3</sup> Japan, 1974 (Pre-harvest)	WP 9 applications		0.03		Spray	0.45, 0.47 0.42, 0.30 0.19, 0.22	PHI 7 PHI 14 PHI 21	Japan 1997
						1.1, 1.1 1.1, 1.1 0.68, 0.77	PHI 7 PHI 14 PHI 21	
						0.40, 0.43 0.38, 0.38 0.36, 0.33	PHI 7 PHI 14 PHI 21	
						1.3, 1.3 0.90, 0.89 0.41, 0.41	PHI 7 PHI 14 PHI 21	
Pear <sup>3</sup> , 1990 USA, CA Bartlett	Mertect 340F, Mertect Fungicide	8.4	0.060 0.20	4.2	Dip + Spray	1.1, 1.1	(2/3)	Norton, 1992b
WA						3.0, 3.2,		
WA						0.89, 0.87		
Bosc NY	Mertect 340F, Mertect Fungicide	8.4	0.060 0.20	4.2	dip plus spray	3.6, 3.7	(2/2)	
NY						4.8, 5.1	(2/2)	
Pear <sup>2</sup> , Blanquilla Spain 1991						1.7, 1.8 2.0, 2.1	DAT 75 DAT 160	Tecnidex, 1992b
Pear Japan, 1974 (Pre-harvest)	WP 5 applications		0.03		spray	0.12, 0.11 0.083, 0.083 0.075, 0.072	PHI 7 PHI 14 PHI 21	Japan, 1997
						0.50, 0.50 0.52, 0.51 0.28, 0.27	PHI 7 PHI 14 PHI 21 PHI 7	
						0.087, 0.081 0.077, 0.072	PHI 14 PHI 21	

<sup>1</sup>Number of analyses per sample/number of samples analysed

<sup>2</sup>Average residues from triplicate analyses of samples from two trials. Summary reports only submitted

<sup>3</sup>Results of duplicate analyses

DAT: days after last treatment

PHI: pre-harvest interval in days

<u>Strawberries</u>. Pre-harvest trials were conducted on strawberries in Mexico and Spain in 1989-1992 with ground spray foliar applications of SC and WP formulations. In Mexico four applications were made 7 days apart, at rates of 0.50-2.0 kg ai/ha. In Spain there were single applications at 1.2 kg ai/ha.

Table 12. Residues of thiabendazole in strawberries from pre-harvest applications of SC and WP formulations of thiabendazole in supervised trials.

Country,		A	pplicatio	n	PHI,	Residues, mg/kg	Reference
Year	Form.	kg	kg	Туре	days		
		ai/ha	ai/hl				
Mexico <sup>1</sup>	Tecto	0.50	0.083	Ground spray	0	0.84, 0.56	Unduraga, 1992a
, 1992	60			(4)	1	1.2, 0.67	
					3	1.6, 0.73	
					7	1.6, 0.70	
					14	0.83, 0.29	
Mexico <sup>1</sup>	Tecto	1.0	0.17	Ground spray	0	1.5, 0.69	
1992	60			(4)	1	4.4, 2.2	
					3	2.7, 1.7	
					7	1.8, 1.6	
					14	1.8, 1.7	
Mexico <sup>1</sup>	Tecto	2.0	0.34	Ground spray	0	4.3, 2.4	
1992	60			(4)	1	6.4, 3.5	
					3	5.9, 2.9	
					7	5.0, 2.0	
					14	1.8, 1.1	
Mexico <sup>1</sup>	Tecto	0.50	0.083	Ground sprav	0	1.1. 0.77	Unduraga, 1992b
1992	60			(4)	1	2.1. 1.3	
				( )	3	4.3. 3.2	
					7	14 0 89	
					14	0.71 0.33	
Mexico <sup>1</sup>	Tecto	1.0	0.17	Ground spray	0	21.12	
1002	60	1.0	0.17	(1)	1	5837	
1772	00			(4)	3	1 4 2 0	
					5	4.4, 2.0 3 1 1 7	
					14	0.83 0.52	
Mexico <sup>1</sup>	Tecto	2.0	0.34	Ground spray	0	3.1.2.1	
1002	60	2.0	0.54	(1)	1	5.1, 2.1 0 7 1 0	
1772	00			(4)	3	9.7, 4.9	
					5	9.5, 4.5	
					14	36.12	
Mariao	Teete	0.50	0.002	Ground aprov	0	1.4	
1002	60	0.50	0.093	(4)	1	1.4	
1992	00			(4)	1	1.2	
					3 7	0.00	
					14	0.41	
Maniaa	Testa	1.0	0.10	C	14	1.0	
Mexico	Tecto	1.0	0.19	Ground spray	0	1.9	
1992	60			(4)	1	1.8	
					3	1.2	
					/	0.87	
		2.0	0.00	G 1	14	0.53	
Mexico	Tecto	2.0	0.38	Ground spray	0	1.8	
1992	60			(4)	1	4.5	
					3	2.6	
					7	1.8	
		1			14	0.90	
Spain <sup>∠</sup>	Tecto	1.2	0.030	Ground spray	0	1.7	Ag Vet, 1991
1989	45			(1)	3	<u>1.6</u>	
					7	1.4	
					14	1.1	

Country,		A	oplicatio	n	PHI,	Residues, mg/kg	Reference
Year	Form.	kg	kg	Туре	days		
		ai/ha	ai/hl				
Spain <sup>2</sup>	Tecto	1.2	0.030	Ground spray	0	0.78	
1989	45			(1)	3	0.33	
					7	0.43	
					14	0.1	

<sup>1</sup>Samples were taken from duplicate plots

<sup>2</sup>Residues are the averages of quadruplicate analyses. The trials were conducted under plastic

<u>Bananas</u>. Post-harvest trials were conducted in the USA, Honduras and Guadeloupe in 1992-1995 with single dips or sprays to run-off of SL and SC formulations of thiabendazole: four dip trials in Guadeloupe in 1992, two dip trials in Hawaii, USA, in 1995 and four spray trials in Honduras in 1992. The fruit were ripened to the green to yellow tip stage (the stage preferred by customers) according to normal commercial practice. At least 10 fingers taken from two clusters were composited for one sample. The samples were stored frozen and analysed within three months of treatment. Benzimdazole residues could not be detected in any of the samples

Table 13. Residues of thiabendazole in or on whole bananas and banana pulp from single post-harvest applications of SC and SL formulations of thiabendazole in supervised trials.

Country			Application		_	Sample	Residues, mg/kg	Remarks	Ref.
Year	Form.	kg ai/ha	kg ai/hl	l/t	Туре				
Hawaii	Mertec	4.2	0.040	10.5	Dip	Green	1.4, 1.3, 1.2, 1.6, 1.4, 1.2,	$(1/10)^{1}$	Norton,
USA, 1995	t				(15  sec)	banana	1.7_1.5, 1.7, 1.4		1995a
	340F								
					Dip		1.8, 1.6, 1.6, 1.6, 1.9, 2.3,	1/10	
					(60 sec)		1.5, 2.0, 1.6, 1.3		
Hawaii	Mertec	4.2	0.040	10.5	Dip	Green	0.94, 1.1, 1.1, 1.2 1.0,	(1/10)	
USA, 1995	t 20S				(15 sec)	banana	0.97, 1.4, 1.0, 1.0, 0.97		
					Dip		1.3, 1.4, 1.4, 1.0, 1.6, 1.3,	(1/10)	
					(60 sec)		1.1, 1.4, 1.5, 0.96		
Honduras	Mertec	4.2	0.040	10.5	Spray	Green	0.96, 0.92, 1.1, 1.0, 0.91,	(2/10)	Norton,
1992	t 20S					banana	0.95, 0.95, 0.98, 1.2, 0.96		1993a
Los Flores							mean: 0.99		
						Ripe	0.023, 0.014, 0.023,		
						banana	0.020, 0.024, 0.005,		
						pulp	0.012, 0.024, 0.029,		
							0.022, mean: 0.019		
Corozal						Green	0.89, 0.88, 0.80, 1.0,		
						banana	0.79, 0.60, 0.67, 1.0,		
							0.90, 0.72		
						Ripe	mean: 0.83		
						banana	0.010, 0.009, 0.008,		
						pulp	0.016, 0.014, 0.012,		
							0.010, 0.016, 0.008,		
							0.006, mean: 0.011		
Honduras	Mertec	4.2	0.040	10.5	Spray	Green	0.67,0.67, 0.79, 0.78,	$(1/10)^{a}$	Norton,
1992	t 340-F					banana	0.70, 0.65, 0.75, 0.68,		1993a
Los Flores							0.64, 0.85		
						Ripe	mean: 0.72		
						banana	0.018, 0.028, 0.008,		
						pulp	0.003, 0.031, 0.025,		
							0.025, 0.030, 0.031,		
							0.015 <u>, mean:</u> 0.021		
Corozal						Green	0.63, 0.76, 0.88, 0.62,	(1/10)	
						banana	0.59, 0.84, 1.0, 0.76,		
							0.63, 0.72		
						Ripe	mean: 0.74		
						banana	0.018, 0.020, 0.026,		

Country			Application			Sample	I	Residues, mg/kg		Remarks	Ref.
Year	Form.	kg ai/ha	kg ai/hl	l/t	Туре						
						pulp	0.025,	0.016,	0.019,		
							0.014,	0.017,	0.016,		
							0.028 m	ean: 0.02			
Guadeloupe,	Mertec		0.045		dip	Green	1.8, 1.6,	1.5		(3/3)	Sing, 1992
1992	t 20S				(2 min)	banana	1.1, 1.3,	0.96			
							1.4, 1.1,	1.6			
Guadeloupe,	Mertec		0.045		dip	Green	1.4, 1.4,	1.9		(3/3)	
1992	t SC				(2 min)	banana	2.6, 2.1,	1.7			
							3.3, 2.8,	3.5			
Guadeloupe,	Mertec		0.090		dip	Green	1.8, 1.8,	1.1		(3/3)	
1992	t 20S				(2  min)	banana	1.0, 2.1,	1.6			
							2.1, 2.6,	2.3			
Guadeloupe,	Mertec		0.090		dip	Green	2.3, 2.6,	1.8		(3/3)	
1992	t SC				(2 min)	banana	3.9, 7.3,	5.3			
							4.7, 4.3,	3.9			

<sup>1</sup>Number of assays per sample/number of samples analysed

<u>Tomatoes</u>. Four pre-harvest trials were conducted on tomatoes grown under plastic in Spain in 1990-1991 with ground spray foliar application of thiabendazole SC and WP formulations. Two trials in 1990 were with two applications, 7 days apart, at 0.50 kg ai/ha, and two in 1991 with single applications at 3.1 kg ai/ha (AgVet, 1991).

Table 14. Residues of thiabendazole in tomatoes grown under plastic in Spain from pre-harvest applications of SC and WP formulations of thiabendazole in supervised trials

	Ар	plication		PHI,	Residues, mg/kg	Remarks <sup>1</sup>
Form.	kg ai/ha	kg ai/hl	Туре	days		
Tecto	3.1	0.090	Ground	0	1.6, 2.3, 2.4	$(3/1)^1$
45			spray	4	1.7, 1.7, 1.8	
			(1)	7	1.6, 1.8, 2.0	
				11	1.4, 1.6, 1.6	
				14	1.3, 1.5, 2.2	
				21	1.0, 1.2,1.4	
Tecto	3.1	0.090	Ground	0	2.0, 2.3, 1.9	(3/1)
45			spray	4	1.9, 2.1, 1.7	
			(1)	7	1.6, 2.0, 1.5	
				11	1.4, 1.9, 1.1	
				14	1.3, 1.5, 0.83	
				21	1.3, 1.3, 0.84	
Tecto	0.50	0.050	Ground	3	0.26, <u>0.32</u> , 0.18, 0.30	(4/1)
60			spray	7	0.25, 0.36, 0.50, 0.37	
			(2)	10	0.44, 0.41, 0.80, 0.73	
Tecto	0.50	0.050	Ground	3	0.28, 0.32, <u>0.40</u> , 0.25	(4/1)
60			spray	7	0.35, 0.30, 0.43, 0.40	
			(2)	10	0.52, 0.32, 0.72, 0.68	

<sup>1</sup>Number of analyses per sample/number of samples

<u>Chicory</u>. Pre-planting trials were conducted in France between 1979 and 1982 with single dip or spray applications of SC and SL formulations of thiabendazole to chicory roots which were grown to harvest. Eleven trials in 1979, 1980 and 1982 were with Flowable SC and 9 trials in 1979 and 1980 with the 20-S formulation at 67-630 g ai/hl. The endive leaves and roots were analysed separately. Residues of thiabendazole in the edible endive leaves did not exceed 0.05 mg thiabendazole/kg.

Table 15. Residues of thiabendazole in or on whole unwashed chicory from single pre-planting applications of SC and SL formulations of thiabendazole in supervised trials (Schreur, 1992).

Country, Year,		Appl	ication			Residu	es, mg/kg
Variety	Form	kg ai/ha	kg	l/t	Туре	Leaf	Root
			a1/n1				
France, 1979	Mertect		0.067		dip	< 0.005 (2)	< 0.065
Witloof	Flowable		0.10		(2 min)	<u>&lt;0.005</u>	0.038
			0.20			< 0.005	< 0.015
France, 1979	Mertect 20S		0.067		dip	< 0.005 (2)	-
Witloof			0.10		(2 min)		< 0.005, (2)
			0.20				< 0.005 0.036
France, 1980	Mertect		0.10		dip	<u>&lt;0.05</u>	9.4
Witloof	Flowable		0.20		(3-5 min)	< 0.05	12
			0.40			< 0.05	4.4
		20	0.25	8	spray	< 0.05	3.7
		40	0.50	8		< 0.05	12
		50	0.63	8		< 0.05	3.7
France, 1980	Mertect 20S		0.099		dip	<u>&lt;0.05</u>	13
Witloof			0.20		(3-5 min)	< 0.05	23
			0.40			1.2*	37
		20	0.25	8	spray	< 0.05	55
		40	0.50	8		< 0.05	7.3
		50	0.63	8		< 0.05	12
France, 1982	Mertect		0.10		dip	<u>&lt;0.05</u> (2)	10, 10
Witloof	Flowable				(2  min)		
		60	0.60	10	spray	< 0.05 (2)	10, 10

\*Probable contamination

<u>Potatoes</u>. Post-harvest residue trials were conducted in the UK and the USA from 1975 to 1990. Seven trials in the UK were with single spray mist applications of a Flowable formulation at 30-80 g ai/t on whole potatoes. Potatoes in the US trials were subjected to an initial seed treatment at 2400 g ai/hl before cutting and planting, followed by an application at 6.2 g ai/t immediately after harvest and before storage, and a second application at 6.2 g ai/t approximately 30 days later. Samples were stored frozen and analysed within 19 months of treatment.

Table 16. Residues of thiabendazole in or on whole potatoes from post-harvest applications of SC formulations of thiabendazole in supervised trials.

Country, Year		A	Application	n		Residues, mg/kg	Remarks	Reference
	Form.	g ai/t	kg ai/hl	l/t	Туре			
USA, ID, 1990	Mertect		2.4		dip		$(2/4)^{1}$	Norton,
Russet	340-F	6.2		0.26	spray	<u>1.8, 1.9, 1.6, 1.6,</u>	3 applications <sup>2</sup>	1993b
		6.2		0.26	spray	<u>1.7, 1.7, 1.2, 1.2,</u>		
WA			2.4				(2/4)	
Burbank		6.2		0.26		<u>7.0, 7.1, 6.0, 6.3,</u>		
		6.2		0.26		<u>7.0, 7.1, 7.0, 7.3</u>		
USA, MI, 1990			2.4		dip		(2/4)	
Yukon gold		6.2		0.26	spray	<u>4.9, 5.1, 4.1, 4.3,</u>	3 applications <sup>2</sup>	
		6.2		0.26	spray	<u>2.8, 3.8, 5.1, 5.5</u>		
USA, ME,			2.4		dip		(2/4)	
1990		6.2		0.26	spray	<u>3.3, 3.4, 2.6, 3.4,</u>	3 applications <sup>2</sup>	
Superior		6.2		0.26	spray	<u>4.0, 4.2, 3.4, 3.6</u>		
UK, 1990	Storite FL	40			spray	<u>0.6, 1.3, 1.0</u>	DAT 0,	McKenzie,
Estima <sup>3</sup>						<u>1.3, 1.9, 1.9</u>	DAT 42	1991
						<u>2.0, 2.0, 2.0</u>	DAT 84	
		80				1.9, 1.6, 1.9	(3/1) DAT 0	
						2.5, 2.9, 3.5	DAT 42	
						3.1, 3.0, 2.8	DAT 84	
Obelix <sup>3</sup>		40			spray	<u>2.0, 2.6, 1.4</u>	DAT 0, 42, 84	
		80				3.3, 2.8, 2.6	DAT 0, 42, 84	

Country, Year		Application				Residues, mg/kg	Remarks	Reference
	Form.	g ai/t	kg ai/hl	l/t	Туре			
Manfora <sup>3</sup>		40			spray	1.7, 1.8, 2.2	DAT 0, 42, 84	
		80				2.0, 3.2, 2.1	DAT 0, 42, 84	
Record	Extractect	30	30		spray	1.2, 2.6	(1/2) DAT 0	Agriserch,
						1.7, <u>2.4</u> , 1.5	DAT 42	1991
Desiree	Exractect	30	30		spray	4.4	DAT 0	
						5.4	DAT 42	
		60	30		spray	6.6, 7.3	(1/2) DAT 0	
						8.2, 8.7	DAT 42	
Cara	Extractect	30	30		spray	12	DAT 0	
						11	DAT 42	

<sup>1</sup>Number of analyses per sample/number of samples analysed

<sup>2</sup>Seed treatment plus 2 post-harvest sprays approximately 30 days apart

<sup>3</sup>Samples were lightly washed before analyses to remove adhering soil

DAT: days after last treatment

<u>Sugar beet</u>. Pre-harvest residue trials were conducted on sugar beet grown in Spain in 1996 with ground spray applications of a thiabendazole SC formulation. Eight trials were with single applications, or 2 applications approximately 33 days apart, at 480 g ai/ha (0.12 kg ai/hl) after development of 4-8 leaves and the crops were grown to harvest (Valcarcel, 1977). Residues of thiabendazole were <0.01 mg/kg in all 16 root samples taken from 0 to 91 days after the last application. The leaves contained the residues shown below:

DAT	Residues in leaves, mg/kg
0	0.07
29-36	0.07, 0.36, 0.05, 0.07
59 –65	<0.01, <0.01, <0.01, 0.41, 0.12
>71	<0.01, 0.019

<u>Mushrooms</u>. Six trials were conducted in the USA in 1990-1991 on mushrooms treated with four applications of an aqueous solution by irrigation at 54 or 108 g ai/100 m<sup>2</sup> or by direct spray at 9.5 or 19 g ai/hl. Applications were made after pinning or after the first harvest break and then after the second, third and fourth breaks according to label instructions. The maximum residues of thiabendazole on mushrooms collected 12 hours after the last application ranged from 2.4 to 13 mg/kg for irrigation and from 30 to 41 mg/kg for spray applications. The residues of benzimidazole were <0.01 mg/kg in all samples. Samples were stored frozen and analysed within 18 months of treatment.

In four trials in Japan in 1988 and two in 1993 mushrooms were treated with a WP formulation using single applications to the bed medium at a rate of 0.120 g ai/kg. The residues of thiabendazole did not exceed 0.25 mg/kg.

Table 17. Residues of thiabendazole in or on whole mushrooms from pre-harvest applications of WP and SC formulations of thiabendazole.

Country, Year		Applicat	ion		Residues, mg/kg <sup>1</sup>	Replication;	Reference
	Form.	g ai/100 m <sup>2</sup>	kg ai/hl	Туре		PHI, days	
USA, 1990	MERTECT 340F	108 54 54 54 54	0.019 0.0095 0.0095 0.0095	Irrigation	3.1 <u>, 3.2</u> (1 & 2) 3.1 <u>, 3.1</u> (3) 3.8 <u>, 3.9</u> (4)	$(2/1)^2$ (2/1) (2/1)	Norton, 1992d
USA, 1990	MERTECT 340F	108 54 54 54	0.019 0.0095 0.0095 0.0095	Irrigation	1.9 <u>, 1.9</u> (1 & 2) 2.0 <u>, 2.2</u> (3) 2.4 <u>, 2.5</u> (4)	(2/1) (2/1) (2/1)	

Country, Year		Applicati	ion		Residues, mg/kg <sup>1</sup>	Replication;	Reference
	Form.	g ai/100 m <sup>2</sup>	kg ai/hl	Туре		PHI, days	
USA, 1990-91	MERTECT	108	0.019	Irrigation	9.3 <u>, 9.6</u> (1)	(2/1)	
	340F	54	0.0095	-	7.0 <u>, 7.3</u> (2)	(2/1)	
		54	0.0095		13 <u>, 13</u> (3)	(2/1)	
		54	0.0095		12 <u>, 12</u> (4)	(2/1)	
USA, 1990-91	MERTECT	108	0.019	Irrigation	5.8 <u>, 6.0</u> (1)	(2/1)	
	340F	54	0.0095	-	3.9, <u>3.9</u> (2)	(2/1)	
		54	0.0095		5.9 <u>, 6.1</u> (3)	(2/1)	
		54	0.0095		7.6 <u>, 8.0</u> (4)	(2/1)	
USA, 1990	MERTECT	108	0.019	Spray	37 <u>, 38</u> (1 & 2)	(2/1)	
	340F	54	0.0095				
		54	0.0095		19 <u>, 21</u> (3)	(2/1)	
		54	0.0095		30 <u>, 31</u> (4)	(2/1)	
USA,	MERTECT	108	0.019	Spray	48, 50, 50, 52 (1)	(2/2)	
1990-1991	340F	54	0.0095		25, 26 <u>, 27,</u> 26 (2)	(2/2)	
		54	0.0095		33 <u>, 34, 35, 36</u> (3)	(2/2)	
		54	0.0095		37, 39, 40 <u>, 41</u> (4)	(2/2)	
Japan, 1988	PANMUSH	120 mg/kg			0.092, 0.089	PHI 125 <sup>3</sup>	Japan, 1997
	WP	of bed			0.12, 0.11	PHI 115	
					0.018	PHI 125	
					0.008	PHI 115	
Japan, 1993	PANMUSH	120 mg/kg	1		0.25, 0.25	PHI 196	1
oupu,	WP	of bed			0.19, 0.19	PHI 188	

<sup>1</sup>Figures in parentheses are breaks at which thiabendazole was applied

<sup>2</sup>Number of analyses per sample/number of samples

<sup>3</sup>Results of 4 replicate trials at the same site

<u>Wheat</u>. Fourteen pre-harvest trials were conducted according to GAP on wheat in the USA in 1990 using single ground or aerial sprays of thiabendazole WG formulation at 620 g ai/ha after development of 2 to 3 tillers but before the first node. The wheat was grown to harvest (Armstrong and Norton, 1993b). The residues of thiabendazole and the metabolite benzimidazole were <0.05 mg/kg in all 14 grain samples. The thiabendazole residues in the straw were in rank order <0.05 (11), 0.11, 0.07 and 0.13 mg/kg. Samples were stored frozen and analysed within 23 months of treatment.

#### Animal feeding studies

<u>Cows</u>. Dairy cattle (3 per group) were dosed once daily by capsule for 28 days with thiabendazole at levels corresponding to 25, 75 and 250 ppm in the feed. The level of 25 ppm represents a likely maximum intake, based on a diet of 70% maize grain and 30% citrus pulp or 50% maize grain, 25% apple pomace and 25% potato waste. There were two control cows. Morning and evening milk samples were collected from all cows on days -1, 1, 2, 4, 7, 14, 21, 28, 29, 35, 42 and 56, and a 500-ml sub-sample from each primary sample was retained. The two sub-samples from each day's milking of the cows in each group were combined and duplicate 500-ml samples were analysed for thiabendazole and 5-hydroxythiabendazole (5-OH-TBZ). The tissues and organs from two of the three cows in each dosed group were collected on day 29 of the study. The remaining cow from each group was slaughtered on day 57. Tissues from each cow were analysed for thiabendazole and 5-OH-TBZ.

The total residues of thiabendazole and 5-OH-TBZ in the milk and tissues increased with increasing dose but not necessarily proportionally. Residues in the milk reached a plateau two days after treatment, but they were  $\leq 0.01$  mg/kg higher than the control value in the low-dose group. This difference is not considered to be significant. The total residues of thiabendazole plus 5-OH-TBZ in the cows dosed at the 25 ppm level were < 0.05 mg/kg in milk and tissues except a single value of 0.05 mg/kg in kidney (Justin, 1990a). No difference was observed between the thiabendazole residues

measured in various muscles. The residues decreased rapidly to control levels when the animals were returned to a thiabendazole-free diet.

Table 18. Residues of thiabendazole and 5-hydroxythiabendazole in milk (daily averages of 3 cows) from cows dosed with thiabendazole.

Sampling	Residues, mg/kg, at dose equivalent to									
day	2	25 ppm	7	/5 ppm	,	250 ppm				
	TBZ	5-OH-TBZ	TBZ	5-OH-TBZ	TBZ	5-OH-TBZ				
-1	0.013	0.003	0.012	0.004	0.013	0.004				
1	0.014	0.009	0.014	0.059	0.014	0.072				
2	0.014	0.012	0.014	0.081	0.017	0.110				
4	0.015	0.013	0.014	0.091	0.015	0.110				
7	0.014	0.013	0.015	0.083	0.014	0.115				
14	0.014	0.013	0.015	0.073	0.016	0.111				
21	0.013	0.012	0.015	0.091	0.017	0.127				
28	0.013	0.013	0.014	0.108	0.016	0.134				
29	0.016	0.004	0.013	0.008	0.015	0.067				
35	0.014	0.003	0.013	0.004	0.012	0.004				
42	0.010	0.002	0.014	0.006	0.014	0.004				
49	0.015	0.004	0.014	0.005	0.018	0.002				
56	0.013	0.004	0.014	0.004	0.018	0.002				

Animals fed a thiabendazole-free diet on days 29-56 5-OH-TBZ: 5-hydroxythiabendazole

Table 19. Residues of thiabendazole and 5-hydroxythiabendazole in tissues from cows dosed with thiabendazole.

Sample (Sampling day)		Residues, mg/kg, at dose equivalent to							
	25	5 ppm	75	ppm	250 ppm				
	TBZ	5-OH-TBZ	TBZ	5-OH-TBZ	TBZ	5-OH-TBZ			
Fat (29)	0.016	0.004	0.013	0.009	0.014	0.007			
	0.018	0.002	0.017	0.012	0.015	0.010			
Fat (57)	0.016	0.003	0.006	0.002	0.017	0.002			
Kidney (29)	0.012	0.038	0.016	0.079	0.024	0.33			
		0.049	0.017	0.42	0.030	0.55			
Kidney (57)	0.020	0.010	0.020	0.008	0.022	0.014			
Liver (29)	0.022	0.026	0.036	0.041	0.056	0.12			
		0.028	0.060	0.130	0.080	0.16			
Liver (57)	0.018	0.016	0.018	0.015	0.020	0.017			
Muscle (29)	0.012	0.002	0.013	0.004	0.015	0.004			
	0.014	0.003	0.014	0.006	0.017	0.005			
Muscle (57)	0.014	< 0.01	0.012	0.002	0.014	0.002			

Animals fed a thiabendazole-free diet on days 29-57

<u>Chickens</u>. Ten groups of birds (25 per group, males and females) were treated continuously for 7 weeks with thiabendazole at levels corresponding to 0, 2, 20, 200 and 2000 ppm in the feed. Four males and four females at each treatment level were killed within four hours of the last dose and the liver, kidney, fat and muscle analysed for thiabendazole and 5-hydroxy-thiabendazole, as were the eggs from the three highest treatment groups. The total residues in the tissues and eggs of birds dosed at the 20 ppm feed level (the expected maximum intake based on a poultry diet of 70% maize grain, 20% potatoes and waste and 10% wheat grain) were <0.1 mg/kg, except a single value of 0.12 mg/kg in kidney (Justin, 1990b).

Table 20. Residues<sup>1</sup> of thiabendazole and 5-hydroxythiabendazole in tissues and eggs from chickens dosed with thiabendazole.

Sample		Residue, mg/kg, at dose equivalent to									
		0	2 ppm		20	20 ppm		200 ppm		2000 ppm	
	TBZ	$5-OH-T^2$	TBZ	5-OH-T	TBZ	5-OH-T	TBZ	5-OH-T	TBZ	5-OH-T	
Fat/skin	0.009	0.009	0.010	0.009	0.010	0.010	0.024	0.029	0.16	0.20	
	0.013	0.013	0.012	0.013	0.015	0.013	0.060	0.055	0.41	0.63	
Kidney	0.01	0.013	0.018	0.022	0.018	0.050	0.038	0.24	0.19	1.5	
-	0.026	0.02	0.040	0.041	0.029	0.093	0.057	0.79	0.54	5.7	
Liver	0.005	0.012	0.006	0.014	0.010	0.046	0.027	0.16	0.29	1.8	
	0.008	0.019	0.012	0.029	0.014	0.067	0.051	0.58	0.60	5.2	
Muscle	0.007	0.005	0.007	0.006	0.009	0.008	0.019	0.016	0.081	0.17	
	0.008	0.007	0.009	0.008	0.013	0.010	0.035	0.036	0.26	0.64	
Egg			-	-	0.007	0.016	0.038	0.39	0.53	1.2	
yolk					0.020	0.031	0.063	1.3	0.67	1.9	
Egg			-	-	0.003	0.004	0.017	0.032	0.18	0.24	
white					0.011	0.012	0.027	0.048	0.21	0.36	

<sup>1</sup>Average residues from two groups at each level

## FATE OF RESIDUES IN STORAGE AND PROCESSING

#### In storage

<u>Potatoes</u>. The effect of cold storage on the residues of thiabendazole in or on potatoes was studied in Greece in 1985. One hundred kg of potatoes were sprayed with a flowable formulation at 30 or 60 g ai/tonne and stored in the dark at  $5^{\circ}$ C and 100% relative humidity. Random samples of six whole tubers or the separated pulp and peel from six tubers were analysed for thiabendazole over a 6-month period. The initial (day 0) samples were analysed after the spray deposit had dried. Unwashed tubers showed an initial loss (probably mechanical) of thiabendazole residues between day 0 and day 14 but thereafter the surface residues did not decline significantly. The results are shown in Table 21 (Lentza-Rizos, 1986).

Table 21. Effect of cold storage on residues of thiabendazole in or on potatoes treated with single post-harvest applications of SC formulations of thiabendazole.

Sample		Thiab	endazole, n	nean of 2 analys	es, mg/kg
	Storage	Treatment w	vith 30 kg a	i/ha	Treatment with 60 kg ai/ha
	period, days	Pulp	Peel	Whole <sup>1</sup>	Whole <sup>2</sup>
Unwashed	0	0.9	108	27	52
tubers	14	1.3	61	15	33
	28	1.2	48	12	32
	56	1.3	56	14	34
	84	1.6	66	16	34
	161	2.2	49	13	35
	189	2.3	69	17	36
Washed	0	0.07	6.2	1.4	3.7
tubers	14	0.07	6.6	1.6	3.4
	28	0.07	5.5	1.4	3.3
	56	0.1	7.6	2.0	5.5
	84	0.1	8.7	2.5	7.0
	161	0.1	8.6	2.1	5.2
	189	0.1	11.5	2.9	5.2

<sup>1</sup>Calculated from the residues in the peel and pulp

<sup>2</sup>Whole potatoes analysed

<u>Apples.</u> The effect of cold storage on the residues of thiabendazole was studied in Spain in 1987. Apples were dipped for 35 seconds in aqueous suspensions of Tecto 60 at an application rate of 100 g ai/hl and the treated fruit stored at 0-2°C and 85-90% relative humidity. The residues of thiabendazole were determined 24 hours after treatment and at monthly intervals during storage. The results are shown in Table 22 (Cano *et al.*, 1987).

Table 22. Effect of cold storage on the residues of thiabendazole in or on unwashed apples treated with single post-harvest dips of WP formulations of thiabendazole. Spain, 1987. Single samples analysed.

Variety		Application	1	Storage	Re	esidues, mg	′kg
	Form	kg ai/hl	Туре	period, days	Whole <sup>1</sup>	Peel	Pulp
Golden Delicious	Tecto 60 WP	0.10	Dip	0 37	3.3	4.5 4.2	0.54
Deficious				62	2.3	3.7	0.19
				90 125	2.3 1.9	3.0 2.1	0.27 0.12
				146	2.0	1.9	0.10
Starking	Tecto 60	0.10	Dip	0	3.5	1.8 4.6	0.16
	WP			37 62	3.0 2.6	3.9 3.8	0.17 0.18
				90	2.0	2.6	0.10
				125 146	1.9 1.4	1.6 1.3	0.10 0.13
				174	0.82	0.83	0.15

<sup>1</sup>Residues in whole apples were calculated from the residues in the peel and pulp

## In processing

<u>Citrus fruit</u>. Two processing trials were conducted in the USA in 1990. Oranges and grapefruit were treated with a post-harvest dip at 12 g ai/t followed by a spray mist application in wax at 500 g ai/hl. Whole, washed fruit were processed.

The effects of simulated home processing on residues of thiabendazole in the preparation of marmalade, both in an open preserving pan and in a microwave oven were studied in the UK in 1993.

The results of all three trials are shown in Table 23.

Table 23. Residues of thiabendazole in processed fractions of washed and unwashed citrus fruit treated post-harvest.

Ref.	Fruit, Country Year	Sample	Mean residue, mg/kg	Processing factor	Replications <sup>1</sup>
Norton, 1992a	Orange, USA, 1990	Washed fruit Juice Molasses Oil Finisher pulp Dried pulp	1.1 0.07 5.4 14 0.16 8.7	0.064 4.9 12.7 0.15 7.9	4/1 2/1 2/1 2/1 2/1 2/1 2/1
	Grapefruit USA, 1990	Washed fruit Juice Molasses Oil	1.55 0.06 9.15 14	0.038 5.9 9.0	2/1 2/1 2/1 2/1

		Finisher pulp	0.15	0.097	2/1
		Dried pulp	12.5	8.1	2/1
Friar and Reynolds,	Orange	Unwashed fruit	$2.41^2$		5/1
1994	UK, 1993	Peel	8.64 <sup>3</sup>	3.6	
		Marmalade (preserving	0.78	0.32	1/3
		pan)	0.90	0.37	1/3
		Marmalade (microwave)			

<sup>1</sup>Number of analyses per sample/number of samples analysed

<sup>2</sup>About 3.5 kg of oranges were processed

<sup>3</sup>Residues in the peel were calculated from the peel/whole orange mass ratio and the residues in the whole oranges. It was assumed that the pulp did not contain any residue.

<u>Apples</u>. Apples were treated with a post-harvest dip at 60 g ai/hl followed by a spray mist application in wax at 8.4 g ai/t approximately 30 days after cold storage in the USA in 1990. Whole unwashed fruit were processed into juice, wet pomace and dried pomace (Norton, 1992c). The thiabendazole residues were 3.85 mg/kg in washed whole apples, 1.05 mg/kg in apple juice, 13.5 mg/kg in wet pomace and 45 mg/kg in dried pomace.

<u>Potatoes</u>. Potatoes were processed to chips in the USA in 1990. Seed potatoes were dipped in an aqueous suspension at 2400 g ai/hl before cutting and planting, and the daughter tubers were sprayed at 6.2 g ai/t immediately after harvest and before cold storage. A second application at 6.2 g ai/t followed approximately 30 days later. The whole washed potatoes were processed by successive washing, abrasive peeling, washing, slicing, washing, frying in vegetable oil at 178-182°C, de-oiling, and salting. The results are shown in Table 24 (Norton, 1993b).

The effect of microwave and oven cooking on the residues of thiabendazole in or on potatoes was studied in the UK in 1990 (Friar and Reynolds, 1991). Potatoes treated post-harvest with a single application of 40 g ai/t were stored for 182 days and the raw peel, raw pulp and unpeeled raw potatoes were subjected to microwave and oven cooking. The residues found in the processed fractions of individual potatoes are shown in Table 25.

Sample	Residues, mg/kg	Processing factor	
Unwashed whole potatoes	6.5		
Wash water	2.2		
Washed potatoes	2.2	0.34	
Wet peel	6.4	0.98	
Dried peel	109	17	
Chips	<0.5	< 0.08	
Flakes	0.2	0.03	

Table 24. Residues of thiabendazole in processed fractions of potatoes.

Table 25. Residues of thiabendazole in processed potato fractions

Sample	Residues, m	Processing factor <sup>1</sup>	
	Individual potatoes	Mean	
whole potato before cooking	1.7, 1.9, 2.4, 2.7, 3.0	2.36	
whole potato, microwave cooked	4.1, 2.9, 2.6, 4.0, 2.9, 3.9	2.84	1.2
whole potato, oven cooked	2.8, 3.2, 2.9, 3.8	3.17	1.34

Sample	Residues, mg/kg		Processing factor <sup>1</sup>
	Individual potatoes	Mean	
raw peel before cooking	9.1, 10, 10, 12,	12.2	
	12, 12, 10, 20, 14		
peel, microwave cooked	17, 14, 17, 25,		
	16, 16, 12, 15	16.4	1.34
peel, oven cooked	13, 13, 12, 16		
	15, 16, 11, 16	14	1.15
raw pulp before cooking	0.05, 0.05, 0.15	0.09	
	0.06, 0.14		
pulp, microwave cooked	0.05, 0.06, 0.03	0.05	0.56
	0.04		
pulp, oven cooked	0.04, 0.04, 0.07, 0.09	0.06	0.67

<sup>1</sup>From raw to cooked whole potato, raw to cooked peel, and raw to cooked pulp

Four trials on the effects of washing, boiling, baking and crisping on the residues of thiabendazole in or on potatoes were conducted in the UK in 1976. Potatoes were treated post-harvest with single applications at 40 or 80 g ai/t. The tubers were processed after storage for 1 and 21 days after treatment and the residues of thiabendazole determined (AgVet, 1976). The results are shown in Table 26.

Table 26. The effect of washing, boiling, baking and crisping on the residues in or on potatoes treated post-harvest with an SC formulation of thiabendazole.

Process Storage,			esidues, mg/k	g <sup>1</sup>	Processing factor from	
	days	40 kg ai/t	80 kg ai/t	Untreated	Raw potatoes	Washed potatoes
Unwashed	1	16.95	24.6	0.095		
	21	20.3	28.4	0.08		
Washed	1	1.5	2.7	0.1	0.088, 0.11	
	21	5.36	7.26	0.075	0.26	
Washed, peeled, chipped	1	0.11	0.15	0.08	0.006	0.073, 0.055
	21	0.24	0.47	0.09	0.012, 0.017	0.044, 0.065
Washed, peeled, crisped	1	0.17	0.17	0.5	0.010, [0.007	
	21	No valid results		0.28		
Washed, peeled, boiled	1	0.22	0.45	0.09	0.013, 0.018	0.15, 0.16
	21	0.25	0.36	0.09	0.012, 0.013	0.047, 0.05
Washed, baked	1	1.8	3.13	0.13	0.18, 0.13	1.2, 1.16
	21	3.0	8.25	0.35	0.15, 0.29	0.55, 1.13

<sup>1</sup>Mean residues from processing Record and Pentland Dell varieties

## **RESIDUES IN FOOD IN COMMERCE OR AT CONSUMPTION**

Monitoring data. The results of retail monitoring carried out in the UK by the Working Party on Pesticide Residues (WPPR) from samples obtained in 1991 are shown in Table 27.

Table 27. Residues of thiabendazole in retail commodities.

Commodity	Source	No. of samples	Residues,	No. of samples in range
			mg/kg	
Main crop potato	UK	176	< 0.1	149
			0.1-0.9	20
			1.2-2.5	7
Cooking apples	UK	24	< 0.1	24
Dessert apples	UK	25	< 0.2	24
			0.2-4.5	1
Dessert apple	imported	36	< 0.2	28
			0.2-4.5	8
Green cabbage	UK	17	< 0.05	17
Green cabbage	imported	5	< 0.05	5
Chicory	UK	8	< 0.2	8
Chicory	imported	3	< 0.2	3
Chicory	unknown	1	< 0.2	1
Grapefruit	imported	25	< 0.5	8
			0.6-6.6	17
Lemon	imported	12	< 0.5	9
			0.6-2.1	3
Strawberry	UK	19	< 0.2	19
Strawberry	imported	20	< 0.2	18
			0.3-0.8	2
Strawberry	unknown	4	< 0.2	4

## NATIONAL MAXIMUM RESIDUE LIMITS

The following national MRLs were reported to the Meeting.

Country, commodity	MRL, mg/kg
Argentina	
citrus fruit (pre-harvest and post-harvest)	10
apple (pre-harvest and post-harvest), banana with peel, pear, quince-(post-harvest)	3
onion, garlic	1
potato-(post-harvest), banana without peel (post-harvest)	0.4
rice	0.2
Austria	
citrus fruit	6
bananas, Chinese cabbage, potatoes, pome fruit, turnip-rooted celery	3
other vegetables	1.5
rape seed	1
cereals	0.5
other	0.1
Belgium	
pome fruit	10
strawberries, potatoes	3
grains	0.2
bulb vegetables, tomatoes	0.1
chicory	0.05
other	0.1*
Brazil	
apples, citrus fruit, pears	10
potato	5

Country, commodity	MRL, mg/kg
banana (unpeeled)	3
banana (without peel)	0.4
cereals (unprocessed)	0.2
mango, papaya, peaches, honeydew melons, squash, cotton seed, soya beans, grasses	0.1* P
Canada	
apples, citrus, pears	10
potatoes	4
bananas (edible pulp)	0.4
sugar beet	0.1*
Chile	
citrus fruits, apples, pears	10
potatoes, sugar beet	5
cereals (raw)	0.2
tomatoes	0.1
milk, carcasses	0.1*
Denmark	
pome and stone fruits, parsley	10
citrus fruits	6
berries and small fruits, other fruits	3
other vegetables	2
potatoes	0.5
European Union	
hanana	3
citrus fruit	6
nome fruit	5
potato ware	5
Strawberry	5
Provisional MRLs set at LOD generally 0.05 or 0.1 mg/kg for various tree nuts	
neaches, grapes, berries, root, bulb, and fruiting vegetables, cucurbits, brassicas, leafy	
and stem vegetables, legumes, pulses, oil seeds, early potatoes, tea, and hops	
established under Council Directive 95/38/EC. MRLs to be incorporated into national	
legislation by Member States.	
Finland	
citrus fruits	6
apples, pears	3
potatoes (industrial use)	1
bananas	0.4
cereal grains	0.2
other potatoes	0.1
Others	2
France	
citrus fruits	6
bananas	3
endive	05
Germany	
potatoes (washed)	4
nome fruits	3
cabbage rape	1
cereals	0.2
other foods of plant origin (except bananas & citrus fruits)	0.1
Hungary	
lemon, grapefruit, orange, mandarin (Imports)	10
bananas (Imports)	3
bananas without peel (Imports)	0.4
Israel	0.1
citrus fruit, pears, apples	10
celerv	5
hananas strawherries	3
Italy	5
notatoes (washed)	Λ
polatoes (washed)	+

Country, commodity	MRL, mg/kg
apples, pears	3
wheat, rice	0.2
onions, garlic	0.1
Japan*	
fruits (except citrus and banana)	3
vegetables	2
sugar beet	0.1
Kenya	
citrus fruit	6
bananas	3
bananas (pulp)	0.4
Mexico	
citrus (dry pulp)	35 (FA)
apples (post-harvest), Citrus fruit, pears (pre-harvest and post-harvest)	10
potatoes (pre-harvest and post-harvest)	3
rice	1
wheat straw	0.2
sova beans, wheat	0.1
sweet potatoes	02*
Netherlands	
pome fruit	10
potato	5
strawherry	3
tomato	2
cereal	0.2
onion	0.1
milk meat	<0.1
other	<0.1
citrus fruit hanana see Preservatives Decision Commodities Act	<0.1
marmalade see Iam & Preservatives Decision Act	
Naw Zaaland	
	10
bananas citrus	3
meat	0.1
Pomonio	0.1
Romania eggs (without shells) whole milk milk products meat	0.1
South Africo	0.1
potatoes nineannles	10
applac citrus pages	6
apples, citus, pears	5
avocauos bananas mustimaton	3
mushroome	1
(all telerances in commedities for legal use)	1
(an tolerances in commodities for local use)	
sitere ferrit	6
	0
washed polatoes	4
chamics, pointe nuns, surawdennes	3
ell ether plant moduate	0.1
	0.1
apple citrus fruits pears	10
appie, ciulus ituits, pears fruit & vagatablas	10
	0.5
polaioes	0.5
Uananas (Without peer)	0.4
ownizerianu	10
bananas (wiloie)	10
vananas (wnote)	3
pananas (puip)	0.4
potatoes	01*
<u><b>NOIE</b></u> : values for citrus fruit and bananas are not tolerances but are upper limits for	

Country, commodity	MRL, mg/kg
the food to be considered fit for human consumption.	
Taiwan	
citrus fruits (peel)	10
mushrooms, tropical fruits (peel)	5
root vegetables	3
rice	2
citrus fruits (pulp)	1
tropical fruits (pulp)	0.5
UK	
potatoes	5
USA-Raw Agricultural Commodities	
apple (post-harvest)	10
avocado	10
banana (Pre-harvest and post-harvest)	3
banana pulp (pre-harvest and post-harvest)	0.4
heans dry	0.1
heets sugar-without tops	0.25
heets sugar-tons	10
cantaloupe	15
carrot (nost-harvest)	10
citrus fruite	10
	10
mango	10
mishroom	10
neusinooni	40
papaya (post-hai vest)	10
pear (post-fial vest)	10
wing nou-h	10
rice, fougli	<u> </u>
	10
	0.1
strawberry	3
sweet potato (post-narvest for seed use)	02
squash, Hubbard	1
wheat grain	1
wheat straw	1
tat of cattle, goats, hogs, horses, sheep	0.1
meat by products of cattle, goats, hogs, horses, poultry, sheep	0.1
meat of cattle, goats, hogs, horses, poultry, sheep	0.1
eggs	0.1
poultry	0.1
milk	0.4
wheat milled fractions (except flour)	3
apple pomace, dried (post-harvest)	33
beets, sugar, pulp (dried and/or dehydrated)	3.5
citrus molasses	20
citrus pulp, dried (post-harvest)	35
grape, pomace (dry or wet)	150
potato processing waste (Pre-harvest and post-harvest)	30
rice, hulls	8
wheat milled fractions (except flour)	3

NS = Not specified

FA = Feed Additive

P = Provisional

\*At or about the limit of determination

Residues are usually defined as thiabendazole except in products of animal origin where they are usually defined as combined residues of thiabendazole and 5-hydroxythiabendazole.

#### APPRAISAL

Thiabendazole was evaluated by the Joint Meeting several times from 1970 to 1981, when MRLs were recommended for a number of commodities. The compound was evaluated by the present Meeting under the periodic review programme of the CCPR.

At its 1992 meeting JECFA noted that total residues of thiabendazole and 5-hydroxythiabendazole were below 0.1 mg/kg in all analysed tissues and milk within a few days of withdrawal and therefore adopted the definition of the residue and the MRLs of 0.1 mg/kg recommended by the 1975 JMPR for animal commodities and milk.

Thiabendazole is registered in many countries for use as a post-harvest and pre-harvest fungicide, veterinary drug and human medicine. The major use for plant protection is the post-harvest application.

The disposition of thiabendazole and its metabolites in humans and farm animals has been extensively studied. Many of the studies have also been published in the open literature. The oral administration of thiabendazole to sheep, cattle, goats, dogs and humans resulted in rapid absorption from the gastrointestinal tract. The time to achieve peak plasma levels varied with species and ranged from about 1 hour in dogs to 7 hours in sheep, goats and cattle. In dogs, goats and cattle, approximately 82% of the dose was excreted in the urine and faeces within the first 72 hours after oral administration. In all the species studied, almost all the recovered <sup>14</sup>C (97-99.6%) was in the urine and faeces. The hydroxylation of the benzimidazole ring at the 5-position to form 5-hydroxythiabendazole and subsequent conjugation to form the glucuronide and sulfate are the major metabolic steps. A minor metabolic pathway found in faeces and tissues involves loss of the thiazolyl group to form benzimidazole (BNZ). None of these residues are likely to persist in edible tissues in view of their relatively low concentrations and rapid elimination. Although the magnitude and profile of the residues differ slightly among different animal species (rats, lactating goats and laying hens), and samples (tissues, milk, eggs and excreta) the major metabolic steps and metabolic steps are the same.

Single gelatine capsules, each containing 120 mg of [<sup>14</sup>C]thiabendazole, were administered daily to lactating goats for 7 consecutive days. Milk was collected twice daily and tissue samples after slaughter on the 8th day, within 24 hours after the final dose. An average of 74% of the administered dose was accounted for at the end of the study in the excreta (urine + faeces), tissues and milk, nearly all of it in the urine (69%) and faeces (28%). In urine, the residues, expressed as thiabendazole, consisted of unconjugated 5hydroxythiabendazole (~7.9 mg/kg) and its O-sulfate conjugate (~9.5 mg/kg). The residues in the faeces consisted of unconjugated 5-hydroxythiabendazole (2.1 mg/kg), together with lower levels of benzimidazole (~0.4 mg/kg) and unmetabolized thiabendazole (~0.3 mg/kg). About 1% of the dose was found in the tissues. The highest tissue residues were in the liver and consisted of low levels of unmetabolized thiabendazole, unconjugated 5-hydroxythiabendazole and benzimidazole, at maximum concentrations of 0.2, 0.12 and 0.08 mg/kg respectively. Total residues in milk reached a steady state in 3 days and averaged about 1% of the orally administered dose (~1 mg/kg) after the final (7-day) dose. In milk the O-sulfate conjugate of 5-hydroxythiabendazole accounted for about 39% of the <sup>14</sup>C (0.4 mg/kg). No other individual residue was detectable ( $\leq 0.5\%$  of the total radioactivity). Fractionation studies indicated that the unidentified residues were mainly products arising from the extensive degradation of thiabendazole followed by incorporation into proteins (20-60%), lipids (12-14%) and polysaccharides (~1%).

Single gelatine capsules, each containing 3.19 mg of  $[^{14}C]$  thiabendazole were orally administered daily to laying hens for 10 consecutive days; eggs and excreta were collected twice and once daily respectively. The hens were killed on the 11th day, within 24 hours after the final dose.

An average of 96.6% of the total administered dose was recovered. About 99.6% of this recovered dose was found in the excreta, and consisted of unconjugated (3.4 mg/kg) and conjugated (4.4 mg/kg) 5-hydroxythiabendazole. Cumulatively, the total residues found in the tissues and eggs accounted for about 0.4% or less of the <sup>14</sup>C. The total residues in eggs attained a level of about 0.1 mg/kg by day 2 and remained

relatively unchanged throughout the next 8 days. The residues in tissues and eggs consisted mainly of unconjugated 5-hydroxythiabendazole, unmetabolized thiabendazole and benzimidazole at maximum concentrations, in the kidneys, of 0.4, 0.11 and 0.12 mg/kg respectively. The proposed metabolic pathway in poultry is the same as in goats.

Neither thiabendazole nor its related residues are likely to persist in milk, eggs or edible tissues because of their relatively low concentrations and rapid elimination.

The fate of [*phenyl*-<sup>14</sup>C]thiabendazole was studied in actively growing wheat (2-3 tiller stage), soya beans (late flowering to early pod set) and sugar beet treated at maximum recommended rates (0.8, 0.68 and 2.015 kg ai/ha respectively). Residues were characterized after a combination of solvent (MeOH, MeOH/H<sub>2</sub>O) and hydrolytic (KOH/MeOH) extractions, by reversed-phase HPLC and electron-impact GC-MS analyses. The same pattern of metabolites was seen in all three crops.

The total residues were about 0.12 mg/kg in wheat grain, 22 mg/kg in the straw, and 67.5 mg/kg in the foliage. Neither thiabendazole nor any individual metabolite was detectable in grain ( $\leq 0.05$  mg/kg). The major individual residue found in the shoots was thiabendazole and the highest level, 65.6 mg/kg, was detected in early foliage. In all wheat tissues examined, only low proportions of the applied thiabendazole were converted to benzimidazole, which was subsequently conjugated with sugars. The benzimidazole could be released from the conjugate(s) by treatment with glucosidase. Benzimidazole was detected only in shoot tissues (<0.05 mg/kg in forage and 7.49 mg/kg in straw), either free or as the sugar conjugate(s). The highest level of unextractable residues was found in immature wheat forage (5.77 mg/kg), constituting about 14% of the total radioactive residue. The unextractable residues were distributed in very small amounts throughout several fractions of natural products, all of which were individually at or below the limit of detection (0.05 mg/kg). These results are consistent with findings in residue trials on wheat, including seed dressing and foliar treatments at or higher than the recommended rates with unlabelled thiabendazole, in which no residue (<0.05 mg/kg) was detectable in the grain at harvest. Since thiabendazole was present at higher levels than benzimidazole in growing wheat plants, the expected levels of benzimidazole in grain will also be undetectable (i.e. <0.05 mg/kg).

The aerial parts of actively growing soya bean crops were sprayed twice, at a 14-day interval, with [<sup>14</sup>C]thiabendazole at a total rate of about 0.68 kg ai/ha. Immature samples (foliage and forage) were taken at intervals of 2 h and 27 days after treatment and mature samples were harvested and separated into grain and straw about 78 days after the first spray. The extractable residues were characterized by both reversed-phase HPLC and GC-MS. The total residues in the seed (~0.9 mg/kg) were less than 10% of those in the straw (~10 mg/kg). At day 27, thiabendazole was the single major residue (59% or 15.12 mg/kg) found in the shoots and benzimidazole-related compounds were present in smaller amounts (1.4% or 0.36 mg/kg). Benzimidazole was released from the conjugate(s) by glucosidase treatment. Thiabendazole (42.9% of the TRR) was the only individual residue detected ( $\geq$ 0.05 mg/kg) in the grain.

The foliage of actively growing sugar beet plants was sprayed five times, at 14-day intervals, with [<sup>14</sup>C]thiabendazole at a total application rate of about 2.02 kg ai/ha. Immature top and root samples were taken about 2 h after the first and last treatments. About 90 days after the first treatment (35 days after the fifth and final spray) mature samples were harvested and separated into tops and roots. The residues were characterized by HPLC. At day 56 the organo-extractable residue in the roots was about 90% thiabendazole, amounting to 55.8% of the TRR. In the mature roots the total residues (~0.40 mg/kg) were about 4% of those in the tops (~10 mg/kg). The main component was the parent thiabendazole, at about 0.10 mg/kg; no other individual component was detectable (<0.05 mg/kg). A level of 2.7 mg/kg of thiabendazole was present in mature tops, where benzimidazole (1.4 mg/kg) was also present.

The distribution of the residues in wheat, soya beans and sugar beet is consistent with other results showing the predominantly axoplasmic movement of thiabendazole which results in measurable levels of thiabendazole residues in shoot tissues such as leaves and straw, and relatively less in storage tissues (grains and roots). It can be concluded that the profile and distribution of residues of thiabendazole in three representative actively growing crops (small grain, legume and root crops), following foliar applications, are the same.

The uptake, distribution and metabolism of thiabendazole by seed potatoes were studied under postharvest storage conditions. Potatoes were briefly immersed in solutions of [<sup>14</sup>C]thiabendazole at concentrations of 50, 100, 200 and 500 mg/kg and pH levels of 2-9. Skin and tissue sections were subsequently analysed. Potato tubers sorbed thiabendazole from aqueous solutions rapidly (within 5 minutes) at all pH levels. Thiabendazole penetrated only about 2 mm into the tubers in 2 weeks and a little more after 12 weeks, most of it (~96%) remaining on the outer skin. Even after 120 days of post-harvest storage, the only radioactive component detected was thiabendazole, accounting for over 80% of the applied <sup>14</sup>C. These results are supported by several additional studies indicating that thiabendazole does not penetrate into the fleshy tissues and does not undergo metabolic transformation. Benzimidazole was not detected (<0.05 mg/kg).

The uptake, distribution and residual fate of  $[^{14}C]$ thiabendazole under typical post-harvest storage conditions were also examined in Valencia oranges. Virtually all (~95%) of the radioactivity was sorbed by the peel and none penetrated into the inner pulp. Radiometric assays of the orange samples over the 28-day storage period demonstrated that practically all (~95%) of the radioactivity was due to thiabendazole itself although the conditions, at 21°C, were favourable for metabolism.

The post-harvest treatment studies on oranges, potatoes and pears gave similar results, showing sorption of thiabendazole by the outer surface of storage tissues without penetration into the fleshy interior.

The uptake of soil residues was studied in three representative crops: wheat (small grain), turnips (root) and lettuce (leafy vegetable). Three sandy loam plots were sprayed with [<sup>14</sup>C]thiabendazole once, or twice two weeks apart, at a total application rate of 2.15 kg ai/ha representing the worst case that might occur in practice. The crops were harvested at maturity. After 137, 223 and 398 days, the extractable residues in the soil amounted to 75.3, 88.6, and 78.1% of the TRR respectively and thiabendazole accounted for 69.6, 86.9 and 63.2% of the TRR at these times. The residues were present in the upper 0.15 cm of the soil; no significant residues were found at 15-30 cm. The major components of the residues in the crops were thiabendazole (0.08 0.23 mg/kg in mature lettuce, 0.08-0.11 mg/kg in turnip roots, 0.63-1.0 mg/kg in turnip tops, <0.05-0.09 mg/kg in wheat grain, 2.61-10.25 mg/kg in wheat straw) and benzimidazole (0.03 mg/kg in mature lettuce, <0.05 mg/kg in turnip roots, 0.05-0.43 in turnip tops, <0.05 mg/kg in wheat grain, and 0.8-2.5 mg/kg in wheat straw), with the benzimidazole both free and as sugar conjugate(s). Lower levels of 5-hydroxythiabendazole (maximum 25-30% of the thiabendazole) were also observed in immature lettuce and wheat forage. Since 5-hydroxythiabendazole is a degradation product in soil, but not a plant metabolite, it is reasonable to conclude that it was produced in the soil and subsequently taken up by the crops. In addition to thiabendazole, benzimidazole, 5-hydroxythiabendazole and the unextractable residues, other radioactive components were also observed in the HPLC radio-chromatograms of various crop extracts, but all of them individually at levels below 0.05 mg/kg. The results demonstrate that the profile and distribution of thiabendazole residues in three representative crops (leafy vegetables, small grains and root crops) planted in treated soil are the same, but the composition of the residue is different from that in actively growing crops following foliar applications.

The fate of thiabendazole in microbially active sandy loam soil was studied under aerobic conditions at  $25 \pm 1^{\circ}$ C. Thiabendazole was degraded with an aerobic half-life of about 737 days. The products consisted of low levels of benzimidazole (<2.5%) and 5-hydroxythiabendazole (<0.5%). Unextractable radiocarbon increased slowly during the study from 1.24% at day 0 to 20.2% at day 120. This increase is consistent with the strong binding of thiabendazole to soil. Volatile material, 96% of which was <sup>14</sup>CO<sub>2</sub>, also increased slowly, attaining its highest level after 12 months and accounting for 5.8% of the applied radioactivity. These results indicate that thiabendazole is fairly stable in soil but will eventually be mineralized under aerobic conditions to CO<sub>2</sub>. Practically no degradation was observed under anaerobic conditions.

Thiabendazole was found to be photolytically stable on the surface of soil, with a calculated half-life of 933 days. Recoveries of <sup>14</sup>C from irradiated and unirradiated soil samples averaged about 98 and 104% respectively, and 90-100% of the radioactivity was due to thiabendazole; no other residue was found.

The adsorption of thiabendazole to soil was studied with silt loam, clay, sandy loam and sand. The results ( $K_{oc}$  values ranged from 1,104 to 22,467) indicate that thiabendazole is bound very tightly to soil. Similarly, the desorption of thiabendazole from these soils was also low, with  $K_{oc}$  values from about 1,336 to 18,325. Column leaching studies with the parent compound and residues aged on soil surfaces indicated that about 98% of the applied radioactivity remained in the top 2.5 cm of the column. On the basis of the high  $K_{oc}$  values and the column leaching studies, thiabendazole is considered to be immobile in soil.

 $[^{14}C]$ Thiabendazole was shown to be degraded rapidly in water when exposed to artificial sunlight, with a half-life of approximately 29 hours. The degradation resulted in the formation of benzimidazole-2-carboxamide (~10%), a polar fraction (8.6%) and relatively low levels (~6%) of benzimidazole. A minor degradation product, with HPLC retention properties consistent with a carboxybenzimidazole, was also present in trace amounts.

Analytical methods for determining residues from supervised trials have been validated with all the crops reported in this review. Validated methods are also available for analysing animal tissues and milk, as well as soil and water. The recoveries in food commodities were above 70% and the typical limits of detection and determination were 0.01-0.05 mg/kg and 0.05-0.1 mg/kg respectively.

Thiabendazole, free and conjugated 5-hydroxythiabendazole, and benzimidazole were found to be stable during frozen storage in crops for periods of 12 to 28 months, and in animal commodities for at least 2 months.

#### Definition of the residue

The studies carried out with labelled thiabendazole and related studies with the unlabelled material show that the only individual detectable residue ( $\geq 0.05 \text{ mg/kg}$ ) in edible crop commodities is likely to be the parent thiabendazole.

The animal metabolism and transfer studies indicate that thiabendazole and 5-hydroxythiabendazole are the major residue components in meat and eggs, while the sulfate conjugate, which was determined in all reported studies, is the major component in milk. The parent thiabendazole occurred at much lower concentrations in all commodities.

The Meeting concluded that the following definitions of the residue are appropriate.

## For compliance with MRLs

For plant products: thiabendazole. For animal products: sum of thiabendazole and 5-hydroxythiabendazole.

#### For estimations of dietary intake

For plant products: thiabendazole. For animal products: sum of thiabendazole, 5-hydroxythiabendazole and its sulfate conjugate.

Post-harvest trials were conducted in the USA and Spain from 1990 to 1994 on oranges, lemons, grapefruit and tangerines. Ten trials were carried out on oranges in Spain with single post-harvest drench applications at 66 g ai/hl and 110 g ai/hl, and eight in the USA on citrus fruit with initial dip applications at

100 g ai/hl, followed by mist applications in wax with 350 or 500 g ai/hl at rates of 8.4 or 12 g ai/t fruit, much higher than the rates of 0.8 5.5 g ai/t specified on the labels. Residues of thiabendazole on unwashed whole fruit from the US trials in rank order were 1.2, 1.8, 2.9, <u>3.0</u>, <u>3.8</u>, 3.9, 4.8 and 5.4 mg/kg. The Spanish trials were reported in a summarized form which did not contain essential details and could not be used to estimate maximum residue levels.

Since there were no residue data from treatments according to GAP, the Meeting recommended the withdrawal of the existing CXL of 10 mg/kg.

Post-harvest residue trials were conducted in the USA (10) and Spain (5) in 1990-1991 on apples and pears. In the US trials, initial dip applications at 60 g ai/hl were followed by mist applications at 200 g ai/hl in wax (about twice the GAP concentration). The US labels provided do not include application in wax for pome fruits, however, in contrast to citrus fruits for which application in wax is specified. The residues on apples and pears (\*) in the US trials were 0.89, 1.1\* 3.0, 3.2, 3.2, 3.4, 3.4, 3.4, 3.7\* and 5.1\* mg/kg whole fruit. The trials in Spain were at 110 g ai/hl, the maximum GAP concentration, but were reported in a summarized form which did not contain essential details and they could not be used for the estimation of maximum residue levels.

Pre-harvest foliar applications on apples at four times the Japanese GAP rate gave rise to residues in the range 0.08-0.52 mg/kg.

As the trials were not according to national GAP, the Meeting recommended the withdrawal of the existing CXLs for apples and pears.

Pre-harvest residue trials on strawberries in Mexico, where there is no GAP, and Spain in 1989-1992 were with ground foliar applications of SC and WP formulations. In Mexico four applications were made 7 days apart, at rates of 0.50-2.0 kg ai/ha. In Spain a single application was carried out at 1.2 kg ai/ha (approx. 1.3 times GAP). The residues from the Spanish trials were 0.33 and 1.6 mg/kg at 3 days PHI. The data were insufficient to estimate a maximum residue level.

Residues following the post-harvest treatment of bananas were determined in a number of trials in Hawaii, Honduras and Guadeloupe. Residues in 10-20 replicate samples taken from individual treated lots indicated that the treatments were fairly uniform. The highest residues of the parent thiabendazole in each trial with 0.04 kg ai/hl in rank order were 0.79, 0.88, 1.0, 1.2, <u>1.4</u>, <u>1.6</u>, 1.7, 1.8, 2.3 and 3.3 mg/kg. Benzimidazole residues could not be detected in any samples. The dip treatments in Hawaii and Guadeloupe gave higher residues than the spray applications in Honduras. The pulp of ripened bananas from four trials contained average residues in the range 0.011-0.021 mg/kg which amounted to 1.3-2.9% of the residues measured in whole green bananas. The highest residues in individual samples from each trial in rank order were 0.016, <u>0.028</u>, <u>0.029</u> and 0.031 mg/kg.

Since the use patterns (20-40 g ai/100 l) for post-harvest applications are very similar in a number of countries, the Meeting estimated a maximum residue level of 5 mg/kg for banana to replace the current CXL (3 mg/kg) and an STMR level of 0.029 mg/kg for banana pulp.

No information was provided on residues in onions. The Meeting therefore recommended the withdrawal of the CXL for bulb onions.

Four pre-harvest residue trials were conducted on tomatoes grown under plastic in Spain in 1990-1991 with ground spray foliar applications of SC and WP formulations. Two trials in 1990 were with two applications 7 days apart, at 0.50 kg ai/ha, and two trials in 1991 were with single applications at 3.1 kg ai/ha (approximately 3 times the GAP rate). The data were insufficient to estimate a maximum residue level and the Meeting recommended the withdrawal of the CXL for tomatoes.

Single dip or spray applications of SC and SL formulations of thiabendazole were used on chicory roots. Twenty trials were conducted with flowable SC and 20-S formulations at 67-630 g ai/hl. The chicory leaves, hearts and roots were all analysed for thiabendazole residues. Residues in the edible witloof chicory sprouts did not exceed 0.05 mg/kg even when the roots were treated at a sixfold rate.

The Meeting estimated a maximum residue level, at or about the limit of determination, of 0.05 mg/kg, and an STMR level of 0.05 mg/kg for witloof chicory (sprouts).

Post-harvest residue trials were conducted on potatoes. In seven trials in the UK whole potatoes were treated with a single spray mist application of a flowable formulation at 30-80 g ai/tonne. Potatoes in the US trials were subjected to an initial seed treatment at 2400 g ai/hl (approximately twice the GAP concentration) before cutting and planting, followed by an application of thiabendazole at 6.2 g ai/t (1.1 times the GAP rate) immediately after harvest and before storage, and a similar application about 30 days later. The residues of thiabendazole on unwashed potatoes from both sets of trials in rank order were 1.9, 2.0, 2.2, 2.4, <u>2.6, 4.2</u>, 5.4, 5.5, 7.3 and 11 mg/kg.

The Meeting estimated a maximum residue level of 15 mg/kg and an STMR of 3.4 mg/kg for potato (adhering soil may be removed by rinsing or gentle brushing, to conform to the commodity to which Codex MRLs apply).

Pre-harvest residue trials on sugar beet were reported from Spain. One or two ground sprays were applied at 480 g ai/ha after development of 4-8 leaves. The residues of thiabendazole were <0.01 mg/kg in all 16 root samples taken from 0 to 91 days after the last application. The leaves and tops contained residues up to 0.41 mg/kg after 59-65 days. Since no GAP or processing studies were reported, the Meeting could not estimate maximum residue levels for sugar beet, sugar beet leaves or tops, molasses or dry pulp, and consequently recommended the withdrawal of the CXLs.

Mushrooms were treated with four applications of an aqueous solution by irrigation at 54-108 g ai/100 m<sup>2</sup> or by direct spray at 9.5-19 g ai/hl. Applications were made after pinning or after the first harvest break and then after the second, third and fourth breaks according to US label instructions. The maximum residues of thiabendazole on mushrooms collected 12 hours after the last application were 1.9, 2.2, 2.4, 2.5, 3.1, 3.2, 3.9, 3.9, 6.0, 6.1, 7.3, 8.0, 9.6, 12 and 13 mg/kg for irrigation and 21, 27, 30, 31, 36, 41 and 52 mg/kg for spray applications. The residues of benzimidazole were <0.01 mg/kg in all samples.

In four residue trials in Japan a WP formulation was applied once to the bed medium at a rate of 0.120 g ai/kg. The residues of thiabendazole were  $\leq 0.25$  mg/kg.

The Meeting evaluated the residues from direct spray applications according to US GAP and estimated a maximum residue level of 60 mg/kg and an STMR of 31 mg/kg for mushrooms.

In fourteen pre-harvest trials on wheat a single ground or aerial spray was applied at 620 g ai/ha (US GAP) after development of 2 to 3 tillers but before the first node, and the wheat was grown to harvest. The residues of thiabendazole and benzimidazole were <0.05 mg/kg in all 14 grain samples. The thiabendazole residues in the straw in rank order were <0.05 (11), 0.07, 0.11 and 0.13 mg/kg.

The Meeting noted that wheat readily takes up thiabendazole residues from soil (<0.05-0.09 mg/kg in wheat grain and 2.61-10.25 mg/kg in wheat straw grown in soil treated at 2.15 kg/ha). Although the pre-harvest use is limited and the application rates (up to 1 kg/ha except onion and garlic 1.4 kg ai/ha) are relatively low, the Meeting concluded that further field-scale rotational crop studies would be required before the pre-harvest use of the compound could be recommended and accordingly recommended the withdrawal of the CXL for cereal grains.

Animal transfer studies were conducted with poultry and cows. Ten groups of chickens (25 per group,

males and females) were treated continuously for 7 weeks with thiabendazole at levels corresponding to 2, 20, 200 and 2000 ppm in the feed. Four males and 4 females at each treatment level were killed within four hours after the last dose and the liver, kidney, fat and muscle analysed for thiabendazole and 5-hydroxythiabendazole, as were eggs from the three highest treatment levels. The sum of thiabendazole and 5-hydroxythiabendazole, including its conjugate released by acid hydrolysis, was 0.02-0.028 mg/kg in fat (taken from different parts of the birds), 0.017-0.023 mg/kg in a 1:1 mixture of breast and leg meat, and 0.06-0.08 mg/kg in liver at the 20 mg/kg feed level (the expected level based on a poultry diet of 70% corn grain, 20% potatoes and waste and 10% wheat grain). At the same feeding level the average residues were 0.023-0.05 mg/kg in egg yolk and 0.007-0.023 mg/kg in egg white.

The Meeting noted the 3.4 mg/kg STMR for potatoes and the processing factor of 17 for processing potatoes to dry potato peel, and concluded that the 20 mg/kg feeding level appropriately covered the residues likely to occur in poultry feed. The Meeting estimated maximum residue and STMR levels of 0.05 mg/kg for poultry meat and 0.1 mg/kg for eggs.

Dairy cattle were treated once daily by capsule for 28 days with thiabendazole at levels corresponding to 25, 75 and 250 ppm in the feed. Milk samples were collected from all cows on days -1, 1, 2, 4, 7, 14, 21, 28, 29, 35, 42 and 56. Tissues and organs from two of the three cows in each treatment group were collected on day 29, and the remaining cow from each group was slaughtered on day 57. All the samples were analysed for thiabendazole and 5-hydroxythiabendazole. The residues in the milk reached plateaus two days after treatment of 0.014 mg/kg thiabendazole and 0.012 mg/kg 5-hydroxythiabendazole in the 25 ppm group and 0.017 mg/kg thiabendazole and 0.11 mg/kg 5-hydroxythiabendazole in the 250 ppm group, but these levels were less than 0.01 mg/kg higher than the control value at the 25 ppm feeding level, and below the limit of determination of the analytical procedure (0.05 mg/kg). The total residues of thiabendazole plus 5-hydroxythiabendazole in the cows of the 25 ppm group were <0.05 mg/kg in the milk and tissues except a single value of 0.05 mg/kg in kidney. At the 250 ppm level the residues were highest in kidney (0.024-0.03 mg/kg thiabendazole, 0.33-0.55 mg/kg 5-hydroxythiabendazole) and liver (0.056-0.08 thiabendazole, 0.12-0.16 mg/kg 5-hydroxythiabendazole), with much lower residues in the muscle and fat (0.014-0.017 mg/kg thiabendazole, 0.004-0.01 mg/kg 5-hydroxythiabendazole). No difference was observed between the thiabendazole residues in various meat tissues. The residues decreased rapidly to control levels when the animals were returned to a thiabendazole-free diet. The level of 25 ppm is a likely maximum rate, based on a diet of 50% maize grain, 25% apple pomace and 25% potato waste.

On the basis of the likely maximum residues in feed items the Meeting estimated maximum residue levels of 0.05 mg/kg for cattle meat and milk and 0.1 mg/kg for cattle edible offal, and STMRs of 0.05 mg/kg for all three commodities.

The metabolism study in goats at a level corresponding to approximately 20 ppm in the feed indicated much higher total residues of 1.1 mg/kg in milk (0.4 mg/kg 5-hydroxythiabendazole), 4.8 mg/kg in liver, 1.4 mg/kg in kidney and 0.1 mg/kg in meat. The Meeting concluded that further feeding studies would be required to estimate maximum residue levels in the meat, milk and edible offals of other animals, and recommended the withdrawal of the CXLs for milks and the meat and edible offals of goats, horses and sheep.

The effect of cold storage was studied with apples and potatoes after post-harvest treatment. The residues decreased during the first 24 hours but then remained relatively constant for 5 to 6 months.

The effects of processing were studied with post-harvest-treated apples, oranges and potatoes. Apples were treated with a post-harvest dip at 60 g ai/hl followed by a spray mist application in wax at 8.4 g ai/t approximately 30 days after cold storage. Whole fruits were processed into juice, wet pomace and dried pomace. The study could not be used to estimate processing factors, because a wax treatment is not specified on the label and the residues on whole unwashed apples were lower than on washed fruit, which cast doubt on the reliability of the results. Properly planned and executed processing studies representing

typical industrial processes would be required before maximum residue levels could be estimated.

Oranges and grapefruit were treated with a post-harvest dip at 12 g ai/t followed by a spray mist application of thiabendazole in wax at 500 g ai/hl. The whole, washed fruits were processed into various fractions. The processing factors were 0.05 for juice and 8 for dried pomace.

The effect of home-processing on residues of thiabendazole in home-made marmalade was studied in the UK in 1993. The processing factors for home-made marmalade prepared in a preserving pan and in a microwave oven were 0.32 and 0.37 respectively.

Since no maximum residue level or STMR could be estimated for citrus fruits, no STMR-P levels could be estimated.

The effect of washing on the thiabendazole residues in potatoes was studied in several trials. The reduction of residues depended mainly on the time which elapsed between treatment and washing, and probably on the efficiency of washing which was not quantified. The processing (i.e. washing) factors calculated from the experiments in rank order were 0.05, 0.09, 0.11, 0.11, 0.12, 0.14, 0.16, 0.16, 0.17, 0.26 and 0.34 with a median of 0.15 and a mean of 0.13. Peeling removed a further substantial proportion of the residues in washed potatoes. The Meeting noted that residues are transferred from the peel to the peeled potatoes during peeling as potatoes peeled before washing contained average residues of 1.54 mg/kg and after washing 0.08 mg/kg. During industrial processing potatoes are always washed before peeling, and in a kitchen operation either before or after peeling or both. The Meeting therefore concluded that it is more appropriate to estimate the effect of peeling washed potatoes. The average ratio of the residue in pulp to that in washed potatoes was 0.045.

Since washing reduced the residues in raw potatoes by an average factor of 0.13 the Meeting estimated STMR-P levels of 0.44 mg/kg (3.4 x 0.13) for washed potatoes, and 0.02 mg/kg (0.44 x 0.045) for washed and peeled potatoes.

In processing trials in the USA seed potatoes were dipped in an aqueous suspension of thiabendazole containing 2400 g ai/hl before cutting and planting followed by a spray application to the daughter tubers at 6.2 g ai/t immediately after harvest and before cold storage, followed by a second application of 6.2 g ai/t approximately 30 days later. The processing of the potatoes involved washing, abrasive peeling, washing, slicing, washing, frying in vegetable oil at 178-182°C, de-oiling, and salting.

The effect of microwave and oven cooking on the residues of thiabendazole in or on potatoes was studied in the UK in 1990. Potatoes were treated post-harvest with a single application at 40 g ai/t. The tubers were stored for 182 days and the raw peel, raw pulp and unpeeled raw potatoes subjected to microwave and oven cooking.

In four trials on the effects of washing, boiling, baking and crisping in the UK in 1976 potatoes were treated post-harvest with single applications at 40 and 80 g ai/t. The tubers were stored for 4 and 21 days after treatment before processing.

The processing factors found in the US and UK trials were 1.13, 1.16, 1.2 (2) and 1.34, mean 1.2, for baked whole potatoes; 0.044, 0.055 and 0.073, mean 0.06, for potato chips; 0.03 for potato flakes and 17 for dried potato peel.

Since baking and frying do not change the residue content substantially, baked potatoes may be consumed with or without peel, and cooked or fried potatoes may be prepared in widely varying ways, the Meeting recommended the use of STMR-Ps for washed potato (0.44 mg/kg) and washed and peeled potato (0.02 mg/kg) for the assessment of dietary intake.

#### RECOMMENDATIONS

The studies carried out with labelled thiabendazole and other related studies with the unlabelled material show that the only residue detectable individually 0.05 mg/kg in edible crop commodities is likely to be the parent thiabendazole.

The animal metabolism and transfer studies indicate that thiabendazole and 5hydroxythiabendazole are the major residue components in meat and eggs, while the sulfate conjugate, which was determined in all studies reported, is the major residue component in milk. The parent thiabendazole occurred at much lower concentration in all commodities.

The Meeting concluded that the following definitions of the residue are appropriate.

For animal products: sum of thiabendazole and 5-hydroxythiabendazole

<u>For estimations of dietary intake for compliance with MRLs</u> For plant products: thiabendazole For animal products: sum of thiabendazole, 5-hydroxythiabendazole and its sulfate conjugate

The Meeting estimated the following maximum residues and STMR levels. The maximum residue levels are recommended for use as MRLs.

Commodity		Recommended MRL, STMR mg/kg		PHI <sup>1</sup>	
CCN	Name	New	Previous	STMR	
FP 0226	Apple	W	10		
FI 0327	Banana	5 PO	3	0.029 <sup>2</sup>	
GC 0080	Cereal grains	W	0.2		
FC 0001	Citrus fruits	W	10 Po		
ML 0812	Cattle milk	0.05		0.05	
MM 0812	Cattle meat	0.05		0.05	
MO 0812	Cattle, edible offal of	0.1			
MO 0096	Edible offal of cattle, goats, horses, pigs & sheep	w	0.1*		
MM 0096	Meat of cattle, goats, horses, pigs & sheep	w	0.1*		
ML 0106	Milks		0.1*		
VO 0450	Mushroom	60		31	12 hrs
VA 0385	Onion, bulb	W	0.1		
FP 0230	Pear	W	10		
VR 0589	Potato	15	5 Po <sup>3</sup>	3.3	
				0.43 (P) <sup>4</sup>	
				0.02 (P) <sup>5</sup>	
PM 0110	Poultry meat	0.05	0.1	0.05	
PE 0112	Eggs	0.1	0.1	0.1	
FB 0275	Strawberry	W	3		
VR 0596	Sugar beet	W	5		
AV 0596	Sugar beet leaves and tops	W	10		
DM 0596	Sugar beet molasses	W	1		
AB 0596	Sugar beet pulp, dry	w	5		
VO 0448	Tomato	W	2		
VS0469	Witloof chicory (sprouts)	0.05*		0.05	Root treatment

PHI on which the recommendations are based

<sup>1</sup>STMR for banana pulp

<sup>2</sup>Washed before analysis

<sup>3</sup>STMR-P for washed potato <sup>4</sup>STMR-P for washed and peeled potato

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