Short-term intake

The international estimated short-term intake (IESTI) for propiconazole was calculated for the food commodities (and their processing fractions) for which maximum residue levels, STMRs and HRs were estimated and for which consumption data were available. The results are shown in Annex 4.

The IESTI varied from 0–1 % of the ARfD (0.3 mg/kg bw) for the general population. The IESTI varied from 0–3% of the ARfD for children 6 years and below. The Meeting concluded that the short-term intake of residues of propiconazole from uses considered by the Meeting was unlikely to present a public health concern.

5.21 PYRIMETHANIL (226)

TOXICOLOGY

Pyrimethanil is the approved ISO name for *N*-(4,6-dimethylpyrimidin-2-yl)aniline (IUPAC), also known as 4,6-dimethyl-*N*-phenyl-2-pyrimidinamine (CAS; CAS No. 53112-28-0). Pyrimethanil is an anilinopyrimidine fungicide that inhibits the secretion of fungal enzymes. It is a fungicide that is intended for the control of *Botrytis cinerea* on grapes and strawberries.

Pyrimethanil has not been evaluated previously by JMPR and was evaluated by the present Meeting at the request of the 39th Session of the CCPR.[43] All pivotal studies with pyrimethanil were certified as complying with GLP.

Biochemical aspects

In rats given radiolabelled pyrimethanil orally, about 80% of the administered dose was absorbed (for the lower dose, 11.8 mg/kg bw, and for the higher dose, 800 mg/kg bw) on the basis of urinary excretion (cage-wash included) in 96 h. About 72% of the dose was absorbed after pre-treatment with pyrimethanil at a dose of 10 mg/kg bw per day for 14-days, on the basis of urinary excretion (cage-wash included). Pyrimethanil was rapidly excreted at both doses, with more than 95% of the lower dose and 63–67% of the higher dose being excreted within the first 24 h. At the lower dose, plasma concentrations of radioactivity peaked at 1 h after dosing. At the higher dose, plasma concentrations of radioactivity initially peaked at 1 h after dosing. After an initial decline, a second peak of plasma radioactivity was observed at 5 h after dosing. The elimination half-life was about 4.8 h and 11.8 h at the lower and higher dose, respectively. Most of a radiolabelled dose was eliminated in the urine (79–81%) with the remainder in faeces (15–23%) at the lower and higher doses. No bioaccumulation of pyrimethanil was observed. A similar excretion pattern was observed in mice and dogs.

Systemically absorbed pyrimethanil was extensively metabolized. The major metabolites of pyrimethanil in the urine and faeces resulted from aromatic oxidation to form phenols in either or both rings and conjugation with glucuronic acid and sulfate. A minor pathway included oxidation of the methyl group on the pyrimidine ring to produce alcohol. The same six metabolites were identified in the urine and faeces. Unchanged pyrimethanil was isolated only in the faeces of males and females (0.3% and 2.1% of the faecal radioactivity at 10 and 1000 mg/kg bw, respectively). Distribution, metabolite profiles and excretion were essentially independent of pre-treatment with unlabelled compound and of sex.

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[43] Codex Alimentarius Commission. *Report of the 39th Session of the Codex Committee on Pesticide Residues, 7–12 May 2007, Beijing, China* (ALINORM07/30/24).

Toxicological data

Pyrimethanil has low acute toxicity when administered by oral, dermal or inhalation routes. The LD_{50} in rats treated orally was 4149 mg/kg bw in males and 5971 mg/kg bw in females. The LD_{50} in rats treated dermally was > 5000 mg/kg bw. The LC_{50} in rats treated by inhalation (nose only) was > 1.98 mg/L (dust). Pyrimethanil was minimally irritating to the eyes of rabbits and not irritating to the skin of rabbits. Pyrimethanil was not a skin sensitizer as determined by Buehler and Magnusson & Kligman (maximization) tests in guinea-pigs. Clinical signs after oral administration consisted of reduced activity, reduced muscle tone, urogenital soiling, coolness to touch, which generally resolved within 1 day. There were no pathological findings.

In short-term and long-term studies in mice, rats and dogs, the major toxicological findings included decreased body weight and body-weight gains, often accompanied by decreased food consumption. The major target organs in mice and rats were liver and thyroid organs as evidenced by organ-weight changes, histopathological alterations, and clinical chemistry parameters (including increased cholesterol, and gamma-glutamyl transferase levels).

In a 90-day dietary study of toxicity in mice, decreased body-weight gains, slightly increased cholesterol and total bilirubin concentrations, an increase in liver weights and histopathological findings in thyroid, kidney and kidney stones were seen at 10000 ppm, equal to1864 mg/kg bw per day. Increases in thyroid weights were associated with exfoliative necrosis and pigmentation of follicular cells. The NOAEL was 900 ppm, equal to 139 mg/kg bw per day).

In a 90-day dietary study of toxicity in rats, decreased body weights, body-weight gains (28–33%) and decreased food consumptions, brown urine and increased urinary proteins, decreased organ weights (heart, adrenal, spleen, thymus), increased liver, kidney, gonad weights, and hypertrophy in liver and thyroid were seen at 8000 ppm, equal to 529.1 mg/kg bw per day, in both sexes. Thyroid effects in rats were manifested as increased incidence and severity of follicular epithelial hypertrophy and follicular brown pigment. The NOAEL was 800 ppm, equal to 54.5 mg/kg bw per day.

Gavage administration of pyrimethanil at > 600 mg/kg bw per day, the highest dose tested, induced vomiting in dogs within 4 h after dosing, suggesting local gastrointestinal tract irritation. This was not considered to be a toxicologically relevant effect for establishing an ARfD. In a 90-day study of toxicity in dogs, diarrhoea, salivation hypoactivity (within 3 h after dosing) and slightly decreased water consumption was observed at 800 mg/kg bw per day. The NOAEL was 80 mg/kg bw per day. In a 52-week study of toxicity in dogs, decreases in body-weight gains (6% and 17% in males and females, respectively), food consumption and feed-conversion efficiency, water consumption, reduced clotting time and increased count of neutrophils were observed at 250 mg/kg bw per day. The NOAEL was 30 mg/kg bw per day. The overall NOAEL was 80 mg/kg bw per day when results of 90-day and 1-year studies of toxicity in dogs were combined.

Pyrimethanil was not mutagenic in an adequate battery of studies of genotoxicity in vitro and in vivo.

The Meeting concluded that pyrimethanil is unlikely to be genotoxic.

The carcinogenicity potential of pyrimethanil was studied in mice and rats. In a study of carcinogenicity in mice, an increased incidence of urinary tract lesions including bladder distension and thickening were observed in male mice during the first weeks at 1600 ppm, equal to 210.9 mg/kg bw per day. The NOAEL was 160 ppm, equal to 20.0 mg/kg bw per day. There were no treatment-related neoplastic findings in the bioassay in mice.

In the study of carcinogenicity in rats, decreased body-weight gains, increased serum cholesterol and GGT levels, necropsy (dark thyroids), and histopathological findings (increases in centrilobular hepatocyte hypertrophy, and increased incidence of colloid depletion and hypertrophy of the follicular epithelium in thyroids) were observed at 5000 ppm, equal to 221 mg/kg bw per day). The NOAEL was 400 ppm, equal to 17 mg/kg bw per day. In rats given pyrimethanil, the thyroid was the only tissue to show a higher incidence of tumours than the controls. The number of benign follicular

cell adenomas in both sexes at the highest dose was higher than in concurrent controls and historical controls.

Special studies were conducted to evaluate the toxicity seen in the liver and thyroid. Mechanistic data suggest that thyroid hormone imbalance caused by increased thyroid hormone clearance by the induction of liver enzymes resulted in increased thyroid-stimulating hormone (TSH) activity and persistent stimulation of the thyroid. Such effects may lead to changes in thyroid homeostasis and alterations in morphology. Rodent thyroid tumours induced by this mode of action are not relevant to humans because rats are much more sensitive to thyroid hormone imbalance and elevations in TSH levels. Thus, the results of bioassays in rats do not raise a cancer concern for humans.

In view of the lack of genotoxicity and the absence of relevant carcinogenicity in rats and mice, the Meeting concluded that pyrimethanil is unlikely to pose a carcinogenic risk to humans.

In a two-generation study of reproduction in rats, reproductive parameters were not affected at the highest dose tested (5000 ppm, equal to 293.4 mg/kg bw per day). The NOAEL for parental systemic toxicity was 400 ppm (equal to 23.1 mg/kg bw per day) on the basis of decreases in body-weight (11–13%) and body-weight gains (11–17%). Offspring toxicity was manifested as a decrease in pup body weights (17%) on postnatal day 21 at 5000 ppm, equal to 293.3 mg/kg bw per day. The NOAEL for offspring toxicity was 400 ppm, equal to 23.1 mg/kg bw per day. Pyrimethanil was not embryotoxic, fetotoxic or teratogenic at doses of up to 1000 mg/kg bw per day in rats. Pyrimethanil was not teratogenic in rabbits. Decreases in foetal body weights were observed at 300 mg/kg bw per day. These decreases in foetal weights (described as “runts” in the study report) were observed in the presence of severe maternal toxicity manifested as a significant decrease in body-weight gain and food consumption, reduced production and size of faecal pellets and death of three rabbits (moribund condition) at 300 mg/kg bw per day. The NOAEL for maternal toxicity in rabbits was 45 mg/kg bw per day and the NOAEL for developmental toxicity was 300 mg/kg bw per day, the highest dose tested.

The Meeting concluded that pyrimethanil is not teratogenic.

In a study of acute neurotoxicity in rats, transient functional observational battery (FOB) effects (gait, ataxia, decreased hind limb-grip strength in males, decreased body temperature) were observed at 1000 mg/kg bw on day 1. Total motor activity was also decreased by $\geq 52\%$ at 1000 mg/kg on day 1 in both sexes compared with controls. All animals appeared normal on days 8 and 15. As these transient and non-specific effects occurred at a high dose administered by gavage, the Meeting concluded that they were not an appropriate basis for establishing an ARfD. The NOAEL was 100 mg/kg bw. In a short-term study of neurotoxicity in rats, no treatment-related changes in mortality, clinical signs, FOB, motor activity, brain measurements (weight, length, and width), gross necropsy, or neurohistopathology were observed at doses of up to 6000 ppm, equal to 391.9 mg/kg bw per day. In females, an overall decrease in body-weight gain of 21% was observed at 6000 ppm, equal to 429.9 mg/kg bw per day. The NOAEL in females was 600 ppm, equal to 38.7 mg/kg bw per day, and 6000 ppm, equal to 319.9 mg/kg bw per day, in males.

The Meeting considered that pyrimethanil is not neurotoxic on the basis of the available data.

No significant adverse effects were reported in personnel working in production plants.

The Meeting concluded that the existing database on pyrimethanil was adequate to characterize the potential hazards to foetuses, infants and children.

Toxicological evaluation

The Meeting established an ADI of 0–0.2 mg/kg bw based on a NOAEL of 400 ppm (equal to 17.0 mg/kg bw per day) on the basis of increased cholesterol and GGT levels, and histopathological changes in the liver and thyroid at 5000 ppm (equal to 221 mg/kg bw per day) in a 2-year study in rats, and using a safety factor of 100. This ADI is supported a by two-generation study of reproduction in rats in which the NOAEL for parental systemic toxicity was 400 ppm, equal to 23.1 mg/kg bw per

day, on the basis of decreased body weights and body-weight gains at 5000 ppm, equal to 293.3 mg/kg bw per day. This ADI is also supported by the NOAEL of 160 ppm, equal to 20.0 mg/kg bw per day, in males in a 2-year study of toxicity in mice; this NOAEL was identified on the basis of increased incidences of urinary tract lesions including bladder distension and thickening seen at 1600 ppm, equal to 210.9 mg/kg bw per day.

The Meeting concluded that it was not necessary to establish an ARfD for pyrimethanil because no toxicity could be attributable to a single exposure in the available database, including a study of developmental toxicity in rats and rabbits. Observations in the study of acute toxicity in rats and clinical signs of toxicity in the pyrimethanil database appeared at doses of 640 mg/kg bw per day and greater were not considered to be relevant for establishing an ARfD since they were transient, non-specific and occurred at high doses. The Meeting also considered clinical signs (vomiting) in several studies of toxicity in dogs; these were considered to be local effects and therefore not relevant in establishing an ARfD.

A toxicological monograph was prepared.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Mouse	Eighty-week study of toxicity and carcinogenicity[a]	Toxicity	160 ppm, equal to 20.0 mg/kg bw per day	1600 ppm, equal to 210.9 mg/kg bw per day
		Carcinogenicity	1600 ppm, equal to 210.9 mg/kg bw per day[c]	—
Rat	Two-year study of toxicity and carcinogenicity[a]	Toxicity	400 ppm, equal to 17 mg/kg bw per day	5000 ppm, equal to 221 mg/kg bw per day
		Carcinogenicity	5000 ppm, equal to 221 mg/kg bw per day[c]	—
	Multigeneration study of reproductive toxicity[a]	Parental toxicity	400 ppm, equal to 23.1 mg/kg bw per day	5000 ppm, equal to 293.3 mg/kg bw per day
		Offspring toxicity	400 ppm equal to 23.1 mg/kg bw per day	5000 ppm, equal to 293.3 mg/kg bw per day
	Developmental toxicity[b]	Maternal toxicity	85 mg/kg bw per day	1000 mg/kg bw per day
		Embryo/fetotoxicity	1000 mg/kg bw per day[c]	____
Rabbit	Developmental toxicity[b]	Maternal toxicity	45 mg/kg bw per day	300 mg/kg bw per day
		Embryo/fetotoxicity	45 mg/kg bw per day	300 mg/kg bw per day
Dog	Ninety-day and 1-year study of toxicity[b]	Toxicity	80 mg/kg bw per day	400/250 mg/kg bw per day

[a] Dietary administration.
[b] Gavage administration.
[c] Highest dose tested.

Estimate of acceptable daily intake for humans

0–0.2 mg/kg bw per day

Estimate of acute reference dose

Unnecessary

Information that would be useful for continued evaluation of the compound

Results from epidemiological, occupational health and other such observational studies of human exposure

Critical end-points for setting guidance values for exposure to pyrimethanil

Absorption, distribution, excretion, and metabolism in mammals	
Rate and extent of oral absorption	Rapid and nearly complete absorption; maximum plasma concentration reached by 1 h
Distribution	Widely distributed in tissues
Potential for accumulation	Low, no evidence of accumulation
Rate and extent of excretion	Approximately 97% (77% in urine and 20% in faeces) within 24 h at 11.8 mg/kg bw per day
Metabolism in animals	Extensive; metabolic pathways include aromatic oxidation to form phenols and conjugation with glucuronic acid and sulfate, minor pathway included oxidation of methyl group to produce alcohol
Toxicologically significant compounds in animals, plants and the environment	Pyrimethanil
Acute toxicity	
Rat, LD_{50}, oral	4149 mg/kg bw for males
Rat, LD_{50}, dermal	> 5000 mg/kg bw
Rat, LC_{50}, inhalation	> 1.98 mg/L dust (4-h exposure, nose only)
Rabbit, skin irritation	Not an irritant
Rabbit, eye irritation	Minimal irritation
Guinea-pig, skin sensitization	Not a sensitizer (Magnussen & Kligman and Buehler test)
Short-term studies of toxicity	
Target/critical effect	Liver and thyroid hypertrophy
Lowest relevant oral NOAEL	54.5 mg/kg bw per day (90-day-rat)
Lowest relevant dermal NOAEL	No data
Lowest relevant inhalation NOAEC	No data
Genotoxicity	
	No genotoxic potential
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	Liver and thyroid
Lowest relevant NOAEL	17 mg/kg bw per day (2-year study of carcinogenicity in rats)
Carcinogenicity	No relevant carcinogenicity in mice and rats
Reproductive toxicity	
Reproduction target/critical effect	No toxicologically relevant effects
Lowest relevant reproductive NOAEL	239.9 mg/kg bw per day (rats; highest dose tested)

Developmental target/critical effect	No developmental toxicity in rats and rabbits
Lowest relevant developmental NOAEL	300 mg/kg bw per day (highest dose tested; rabbits)
Neurotoxicity/delayed neurotoxicity	
Acute neurotoxicity	No sign of specific neurotoxicity
Mechanistic data	
	Studies on hepatic clearance and thyroid hormone perturbations
Medical data	
	No significant adverse health effects reported

Summary

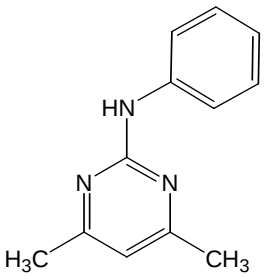
	Value	Study	Safety factor
ADI	0–0.2 mg/kg bw per day	Rats, 2-year study of toxicity	100
ARfD	Unnecessary	—	—

RESIDUE AND ANALYTICAL ASPECTS

Pyrimethanil is an anilinopyrimidine fungicide that inhibits the secretion of hydrolytic enzymes by the fungi that are needed during the infection process. Pyrimethanil blocks the ability of fungi to degrade and digest the plant tissues, thus stopping penetration and development of the disease.

At the 37th session of the CCPR (ALINORM 04/27/24), pyrimethanil was listed as a candidate for evaluation of a new compound by the 2007 JMPR.

Chemical name: N-(4,6-dimethylpyrimidin-2-yl) aniline



Animal metabolism

The Meeting received results of an animal metabolism study in lactating dairy cows. A lactating dairy cow was orally dosed for seven consecutive days with [^{14}C]pyrimethanil at a daily dose rate of 10 ppm in the diet, which corresponds to 0.4 mg/kg bw per day for a 600 kg cow. Residues in muscle and fat were too low to isolate and identify (0.02–0.04mg/kg total radioactive residue, TRR). The TRR in milk reached a plateau on about day 5 (0.07 mg/kg). No pyrimethanil was found in the milk from any day of the treatment. The major metabolite present in milk (64% TRR) was identified 2-anilino-4,6-dimethylpyrimidin-5-ol. Also present in milk were metabolites (27% TRR) characterized as highly polar.

Parent pyrimethanil was not found in kidney or liver. The TRR in kidney was identified as 46% 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine, 5% 2-anilino-4,6-dimethylpyrimidin-5-ol, and 7% 2-(4-hydroxyanilino)-4-hydroxymethyl-6-methylpyrimidine. Again, 42% TRR was characterized as

highly polar. No metabolite was identified in liver, but the TRR was characterized as 48% protein, 9% lipid, 7% ribonucleic acid and 6% sulfurated glycoamino-glycans.

Metabolism in the rat was quite similar to that of the cow. In the rat, only small amounts of the administered pyrimethanil were found in faeces and none was found in urine. The major metabolite in urine and faeces was 2-(4-hydroxyanalino)-4,6-dimethylpyrimidine and its sulfate, 13–52%. Other metabolites, generally < 10% of total extracted radioactivity in the excreta, were 2-anilino-4,6-dimethylpyrimidin-5-ol, 2-(4-hydroxyanilino)-4-hydroxymethyl-6-methylpyrimidine, 2-(4-hydroxyanilino)-6-dimethyl-pyrimidin-5-ol and 2-anilino-6-methylpyrimidine-4-methanol.

The Meeting concluded that pyrimethanil is very extensively metabolised in cattle, forming monohydroxy and dihydroxy derivatives in milk and kidney, and being incorporated into biological substrates in liver. No accumulation occurs in muscle or fat.

Plant metabolism

The Meeting received plant metabolism studies for the foliar application of [^{14}C]pyrimethanil, radiolabelled either on the aniline ring or at C-2 of the pyrimidine ring, for apples, grapes, carrots, tomato, leaf lettuce and strawberry. Generally the majority of the radioactivity was removed in a dichloromethane surface wash (56% grapes, 90% tomato). In all instances, the major component of the TRR was pyrimethanil (apple fruit, 70–77%; carrot root, 70–89%; tomato fruit, 95–96%; leaf lettuce 44%; strawberry fruits, no identifications made). Minor metabolites identified included hyrdoxylated and conjugated derivatives of pyrimethanil 2% TRR, and the ß-O-glucoside of 2-anilino-4-hydroxymethyl-6-hydroxymethylpyrimidine 3% TRR in apples; malonyl-β-O-glucoside of 2-anilino-hydroxymethyl-6-methylpyrimidine 6% TRR, and the β-glucoside of 2-anilino-4-hydroxymethyl-6-methylpyrimidine 6% TRR on carrot foliage (< 1% TRR each on carrot root); hydroxylated and conjugated compounds of pyrimethanil 6–28% TRR on tomato leaves; conjugate of 2-(4-hydroxyanilino)-4,6-dimethylpyridine 5% TRR and conjugate of 2-anilino-4,6-dimethylpyrimidin-5-ol, 8% TRR on leaf lettuce. Where both radiolabels were tested on the same crop, no significant differences were found in the compositions of the TRRs.

The Meeting concluded that the metabolism of pyrimethanil had been adequately defined via studies on three distinct crop types: fruit, root and leafy. Very little metabolism occurs, and the major portion of the residue is the parent pyrimethanil. The similarity in metabolic profiles between studies conducted with the radiolabel in either the aniline ring or the pyrimidine ring indicates no cleavage at the ring junction (aniline amino group). Minor metabolites identified are hydroxylated and conjugated derivatives of pyrimethanil, and are generally less than 10% TRR.

Environmental fate

The Meeting received studies on aqueous hydrolysis, aerobic and anaerobic degradation in soil, photolysis in water and residues in succeeding crops. Pyrimethanil is stable to hydrolysis in water at pH 5, 7 and 9 at 20 °C.

Under aerobic conditions, pyrimethanil slowly degraded in soil with about 80% remaining after 130 days. This was followed by a rapid decline in both extractable radioactivity and pyrimethanil levels. At higher soil treatment rates (500 mg/kg) differences were seen in the apparent degradation of the pyrimidine and aniline labels. With the pyrimidinyl label, about 60% of the extractable radioactivity was identified as 2-amino-4,6-dimethylpyrimidine. Cleavage of the aniline linkage is indicated.

Pyrimethanil does undergo photolytic degradation in water (sterile buffer) at pH 4 and pH 7 with estimated half-lives of 1 and 80 days, respectively. In a separate experiment using in sterile water containing humic acids, the half-life was reduced to less than 2 days at pH 7.

The Meeting concluded that pyrimethanil is stable under aqueous hydrolysis at pH 2–9 and is relatively stable on soil under aerobic conditions. It was also concluded that pyrimethanil is not stable in water under photolysis.

The uptake of 2-[^{14}C]pyrimidinyl-labelled pyrimethanil in *rotational crops* under confined conditions was reported to the Meeting. The pyrimethanil was applied to soil at a rate of 2.4 kg ai/ha. Substantial residues were found in crops planted 30 days after the treatment, 0.23 to 8.2 mg/kg TRR as pyrimethanil. Pyrimethanil comprised 1% (radish top) to 45% (wheat forage) of the TRR. The major identified metabolite (> 10% TRR) was 2-anilino-4-hydroxymethyl-6-methylprimidine in wheat forage and lettuce. Pyrimethanil was < 0.05 mg/kg in all rotational crops at the 30 day plantback interval, *except* for wheat grain (73 day, 0.41 mg/kg TRR, < 0.001 mg/kg pyrimethanil), forage (35 day immature, 1 mg/kg TRR, 1.1 mg/kg pyrimethanil), and straw (73 day, 8.2 mg/kg TRR, 0.22 mg/kg pyrimethanil). At a 130 day plantback interval, total residues in the crops declined to 0.01 to 0.03 mg/kg, with parent comprising 1–26% of the TRR. No extractable metabolite exceeded 10% TRR.

Three field rotational crop studies with a single crop, wheat, were conducted. Using a 30 day plantback interval following harvest of treated potatoes (3 applications at 0.8 kg ai/ha), residues of pyrimethanil and 2-anilino-4-hydroxymethyl-6-methylprimidine were below the limits of detection (< 0.012 mg/kg for pyrimethanil and < 0.015 mg/kg for 2-anilino-4-hydroxymethyl-6-methylprimidine), except for one wheat forage sample (< 0.05 mg/kg LOQ). The intervals from plantback to harvest were 128–232 days for forage and 190–316 days for straw.

The Meeting concluded that residues of pyrimethanil, in rotational crops planted 30 days or more after the final application of pyrimethanil to the primary crop, will most likely be below the LOQ (< 0.05 mg/kg), with the possible exception of forages and straws.

Methods of Analysis

The Meeting received information for analytical methods on the quantitative determination of pyrimethanil in a variety of crops and for the determination of pyrimethanil and metabolites 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine and 2-anilino-4,6-dimethylpyrimidine in bovine commodities.

The plant commodity methods consist of organic solvent extraction (acetone or methanol), clean-up, and analysis by either gas chromatography, with a mass spectrometer detector (GC/MS, m/z 198), or by high performance liquid chromatography with an ultraviolet detector (HPLC). The HPLC method was validated for apples, tomatoes, grapes, green beans, wine, grape juice, and grape pomace. The validated limits of quantitation (LOQs) are 0.05, 0.05, 0.02, 0.05, 0.02 and 0.02 mg/kg, respectively. The GC/MS method was validated for potatoes, carrots, tomatoes, green beans, lettuce, sweet peppers, strawberries, raspberries, apples, peaches, plums and oranges. A LOQ of 0.05 mg/kg was demonstrated for all of these commodities.

A radiovalidation study was conducted for the GC/MS procedure. Lettuce from the metabolism study was subjected to the extraction and analysis procedures of the method. Extraction efficiency was 97%.

A GC/MS method was described for the determination of pyrimethanil and metabolites 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine and 2-anilino-4,6-dimethylpyrimidin-5-ol in milk, fat, muscle, liver and kidney. The metabolites are converted to methylated derivatives prior to analysis. The demonstrated LOQs are 0.01 mg/kg for each of the analytes in milk and 0.05 mg/kg in each of the analytes in the various tissues. The independent laboratory validation encountered considerable problems and did not achieve acceptable validation for precision for pyrimethanil in meat at 0.05 mg/kg and overall at levels of 0.05 and 0.5 mg/kg. No radiovalidation of the method was reported.

Multiresidue methods (US FDA and DFG S 19) were reported for pyrimethanil in various plant commodities.

The Meeting concluded that adequate analytical methods exist for both data collection and enforcement purposes for pyrimethanil residues in plant commodities and for pyrimethanil, 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine (SN 614276), and 2-anilino-4,6-dimethylpyrimidin-5-ol (SN 614277) in milk and bovine tissues.

Stability of pesticide residues in stored analytical samples

The Meeting received information on the stability of pyrimethanil in a variety of crop matrices, but no information on stability in livestock commodities. Pyrimethanil is stable (< 30% loss) in apples, grapes, tomatoes, lettuce, carrots, peas (dried), peaches and plums for at least 365 days when the commodities are stored frozen at about -20 °C.

The Meeting concluded that pyrimethanil is stable on frozen plant commodities for at least one year. No conclusions are possible on the stability of pyrimethanil or its metabolites in livestock commodities.

Residue definition

The major component of the residue on numerous plant commodities, from the foliar application of pyrimethanil, is pyrimethanil. Minor amounts of hydroxylated pyrimethanil derivatives are found, generally < 10% each of the total residue. The two analytical methods determine only pyrimethanil.

In livestock (cow) commodities, pyrimethanil is not found following oral administration of the compound. The major metabolites are 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine and 2-anilino-4,6-dimethylpyrimidin-5-ol, in kidney and milk, respectively. The analytical method provided determines the parent and the two named metabolites.

The log of the octanol/water partition coefficient is 2.8. In the cow feeding study, no pyrimethanil (< 0.05 mg/kg) was found in either fat or muscle at a 50 ppm feeding level. In the same study, the milk fat contained 0.031 mg/kg of 2-anilino-4,6-dimethylpyrimidin-5-ol, and the skim milk contained 0.064 mg/kg of 2-anilino-4,6-dimethylpyrimidin-5-ol and 0.015 mg/kg 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine. Thus, the total residue concentrated slightly in the non-fat portion of milk.

The Meeting concluded that the residue definition for both enforcement and dietary exposure considerations for plant commodities is pyrimethanil. The Meeting further concluded that the residue definition for both enforcement and dietary exposure considerations for milk is the sum of pyrimethanil and 2-anilino-4,6-dimethylpyrimidin-5-ol, expressed as pyrimethanil and for livestock tissues (excluding poultry) is the sum of pyrimethanil and 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine, expressed as pyrimethanil.

The Meeting also decided that pyrimethanil is not fat-soluble.

Results of supervised trials on crops

The Meeting received supervised trials data for the foliar application of pyrimethanil as a suspension concentrate formulation (SC) to a variety of fruit, vegetable, and nut crops. Additionally, supervised trial data reports were received for the post-harvest treatment of citrus, pome fruit and cherries.

Citrus

Various post-harvest treatments of lemon, orange, tangelo, tangerine, and grapefruit were reported for 45 trials from the USA. The USA GAP is: 204 g/L pyrimethanil + 263 g/L imazalil SC, dip or wash at 0.08 kg ai/hL or drench at 0.08 kg ai/hL or aqueous line spray at 0.1 kg ai/hL or wax line spray/storage and pack wax at 0.2 kg ai/hL, with a maximum of two treatments (of all types); 400 g/L pyrimethanil SC, dip or wash at 0.1 kg ai/hL or drench at 0.05 kg ai/hL or aqueous line spray at 0.2 kg ai/hL or wax line spray/storage and pack wax at 0.2 kg ai/hL, with a maximum of 2 or 3 treatments. Additionally, eight trials for the post-harvest treatment of oranges and mandarins in Spain were reported. No GAP was supplied, and the GAP of the USA was utilized. Thirty-three USA trials (9 × lemon, 10 × orange, 5 × grapefruit, 4 × tangelo and 4 × tangerines) were at maximum GAP. No Spanish trials matched the USA GAP.

Residues in the 32 trials in ranked order (median underlined) were: 1.2 (3), 1.4, 1.5 (2), 1.7 (2), 1.9, 2.1, 2.2, 2.3, 2.6, 2.7 (3), 2.8 (3), 2.9, 3.1, 3.3, 3.4 (2), 3.6, 4.1 (2), 4.2, 4.3, 4.6, 5.5,

5.8 mg/kg. No data were provided on the analysis of the edible portion (pulp). The Meeting estimated a maximum residue level of 7 mg/kg (Po) and an STMR of 2.8 mg/kg.

Pome fruit

Pre-harvest apple trials were reported from Europe and the USA. Pear trials were reported from the USA.

Two apple trials were conducted in Germany, two in northern France, and one in the UK. None of the trials matched the GAP of Belgium, 400 g/L SC, 0.45 kg ai/ha, 0.22 kg ai/hL, 5 applications, 28 day PHI. Two apple trials were conducted in southern France, two in Italy and one in Spain. One trial matched the GAP of Italy, 400 g/L SC, 0.04 kg ai/hL, 5 applications, 14 day PHI. The residue (Italy) was 0.56 mg/kg.

Twelve apple trials were conducted in the USA at the GAP, 400 g/L SC, 0.45 kg ai/ha, 1.8 kg ai/ha per season, 72 day PHI. The residues in ranked order are: < 0.05 (7), 0.06, 0.10, 0.12, 0.15, 0.16 mg/kg.

Six pear trials were conducted in the USA under the same USA GAP as apples. The residues found were: < 0.05 (6) mg/kg.

Post-harvest treatment of apples was reported from Spain and France and the USA. The GAP of Belgium is 200 g/L pyrimethanil + 200 g/L imazalil SC, spray or dip at 0.04 kg ai/hL, one treatment. Two of nine European trials were at the maximum GAP, and residues are 0.57 and 1.7 mg/kg. An additional trial matched the GAP of Chile, 3.78 mg/kg.

The GAP of the USA is dipping, drenching or aqueous line spray at 0.1 kg ai/hL or wax line spray at 0.2 kg ai/hL. Up to 2 treatments (of any combination) may be used. The GAP of Chile is identical, but only one treatment is permitted. Using the GAP of the USA, no trials are at GAP. Using the GAP of Chile, 10 of 32 trials were at maximum GAP. The residues in ranked order on apples were: 0.27, 0.28, 0.33, 0.39, 0.64, 0.70, 1.1 (2), 1.2, 1.5 mg/kg. Studies on the post-harvest treatment of pears in the USA were also reported. The GAPs of Chile and the USA are the same as for apples. Using the GAP of the USA, the residues of two trials are at GAP 1.01 and 1.18 mg/kg. Using the GAP of Chile, an additional eight of 35 trials were at the maximum GAP. Residues of pyrimethanil in ranked order were: 0.13, 0.18, 0.32, 0.45, 0.56, 0.86, 1.1 (2) mg/kg. Six post-harvest treatment trials on pears were reported from France, Spain and Belgium. No trials matched the GAPs of Chile or the USA. Two trials (BE, FR) matched the GAP of Belgium (200 g/L pyrimethanil + 200 g/L imazalil SC, spray or dip at 0.04 kg ai/hL, one treatment), and the residue values are 0.32 and 0.55 mg/kg.

Studies on the thermofogging post-harvest treatment of apples and pears in Europe was reported. However, the only GAP supplied (Chile) has yet to be approved by the national government. The Meeting noted that the maximum residue under the proposed GAP was 3.5 mg/kg on pears in Italy.

The residue values for post-harvest treatment of apples and pears in the USA and Europe at the GAPs of Chile or the USA are from the same population and may be combined. Residues in the 21 trials in ranked order (median underlined) were: 0.13, 0.18, 0.27, 0.28, 0.32, 0.33, 0.39, 0.45, 0.56, 0.64, 0.70, 0.86, 1.0, 1.1 (4), 1.2 (2), 1.5, 3.8 mg/kg. Based on the post-harvest treatments, the Meeting estimated an STMR of 0.70 mg/kg and a maximum residue level of 7 mg/kg for pome fruit (Po).

Stone fruit

Apricot, peach and plum trials were reported from the USA. The GAP is identical for all: 600 g/L SC, 0.8 kg ai/ha, 2.4 kg ai/ha/season, 2 day PHI. Five apricot trials were at maximum GAP: 0.61, 0.64, 1.2, 1.3, 1.7 mg/kg. Twelve peach trials were at maximum GAP: 0.38, 0.54, 0.94, 1.1, 1.2, 1.3 (3), 1.5, 1.6, 2.6 mg/kg. Eight plum trials were at maximum GAP: 0.05, 0.44, 0.58, 0.59 (2), 0.61, 0.62, 1.2 mg/kg.

The Meeting considered the apricot, peach and plum trials not to be from the same population. The Meeting estimated an STMR of 1.2 mg/kg and a maximum residue level of 3 mg/kg for apricots.

The meeting estimated an STMR of 1.3 mg/kg and a maximum residue level of 4 mg/kg for peaches and for nectarines. The Meeting estimated an STMR of 0.59 mg/kg and a maximum residue level of 2 mg/kg for plums.

Reports on the post-harvest treatment of peaches and plums in the USA were reported, but no GAP was provided.

Reports on the post-harvest treatment of cherries in Germany were reported. A GAP was supplied for Chile (400 g/L SC, dipping, 0.04 kg ai/hL, 1 application. Eight trials were at maximum GAP, and the values in ranked order were: 0.82, 1.0, 1.1, 1.2, 1.4(3), 2.5 mg/kg. The Meeting estimated an STMR of 1.3 mg/kg and a maximum residue level of 4 mg/kg (Po) for cherries.

Berries and other small fruits

Supervised trials for the foliar application of pyrimethanil to grapes were reported from the EU and the USA. Five trials in northern Europe (two from Germany and three from France) were evaluated against the GAP of France (400 g/L SC, 1 kg ai/ha, 1 application, 21 days PHI: 0.37, 0.44, 0.59, 0.97, 1.1 mg/kg); and 10 trials in southern Europe (2 Spain, 6 France, 2 Italy: 0.28, 0.48, 1.0, 1.5 mg/kg) were evaluated against the GAP of Spain (400 g/L SC, 0.08 kg ai/hL, one application, 21 day PHI). Nine trials were at maximum GAP, and the residues in ranked order were: 0.28, 0.37, 0.44, 0.48, 0.59, 0.92, 1.0, 1.1, 1.5 mg/kg.

Twelve trials were reported from the USA (USA GAP: 600 g/L SC, 0.8 ka ai/ha, 1.6 kg ai/ha/season, 7 day PHI). All trials were at maximum GAP, and the residues found were: 0.12, 0.44, 0.49, 0.64, 0.66, 0.71, 0.89, 1.2, 1.5, 1.6, 2.0, 2.5 mg/kg.

The Meeting considered the EU and USA trials to be from the same population and combined the results. Residues in the 21 trials in ranked order (median underlined) were: 0.12, 0.28, 0.37, 0.44(2), 0.48, 0.49, 0.59, 0.64, 0.66, 0.71, 0.89, 0.92, 1.0, 1.1, 1.2, 1.5 (2), 1.6, 2.0, 2.5 mg/kg. The Meeting estimated an STMR of 0.71 mg/kg and a maximum residue level of 4 mg/kg for grapes.

Eight trial were conducted on the foliar application of pyrimethanil to strawberries in the USA, where the GAP is 600 g/L SC, 0.8 kg ai/ha, 2.4 kg ai/ha/season, 1 day PHI. All trials were at maximum GAP, and the residues in ranked order (median underlined) were: 0.79, 0.93, 0.99, 1.1, 1.2, 1.3(2), and 2.3 mg/kg. The Meeting estimated an STMR of 1.2 mg/kg and a maximum residue level of 3 mg/kg for strawberries.

Bananas

Eleven trials each on the foliar treatment of bagged and unbagged bananas with pyrimethanil were reported from Costa Rica (3), Ecuador (3), Colombia (3) and Guatemala (2). The GAP is identical in all these countries: 600 g/L SC, 0.3 kg ai/ha, 6 applications, 0 day PHI (constant harvesting). All residues were below the LOQ except one bagged banana sample in Ecuador. The residues in ranked order were: < 0.05 (21), 0.09 mg/kg. All pulp samples were < 0.05 mg/kg. The Meeting estimated an STMR of 0.05 mg/kg and a maximum residue level of 0.1 mg/kg for bananas.

Bulb Vegetables

Nine trials were conducted on the foliar application of pyrimethanil to dry bulb onions and spring onions in the USA, where the GAP is: 600 g/L SC, 0.8 kg ai/ha, 2.4 kg ai/ha/season, 7 days PHI. All trials were conducted at maximum GAP, and the residues in ranked order on bulb onions were: < 0.05 (3), 0.075, 0.087, 0.095 mg/kg. Residues on green onions in ranked order are: 0.26, 0.38, 1.6 mg/kg. The Meeting estimated an STMR of 0.062 mg/kg and a maximum residue level of 0.2 mg/kg for bulb onions (dry). The Meeting estimated an STMR of 0.38 mg/kg and a maximum residue level of 3 mg/kg for spring onions.

Fruiting Vegetables, Other than Cucurbits

Sixteen trials were conducted on the foliar application of pyrimethanil to tomatoes in the USA, where the GAP is: 600 g/L SC, 0.3 kg ai/ha, 1.6kg ai/ha/season, 1 day PHI. All trials were at maximum

GAP, and the residues in ranked order were: 0.06, 0.07 (3), 0.10, 0.13, 0.14 (2), 0.15, 0.16, 0.17, 0.20, 0.22, 0.23, 0.35, 0.37 mg/kg.

Eight glasshouse trials were conducted in Europe, 2 in France and 6 in the Netherlands. The GAP of France is 400 g/L SC, 0.8 kg ai/ha, 2 applications, 3 day PHI. All trials were at maximum GAP, and the residues in ranked order (median underlined) were: 0.26 (2), 0.31 (2), 0.33 (2), 0.36 (2) mg/kg.

The USA and EU trials were not considered to be from the same population, and the Meeting used the EU trials to estimate an STMR of 0.32 mg/kg and a maximum residue level of 0.7 mg/kg for tomatoes.

Leafy Vegetables

Trials were conducted on both head lettuce and leaf lettuce in Europe. The GAP of France (400 g/L SC, 0.8 kg ai/ha, 2 applications, 21 day PHI) was applied to field trials in the UK (4), the Netherlands (1), France (North, 2), and Germany (2): < 0.05 (5), 0.11, 0.13, 0.28, 0.43 mg/kg. The GAP of Italy (400 g/L SC, 0.8 kg ai/ha, 2 applications, 14 day PHI) were applied to trials in Italy (2), Greece (1), France (South, 1), and Spain (1): 0.05, 0.14, 0.31, 0.77, 1.2 mg/kg. The residues in ranked order for head lettuce were: < 0.05 (5), 0.05, 0.11, 0.13, 0.14, 0.28, 0.31, 0.43, 0.77, 1.2 mg/kg.

Glasshouse trials were also reported from Europe (UK, Netherlands and Germany) for head lettuce. The GAP of Italy is 400 g/L SC, 0.8 kg ai/ha low volume, 0.08 kg ai/hL high volume, 2 applications, 14 day PHI. All trials were at maximum GAP, using high volume, and the residues in ranked order were: 0.37, 0.41, 0.49, 0.61, 0.85, 0.97 (2), 1.4, 1.6 mg/kg.

The Meeting considered the field and glasshouse trials in Europe not to be from the same population and used the glasshouse trials to estimate an STMR of 0.85 mg/kg and a maximum residue level of 3 mg/kg for head lettuce.

Field trials were also conducted in France, Greece, Italy and Portugal for leaf lettuce. Using the GAP of Italy (400 g/L SC, 0.8 kg ai/ha, 2 applications, with a 14 day PHI), three of the four trials were at maximum GAP. The residues in ranked order are 0.62, 0.68, 7.5 mg/kg. The Meeting considered three trials an insufficient number for the estimation of an STMR and a maximum residue level for leaf lettuce.

Legume Vegetables

Trials for the application of pyrimethanil to common beans (green beans) were reported from France (4) and Germany (3). The GAP in France is 400 g/L SC, 0.6 kg ai/ha, 1 application, 14 day PHI. Residues in ranked order were: < 0.05 (3), 0.05, 0.07, 0.08, 0.09.

Trials were also reported for the treatment of green beans in glasshouses in France (2), Italy (1), Spain (3), and Greece (2). The GAP of France is 400 g/L SC, 0.6 kg ai/ha, 14 day PHI. The residues in ranked order (median underlined) were: < 0.05, 0.12, 0.13, 0.20, 0.25, 0.28, 0.91, 1.9 mg/kg.

The Meeting considered the field and glasshouse trials on green beans not to be from the same population and used the glasshouse trials to estimate an STMR of 0.22 mg/kg and a maximum residue level of 3 mg/kg for common beans.

Root and tuber vegetables

Trials were reported on the foliar application of pyrimethanil to carrots in Brazil and Europe. Two trials in Brazil did not match the GAP of Brazil (300 g/L SC, 0.6 kg ai/ha, with a 14 day PHI). Nine trials, conducted in Northern Europe were received from the UK, France, Germany and the Netherlands. Eight trials were at the maximum GAP of France, i.e., 400 g/L SC, 0.8 kg ai/ha × 2 applications, with a 21 day PHI. Residues in rank order were: < 0.05 (2), 0.07 (2), 0.24, 0.28, 0.35, 0.36 mg/kg. Nine trials were conducted in Southern Europe in Spain, France, Greece, Italy and Portugal, and all were conducted at the maximum GAP of Italy (400 g/L SC, 0.8 kg ai/ha × 2

applications, with a 7 day PHI), residues in rank order were: < 0.05, 0.05, 0.08, 0.09, 0.14, 0.21, 0.33, 0.44, 0.54 mg/kg. Residues in the two areas were comparable, and the combined residue values in ranked order (median underlined) were: < 0.05 (3), 0.07 (3), 0.08, 0.09, 0.13, 0.14, 0.21, 0.24, 0.28, 0.33, 0.35, 0.36, 0.44, 0.54 mg/kg. The Meeting estimated an STMR of 0.14 mg/kg and a maximum residue level of 1 mg/kg for carrots.

Supervised trials for the foliar application of pyrimethanil to potatoes were reported from the USA where the GAP is 0.3 kg ai/ha (600 g/L SC), with a maximum of 1.6 kg ai/ha/season, with a 7 day PHI. The ranked order of residue values for 16 trials at maximum GAP was: < 0.05(16). The Meeting estimated an STMR of 0.05 mg/kg and a maximum residue level of 0.05* mg/kg for potatoes.

Tree Nuts

The Meeting received a report on supervised field trials on almonds in the USA, where the GAP is 0.8 kg ai/ha (600 g/L SC), with a maximum of 2.4 kg ai/ha/season, and a 30 day PHI. Six trials were at the maximum GAP and the ranked order of residue values on almond hulls were: 1.9, 2.4, 2.6, 2.7, 3.6, 9.2 mg/kg. The ranked order of values on almond nutmeat was: < 0.05(4), 0.06, 0.10 mg/kg. The Meeting estimated an STMR of 2.6 mg/kg and a maximum residue level of 12 mg/kg for almond hulls. The Meeting also estimated an STMR of 0.05 and a maximum residue level of 0.2 mg/kg for almond nutmeats.

Legume Animal Feeds

Thirteen supervised trials were carried out in Europe (France, Germany and the UK) for the foliar application of pyrimethanil to fodder peas (field peas, combining peas, protein peas). The GAP in France is 400 g/L SC, 0.6 kg ai/ha, with a 28 day PHI. Eleven trials were conducted at this maximum GAP, and the values in ranked order for dry seeds were: < 0.05 (4), 0.08, 0.09, 0.11, 0.12, 0.22, 0.25, 0.30 mg/kg. The highest residue was 0.30 mg/kg. The values in ranked order for straw were: < 0.05 (3), 0.15(2), 0.24, 0.28, 0.64, 0.66, 1.0 mg/kg. The highest residue was 1.0 mg/kg. The Meeting estimated an STMR of 0.09 mg/kg and a maximum residue level of 0.5 mg/kg for fodder pea seed (dry) and an STMR of 0.20 mg/kg and a maximum residue level of 3 mg/kg for fodder pea straw.

Fate of residues during processing

The Meeting received processing studies for oranges, apples, grapes, tomatoes, green beans and carrots. No information was supplied on the fate of radiolabelled pyrimethanil under general processing conditions.

Oranges with incurred residues of pyrimethanil from post-harvest treatment (2.9 mg/kg; 7.5 mg/kg) were processed by a commercial process into juice, dried pulp and citrus oil. The average processing factors were 0.01 for juice, 0.45 for pulp (dried), and 20 for citrus oil. Applying these factors to the STMR for citrus (2.8 mg/kg), the Meeting estimated the following STMR-Ps for citrus juice, citrus pulp (dried) and citrus oil, respectively: 0.028 mg/kg; 1.3 mg/kg; 56 mg/kg.

Apple processing studies were conducted in Germany (four trials) and the USA (one trial). The median processing factor for juice was 0.45 (n=5), the average factor for puree (n=2) was 0.37, and the factor for wet pomace (n=1) was 4.1. Applying these factors to the STMR, the Meeting estimated: STMR-P of 0.32 mg/kg for juice; a STMR-P of 2.9 mg/kg for wet apple pomace, and a STMR-P of 0.26 mg/kg for apple puree. The STMR-P and maximum residue limit estimates for dry apple pomace are 7.2 mg/kg (0.7 mg/kg × 4.1/0.40) and 40 mg/kg (3.8 mg/kg × 4.1/0.4), respectively, assuming that wet apple pomace contains 40% dry matter (*Table of OECD Feedstuffs Derived from Field Crop).*

A plum to prune processing study was conducted in the USA. The processing factor of 0.81 applied to the STMR of fresh plums (0.59 mg/kg) yields an STMR-P of 0.48 mg/kg for (dried) prunes.

Processing studies for the conversion of grapes to white wine was reported from Italy. The median processing factor (n=11, one value > 1 with all others < 1) was 0.48. Applying this factor to the STMR for grapes of 0.71 mg/kg yields a STMR-P of 0.34 mg/kg for wine.

A processing study for the conversion of grapes to juice and raisin (USA) was reported to the Meeting. The processing factors for juice, wet pomace and raisins are 0.7, 2.4 and 1.6, respectively (n=1). Applying these factors to the appropriate STMRs or HR levels the Meeting estimated the following: STMR-P for juice 0.50 mg/kg; STMR-P for wet grape pomace 1.7 mg/kg; STMR-P for grape raisins 1.1. The Meeting also estimated a maximum residue level of 5 mg/kg for grape raisins.

A tomato processing study was conducted in the USA in which tomatoes with incurred residues were processed by a commercial-type method into puree and paste, with processing factors (n=1) of 0.31 and 1.1, respectively. Applying these factors to the STMR for tomatoes (0.32 mg/kg) yields STMR-Ps of 0.10 mg/kg and 0.35 mg/kg for tomato puree and tomato paste, respectively.

Samples of green beans with incurred pyrimethanil residues (Europe) were processed utilizing commercial canning and freezing techniques (n=4). The median processing factor was 0.40 for canning and the median factor for freezing was 0.50. Using the freezing factor, the STMR-P for processed green (common) beans was estimated as 0.11 mg/kg (0.50 × 0.22).

Samples of carrot from four locations in Southern Europe with incurred residues of pyrimethanil were processed by commercial-type procedures into canned carrots, frozen carrots, carrot juice and carrot puree. The median processing factors (n=4) for canned carrots and frozen carrots were 0.59 and 0.45, respectively. The median processing factors (n=4) for juice and puree were 0.20 and 0.45, respectively. Using these factors, STMRs were derived for canned carrots, 0.083 mg/kg, and frozen carrots, 0.063 mg/kg; the average STMR for canned/frozen carrots, 0.073 mg/kg; carrot juice 0.028 mg/kg; and carrot puree 0.063 mg/kg. The HR for canned/frozen carrots is 0.28 mg/kg (the average of 0.59 × 0.54 mg/kg and 0.45 × 0.54 mg/kg).

Livestock dietary burden

Based on the *Table of OECD Feedstuffs Derived from Field Crops*, Annex 4, ENV/JM/MONO (2006) 32, also published as Annex 6 of the 2006 JMPR *Report*, the following feed items are potentially available: pea hay (straw), carrot culls, potato culls, pea seed, almond hulls, apple pomace (wet), citrus (dried pulp), potato (processed waste), grape pomace (wet). Calculation from highest residue, STMR (some bulk commodities) and STMR-P values provides the levels in feed suitable for estimating MRLs, while calculation from STMR and STMR-P values for feed is suitable for estimating STMR values for animal commodities. The percentage dry matter is taken as 100% when the highest residue levels and STMRs are already expressed as dry weight.

Estimated maximum and mean livestock dietary burdens

Dietary burden calculations for beef cattle and dairy cattle are provided below. The calculations were made according to the animal diets from US-Canada, EU and Australia in the *Table of OECD Feedstuffs Derived from Field Crop* (Annex 6 of the 2006 JMPR Report).

Poultry metabolism, poultry analytical methods and poultry feeding studies were not provided. The manufacturers noted a lack of poultry feed items. However, the *Table of OECD Feedstuffs Derived from Field Crop* indicates several poultry feeding items that potentially contain pyrimethanil residues: carrot culls (10% Australia); pea seed (20% US, EU), pea hay (straw) (10% Europe) and potato culls (10% Europe).

	Animal dietary burden, pyrimethanil, ppm of dry matter diet					
	US-Canada		EU		Australia	
	max	mean	max	mean	max	mean
Beef cattle	2.42	1.90	2.49	1.70	3.52[1]	2.76
Dairy cattle	1.69	1.18	1.76	0.93	3.52[1]	2.86[2]

[1] Highest maximum beef or dairy cattle dietary burden suitable for MRL estimates for mammalian meat and milk.

[2] Highest mean beef or dairy cattle dietary burden suitable for STMR estimates for mammalian meat and milk.

Animal commodity maximum residue levels

The Meeting received a report on the feeding of Holstein lactating cattle for 28 days with pyrimethanil. Dosing was made on a daily basis at the nominal dose rates of 1, 3, 10 and 50 ppm in the diet. The total residue (pyrimethanil + 2-(4-hydroxyanilino-4,6-dimethylpyrimidine + 2-anilino-4,6-dimethylpyrimidin-5-ol) reached a plateau in milk between day 15 and day 22 at the 50 ppm dosing level.

Residues in milk (final day 27) were below the LOQ (0.01 mg/kg per compound) at the 50 ppm dosing level for each of pyrimethanil and 2-(4-hydroxyanilino-4,6-dimethylpyrimidine. The metabolite 2-anilino-4,6-dimethylpyrimidin-5-ol had a maximum concentration of 0.088 mg/kg and an average concentration of 0.069 mg/kg in final milk from the 50 ppm dosing regimen. The same metabolite was found at a maximum concentration of 0.017 mg/kg in milk at the 10 ppm feeding level and was absent (< 0.01 mg/kg) at the 3 ppm dosing level.

A milk sample from day 27 was separated into skim milk and milk fat. The residue in skim milk consisted of 0.015 mg/kg 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine and 0.064 mg/kg 2-anilino-4,6-dimethylpyrimidin-5-ol. Milk fat contained 0.031 mg/kg 2-anilino-4,6-dimethylpyrimidin-5-ol. Thus, the residue is not fat soluble.

At the 50 ppm level, each of the parent and metabolite 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine was absent at the LOQ (0.05 mg/kg) in all tissues except kidney. Pyrimethanil was absent in kidney (at the 50 ppm feeding level). The average concentration of 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine in kidney was 0.63 mg/kg and the maximum residue was 0.88 mg/kg. At the 3 ppm feeding level, the average concentration of 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine in kidney was 0.066 mg/kg and the maximum was 0.08 mg/kg. At the 10 ppm feeding level, the average concentration of 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine in kidney was 0.12 mg/kg and the maximum was 0.13 mg/kg.

In the table below, dietary burdens are shown in round brackets (), feeding levels and residue concentrations from the feeding study are shown in square brackets [] and estimated concentrations related to the dietary burdens are shown without brackets.

Pyrimethanil total residues[1], mg/kg

Dietary burden (ppm) Feeding level [ppm]	Milk	Muscle	Liver	Kidney	Fat
MRL					
	Mean	Highest	Highest	Highest	Highest
MRL, beef cattle (3.52) [3.0]		(< 0.1) [< 0.1]	(< 0.1) [< 0.1]	(0.09[2] + < 0.05[3]) [0.08[2] + < 0.05[3]]	(< 0.1) [< 0.1]
MRL, dairy cattle (3.52) [3.0]	(< 0.03) [< 0.03[4]]	(< 0.1) [< 0.1]	(< 0.1) [< 0.1]	(0.09[2] + < 0.05[3]) [0.08[2] + < 0.05}	(< 0.1) [< 0.1]
STMR					
	Mean	Mean	Mean	Mean	Mean
STMR beet cattle (2.76) [3.0]		(< 0.1) [< 0.1]	(< 0.1) [< 0.1]	(0.058 [2]+ < 0.05[3]) [0.066[2] + < 0.05[3]]	(< 0.1) [< 0.1]
STMR dairy cattle (2.86) [3.0]	(< 0.02) [< 0.02]	(< 0.1) [< 0.1]	(< 0.1) [< 0.1]	(0.060 + < 0.05[3]) [0.066 [2]+ < 0.05[3]]	(< 0.1) [< 0.1]

[1]The LOQ is 0.05 for each of pyrimethanil and 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine, in animal tissues. The LOQ is 0.01 mg/kg for each of pyrimethanil, 2-anilino-4,6-dimethylpyrimidin-5-ol, 2-anilino-4,6-dimethylpyrimidin-5-ol in milk.
[2] 2-(4-hydroxyanilino)-4,6-dimethylpyrimidine.
[3] Pyrimethanil. At a 50 ppm pyrimethanil feeding level, pyrimethanil was < 0.05 mg/kg. By extrapolation, at the 3 ppm feeding level, the pyrimethanil concentration would be < 0.005 mg/kg.
[4] pyrimethanil + 2-(4-hydroxyanilino-4,6-dimethylpyrimidine + 2-anilino-4,6-dimethylpyrimidin-5-ol. At a 50 ppm feeding level only 2-anilino-4,6-dimethylpyrimidin-5-ol had quantifiable residues.

The Meeting estimated an STMR of 0.01 mg/kg for milk and estimated a maximum residue level of 0.01 mg/kg for milk. The Meeting estimated STMRs of 0.0 mg/kg for each of meat and fat and maximum residue levels of 0.05 (*) mg/kg for meat. The Meeting estimated an STMR of 0.065 mg/kg for edible offal based on the STMR value for dairy cow kidney. The Meeting estimated a maximum residue level of 0.1 mg/kg for edible offal (mammalian) based on the value of kidney.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes (IEDI) of pyrimethanil based on the STMRs estimated for 32 commodities for the thirteen GEMS/Food cluster diets were in the range of 0% to 5% of the maximum ADI (0.2 mg/kg bw). The Meeting concluded that the long-term intake of residues of pyrimethanil resulting from its uses that have been considered by JMPR is unlikely to present a public health concern.

Short-term intake

The 2007 JMPR decided that an ARfD is unnecessary. The Meeting therefore concluded that the short-term intake of pyrimethanil residues is unlikely to present a public health concern.

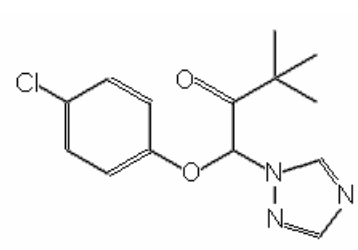
5.22 TRIADIMEFON (133)/ TRIADIMENOL (168)

RESIDUE AND ANALYTICAL ASPECTS

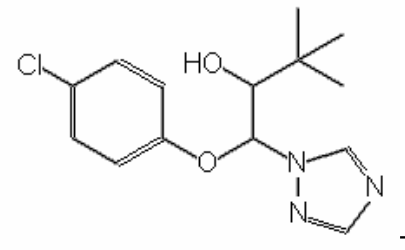
Triadimenol and triadimefon are related substances and follow the same metabolic pathways in all matrices investigated. Both compounds were evaluated by JMPR several times since 1978 and the last time in 2004, when an ADI of 0–0.03 mg/kg bw and an ARfD of 0.08 mg/kg bw were established for triadimefon and triadimenol each. The residue evaluation of the compounds was completed by the current Meeting within the periodic re-evaluation program.

Data submitted by the manufacturer and evaluated at this Meeting include metabolism in animal and plants, degradation in soil, residues in succeeding crops, analytical methods, supervised residue trials and processing studies.

The following appraisal includes the evaluation of the residue behaviour for both triadimefon and triadimenol.



ohenoxy)-3,3-dı



-butanone

Triadimenol β-(4-chlorophenoxy)-α-(1,1-dimethylethyl)-1H-1,2,4-triazole-1-ethanol

Triadimefon and triadimenol are structurally related systemic fungicides with registered uses in many countries. Their main mode of action is inhibitors of ergosterol biosyntheses in fungi.

The following abbreviations are used for the metabolites discussed below:

M02	γ-(4-chlorophenoxy)-β-hydroxy-α,α-dimethyl-1H-1,2,4-triazole-1-butanoic acid