5.26 QUINCLORAC (287)

TOXICOLOGY

Quinclorac is the ISO-approved common name for 3,7-dichloroquinoline-8-carboxylic acid (IUPAC), with CAS number 84087-01-4. It is a herbicide of the quinoline carboxylic acid class. The pesticidal mode of action is as a mimic of the plant hormone auxin.

Quinclorac has not been evaluated previously by JMPR and was reviewed by the present Meeting at the request of CCPR.

All critical studies contained statements of compliance with GLP.

Initial production batches of quinclorac contained cinnoline impurities that were associated with positive results in genotoxicity studies. Improved production methods have reduced the levels of these impurities, and current batches are reported to contain cinnolines at concentrations below 1 ppm. The sponsor has confirmed that current technical quinclorac has a purity of greater than 99% and that the material tested in the submitted toxicity studies adequately covers the impurities in current production material.

Biochemical aspects

The toxicokinetics and biotransformation of quinclorac were investigated in rats administered (2,3,4-^{14}C)-labelled quinclorac at single doses of 15, 100, 600 or 1200 mg/kg bw by gavage or at 15 000 ppm in the diet (equivalent to 1200 mg/kg bw); 7 daily doses of 15 or 600 mg/kg bw per day by gavage or at 15 000 ppm in the diet (equivalent to 1200 mg/kg bw per day); or 14 daily doses of 15 mg/kg bw per day of unlabelled quinclorac followed by a single labelled dose of 15 mg/kg bw. Absorption was rapid, with maximal blood concentrations achieved between 0.25 and 1 hour for single doses of 600 mg/kg bw and below. The extent of oral absorption was high (> 90%) at all dose levels, based on urinary and biliary data, with some of the biliary component being reabsorbed. Quinclorac was widely distributed in the body, with highest concentrations of radiolabel present in the blood, kidney and plasma. The labelled material was excreted primarily via urine (50–90% in 24 hours). Clearance from the blood was slower following repeated dosing with 600 mg/kg bw and a single dose of 1200 mg/kg bw, resulting in non-proportionate increases in AUC with dose. Absorbed quinclorac was metabolized to only a limited extent, with unchanged parent compound representing approximately 80% of the excreted radiolabel. The major biotransformation product was quinclorac–glucuronide conjugate at approximately 5% of the administered dose. The excretion pattern, tissue distribution of radioactivity and/or metabolite profile were similar across administered dose levels and with single or repeated administration.

Toxicological data

Quinclorac was of low acute toxicity in rats via the oral route (LD_{50} = 2680 mg/kg bw) or dermal route (LD_{50} > 2000 mg/kg bw) and by inhalation (LC_{50} > 5.15 mg/L air). Quinclorac was not irritating to the skin of rabbits, but was transiently and mildly irritating to the eyes of rabbits. Modern material of a high purity (99.4%) was not a skin sensitizer in guinea-pigs, but a positive result was seen with older, less pure quinclorac (97.4%).

In repeated-dose toxicity studies in mice, rats and dogs, the predominant effect was reduced body weight gain, often associated with reductions in feed consumption. The only organ showing consistency of effects was the kidney, with increases in organ weight and histopathological changes (e.g. interstitial nephritis) at high dose levels.

In a 90-day study of toxicity in mice, dietary concentrations of quinclorac were 0, 4000, 8000 and 16 000 ppm (equal to 0, 1001, 1992 and 4555 mg/kg bw per day for males and 0, 1466, 2735 and 5953 mg/kg bw per day for females, respectively). The NOAEL was 4000 ppm (equal to 1001 mg/kg bw per day), based on increases in blood urea levels and water consumption at 8000 ppm (equal to 1992 mg/kg bw per day). Slight changes in body weight and mean red blood cell volume were considered not to be adverse. In a subsequent 90-day dietary study of toxicity in mice administered

500 ppm quinclorac (equal to 85 mg/kg bw per day for males and 130 mg/kg bw per day for females), there were no treatment-related effects; the NOAEL was 500 ppm (equal to 85 mg/kg bw per day), the only dose tested.

In a 90-day study of toxicity in rats, dietary concentrations of quinclorac were 0, 1000, 4000 and 12 000 ppm (equal to 0, 77, 302 and 930 mg/kg bw per day for males and 0, 87, 358 and 1035 mg/kg bw per day for females, respectively). The NOAEL was 4000 ppm (equal to 302 mg/kg bw per day), on the basis of a range of clinical chemistry and haematology changes in both sexes and urothelial hyperplasia and interstitial nephritis in males at 12 000 ppm (equal to 930 mg/kg bw per day).

In a 28-day dietary study in which dogs were administered quinclorac at 0, 1000, 3000, 9000 or 27 000 ppm (equal to 0, 31, 95, 278 and 912 mg/kg bw per day for males and 0, 36, 108, 315 and 956 mg/kg bw per day for females, respectively), the NOAEL was 9000 ppm (equal to 278 mg/kg bw per day), based on body weight loss and kidney lesions at 27 000 ppm (equal to 912 mg/kg bw per day).

In a 1-year study in dogs in which quinclorac was administered in the diet at 0, 1000, 4000 or 12 000 ppm (equal to 0, 35, 139 and 490 mg/kg bw per day for males and 0, 35, 141 and 472 mg/kg bw per day for females, respectively), the NOAEL was 1000 ppm (equal to 35 mg/kg bw per day), on the basis of an increase in relative kidney weights in males at 4000 ppm (equal to 139 mg/kg bw per day).

In a 78-week toxicity and carcinogenicity study in mice, dietary concentrations of quinclorac were 0, 1000, 4000 and 8000 ppm (equal to 0, 170, 711 and 1444 mg/kg bw per day for males and 0, 213, 869 and 1828 mg/kg bw per day for females, respectively). No NOAEL could be identified, as reductions in body weight were observed in females at all doses. Quinclorac did not produce any increase in the incidences of benign or malignant tumours.

A subsequent 78-week toxicity study in mice used a single dietary level of 250 ppm (equal to 42 mg/kg bw per day for males and 52 mg/kg bw per day for females). There were no adverse effects.

The Meeting concluded that the overall NOAEL for the 78-week toxicity studies in mice was 250 ppm (equal to 52 mg/kg bw per day), based on reductions in body weight in females at 1000 ppm (equal to 213 mg/kg bw per day).

In a 2-year toxicity and carcinogenicity study in rats, dietary concentrations of quinclorac were 0, 1000, 4000 and 8000 ppm (equal to 0, 55, 221 and 444 mg/kg bw per day for males and 0, 66, 262 and 529 mg/kg bw per day for females, respectively) for evaluation of carcinogenic potential. Satellite groups received diets containing quinclorac at 0, 1000, 4000, 8000 or 12 000 ppm (equal to 0, 55, 221, 444 and 675 mg/kg bw per day for males and 0, 66, 262, 529 and 832 mg/kg bw per day for females, respectively) for the evaluation of toxicity. The only significant effect was a decrease in the body weight of top-dose females in the satellite groups. The NOAEL was 8000 ppm (equal to 529 mg/kg bw per day), on the basis of reductions in body weight in females at 12 000 ppm (equal to 832 mg/kg bw per day). Quinclorac did not increase the incidence of benign or malignant tumours.

The Meeting concluded that quinclorac is not carcinogenic in mice or rats.

Quinclorac was tested for genotoxicity in an adequate range of assays, both in vitro and in vivo. The majority of studies produced negative results. Positive results were seen at high concentrations in a cytogenicity assay in human lymphocytes. In vivo assays of bone marrow micronucleus induction and UDS in hepatocytes gave negative results.

The Meeting concluded that quinclorac is unlikely to be genotoxic in vivo.

In view of the fact that quinclorac is unlikely to be genotoxic in vivo and the absence of carcinogenicity in mice and rats, the Meeting concluded that quinclorac is unlikely to pose a carcinogenic risk to humans from the diet.

In a two-generation study of reproductive toxicity in rats, with two matings in the F_1 generation and one in the F_2 generation, dietary concentrations of quinclorac were 0, 1000, 4000 and

12 000 ppm (equivalent to mean intakes of 0, 96, 381 and 1180 mg/kg bw per day, respectively). The NOAEL for reproductive effects was 12 000 ppm (equivalent to 1180 mg/kg bw per day), the highest dose tested. The NOAEL for parental toxicity was 4000 ppm (equivalent to 381 mg/kg bw per day), based on an increase in the incidence of interstitial nephritis at 12 000 ppm (equivalent to 1180 mg/kg bw per day) in females of both generations. The NOAEL for effects on offspring was 4000 ppm (equivalent to 381 mg/kg bw per day), based on reduced pup weight during lactation at 12 000 ppm (equivalent to 1180 mg/kg bw per day).

In a study of developmental toxicity in rats dosed with quinclorac at 0, 24.4, 146 or 438 mg/kg bw per day by gavage in 0.5% carboxymethyl cellulose, there were no effects on any measured fetal parameters. The NOAEL for maternal toxicity was 146 mg/kg bw per day, on the basis of deaths, reduced feed intake, increased water intake and severe ulceration of the glandular stomach at 438 mg/kg bw per day. The NOAEL for embryo and fetal toxicity was 438 mg/kg bw per day, the highest dose tested.

In a study of developmental toxicity in rabbits dosed with quinclorac at 0, 70, 200 or 600 mg/kg bw per day by gavage in 0.5% carboxymethyl cellulose, severe maternal toxicity, including deaths, was observed at 600 mg/kg bw per day. Live pup numbers were reduced at 600 mg/kg bw per day. At the top dose level, there was an increase in the number of pups with skeletal variations, although there was no significant increase in any specific variation. There was no increase in the number of pups with malformations. The NOAEL for maternal toxicity was 200 mg/kg bw per day, based on mortality and body weight loss at 600 mg/kg bw per day. The NOAEL for embryo and fetal toxicity was 200 mg/kg bw per day, based on an increase in fetuses with skeletal variations, reduced numbers of viable fetuses and reduced fetal weights at 600 mg/kg bw per day.

The Meeting concluded that quinclorac is not teratogenic in rats or rabbits.

The acute neurotoxicity of quinclorac was investigated in rats administered dose levels of 0, 150, 500 or 1500 mg/kg bw by gavage in 1% carboxymethyl cellulose. Dose-related reductions in locomotor activity were seen at 4–5 hours post-dosing, but not subsequently, in the mid- and high-dose groups. Motor activity reductions in males in the low-dose group were considered not to be treatment related, as the background activity in this group was consistently lower than in the other groups. There were no indications of neuropathy. The NOAEL was 150 mg/kg bw, based on reduced motor activity at 500 mg/kg bw.

In a subchronic (90-day) neurotoxicity study in rats, dietary concentrations of quinclorac were 0, 1500, 5000 and 15 000 ppm (equal to 0, 96, 301 and 976 mg/kg bw per day for males and 0, 112, 368 and 1142 mg/kg bw per day for females, respectively). No adverse effects were reported. The NOAEL for neurotoxicity was 15 000 ppm (equal to 976 mg/kg bw per day), the highest dose tested.

The reduced motor activity seen in the acute neurotoxicity study is a relatively general finding, not specific to a neurotoxic mode of action; there was no evidence of specific neurotoxic findings in other studies. The Meeting concluded that quinclorac is not neurotoxic.

In a 28-day immunotoxicity study in female mice, dietary concentrations were 0, 500, 1500 and 5000 ppm (equal to 0, 176, 439 and 1760 mg/kg bw per day, respectively). No adverse effects were reported. The NOAEL for immunotoxicity was 5000 ppm (equal to 1760 mg/kg bw per day), the highest dose tested.

The Meeting concluded that quinclorac is not immunotoxic.

Biochemical and toxicological data on metabolites and/or degradates

[3-^{14}C]Quinclorac methyl ester, a plant metabolite, administered to rats at 15, 50 or 600 mg/kg bw by gavage was rapidly and extensively absorbed and excreted via urine and bile. The proportion of radiolabel in the bile increased from 30% at 15 mg/kg bw to 51% at 600 mg/kg bw, with a corresponding decrease in radiolabel in urine (51% and 32%, respectively). The initial steps in biotransformation involved extensive demethylation to release free quinclorac (approximately 50% of the administered dose). Other metabolic steps, identified from biliary metabolites, were arene oxide

formation and conjugation with glutathione, with subsequent transformation of the glutathione moiety, hydroxylation of the quinoline structure and dimerization.

Quinclorac methyl ester has a low acute oral toxicity to rats (LD_{50} > 2000 mg/kg bw); clinical signs (poor general state, dyspnoea and piloerection) were noted.

In a repeated-dose study of toxicity in rats, quinclorac methyl ester was administered in the diet at 0, 2000, 4000 and 8000 ppm (equal to 0, 128, 252 and 518 mg/kg bw per day for males and 0, 145, 274 and 509 mg/kg bw per day for females, respectively) for 3 months. The main findings were reduced body weight, increased relative organ weights and histopathological changes of the liver, thyroid and kidney. A NOAEL could not be identified, as increased relative liver weights, hepatocellular hypertrophy, increased relative thyroid gland weights, thyroid hypertrophy/hyperplasia and "nuclear crowding" of the kidney were observed at 2000 ppm (equal to 128 mg/kg bw per day), the lowest dose tested.

The pattern of toxicity seen with the methyl ester is not the same as that seen with quinclorac; therefore, a comparison of relative toxic potency is not straightforward. A comparison of the 90-day studies of toxicity in rats for quinclorac and quinclorac methyl ester results in a ratio of 2.4 (302/128) between the NOAEL for quinclorac and the LOAEL for the ester and a ratio of 7.3 (930/128) between the LOAEL for quinclorac and the LOAEL for the ester. The main metabolic step of the methyl ester is demethylation to quinclorac, which suggests that some aspects of the toxicity of the methyl ester will have been addressed by studies with quinclorac. In acute oral toxicity studies, similar clinical signs (poor general state, dyspnoea, piloerection) were reported at a dose of 2000 mg/kg bw for the methyl ester and a similar dose of 1780 mg/kg bw used in the oral LD_{50} study with quinclorac. The Meeting concluded that quinclorac methyl ester was likely to be less than 10-fold more toxic than quinclorac.

Several quinclorac conjugates were identified as plant metabolites. No specific toxicity data were available on these conjugates, but a structure–activity relationship analysis identified no alerts that were not also present for quinclorac. The Meeting concluded that these conjugates were likely to be of lower or equivalent toxicity to the parent compound, because they are expected to be readily hydrolysed to the parent in the gastrointestinal tract.

Human data

No adverse effects have been reported in quinclorac production and formulation plant workers, and no significant effects have been reported in exposed users of quinclorac-based products.

The Meeting concluded that the existing database on quinclorac was adequate to characterize the potential hazards to the general population, including fetuses, infants and children.

Toxicological evaluation

The Meeting established an ADI for quinclorac of 0–0.4 mg/kg bw, on the basis of the NOAEL of 35 mg/kg bw per day for increased relative kidney weights from the 1-year dog study. A safety factor of 100 was applied.

The Meeting established an ARfD for quinclorac of 2 mg/kg bw, on the basis of the NOAEL of 150 mg/kg bw per day for reductions in motor activity in the acute neurotoxicity study in rats. A safety factor of 100 was applied.

The plant metabolite quinclorac methyl ester is not found in rats administered quinclorac. The main metabolic step for the methyl ester in rats is demethylation to quinclorac. Similar clinical signs were seen at similar doses in the acute oral toxicity studies with quinclorac and the methyl ester. In a 90-day study of toxicity in rats, the methyl ester produced a pattern of liver, kidney and thyroid effects that differed from that seen in the equivalent study with quinclorac, and the LOAEL for the methyl ester was below the NOAEL for quinclorac.

The Meeting concluded that the methyl ester is 10-fold more toxic than quinclorac and that a 10-fold potency factor should be applied to the residue levels for use in both the acute and chronic

dietary exposure estimates for quinclorac and that these should be added to the dietary exposures for quinclorac and compared with the ARfD and ADI for quinclorac, respectively.

The Meeting concluded that the quinclorac conjugates were of no greater toxicity than the parent.

Both the ADI and ARfD are established for the sum of quinclorac and its conjugates, and quinclorac methyl ester (×10), expressed as quinclorac.

A toxicological monograph was prepared.

Levels relevant to risk assessment of quinclorac and quinclorac methyl ester

Species	Study	Effect	NOAEL	LOAEL
Mouse	Seventy-eight-week studies of toxicity and carcinogenicity[a,b]	Toxicity	250 ppm, equal to 52 mg/kg bw per day	1 000 ppm, equal to 213 mg/kg bw per day
		Carcinogenicity	8 000 ppm, equal to 1 444 mg/kg bw per day[c]	–
Rat	Acute neurotoxicity study[d]	Neurotoxicity	150 mg/kg bw	500 mg/kg bw
	Two-year study of toxicity and carcinogenicity[a]	Toxicity	8 000 ppm, equal to 529 mg/kg bw per day	12 000 ppm, equal to 832 mg/kg bw per day
		Carcinogenicity	8 000 ppm, equal to 444 mg/kg bw per day[c]	–
	Two-generation study of reproductive toxicity[a]	Reproductive toxicity	12 000 ppm, equivalent to 1 180 mg/kg bw per day[c]	–
		Parental toxicity	4 000 ppm, equivalent to 381 mg/kg bw per day	12 000 ppm, equivalent to 1 180 mg/kg bw per day
		Offspring toxicity	4 000 ppm, equivalent to 381 mg/kg bw per day	12 000 ppm, equivalent to 1 180 mg/kg bw per day
	Developmental toxicity study[d]	Maternal toxicity	146 mg/kg bw per day	438 mg/kg bw per day
		Embryo and fetal toxicity	438 mg/kg bw per day[c]	–
Rabbit	Developmental toxicity study[d]	Maternal toxicity	200 mg/kg bw per day	600 mg/kg bw per day
		Embryo and fetal toxicity	200 mg/kg bw per day	600 mg/kg bw per day
Dog	One-year study of toxicity[a]	Toxicity	1 000 ppm, equal to 35 mg/kg bw per day	4 000 ppm, equal to 139 mg/kg bw per day
Metabolite: Quinclorac methyl ester				
Rat	Ninety-day study of	Toxicity	–	2 000 ppm, equal to

Species	Study	Effect	NOAEL	LOAEL
	toxicity			128 mg/kg bw per day[e]

[a] Dietary administration.
[b] Two or more studies combined.
[c] Highest dose tested.
[d] Gavage administration.
[e] Lowest dose tested.

Estimate of acceptable daily intake (ADI) for the sum of quinclorac and its conjugates, and quinclorac methyl ester (×10), expressed as quinclorac

0–0.4 mg/kg bw

Estimate of acute reference dose (ARfD) for the sum of quinclorac and its conjugates, and quinclorac methyl ester (×10), expressed as quinclorac

2 mg/kg bw

Information that would be useful for the 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 quinclorac

Absorption, distribution, excretion and metabolism in mammals	
Rate and extent of oral absorption	Rapid (T_{max} = 0.25–1 h) and extensive (> 90%)
Dermal absorption	No data
Distribution	Widely distributed; highest levels in blood, kidney and plasma
Potential for accumulation	None
Rate and extent of excretion	Rapid (up to 90% excreted in urine within 24 h)
Metabolism in animals	Limited; 80% excreted unchanged; some glucuronidation
Toxicologically significant compounds in animals and plants	Quinclorac; quinclorac methyl ester; conjugates
Acute toxicity	
Rat, LD_{50}, oral	2 680 mg/kg bw
Rat, LD_{50}, dermal	> 2 000 mg/kg bw
Rat, LC_{50}, inhalation	> 5.15 mg/L
Rabbit, dermal irritation	Not irritating
Rabbit, ocular irritation	Mildly, transiently irritating
Guinea-pig, dermal sensitization	Negative (maximization test)
Short-term studies of toxicity	
Target/critical effect	Reduced body weights; increased kidney weight, interstitial nephritis, urothelial hyperplasia
Lowest relevant oral NOAEL	35 mg/kg bw per day (12 months; dog)

Lowest relevant dermal NOAEL	1 000 mg/kg bw per day (rabbit; highest dose tested)
Lowest relevant inhalation NOAEC	No data
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	Reduced body weight
Lowest relevant NOAEL	52 mg/kg bw per day (mouse)
Carcinogenicity	Not carcinogenic in mice or rats[a]
Genotoxicity	
	Unlikely to be genotoxic in vivo[a]
Reproductive toxicity	
Target/critical effect	No effects on reproduction; reduced pup weight during lactation
Lowest relevant parental NOAEL	381 mg/kg bw per day (rat)
Lowest relevant offspring NOAEL	381 mg/kg bw per day (rat)
Lowest relevant reproductive NOAEL	1 180 mg/kg bw per day (rat)
Developmental toxicity	
Target/critical effect	No effects in rats; reduction in viable fetuses, decreased fetal weight, increase in skeletal variations (rabbit)
Lowest relevant maternal NOAEL	146 mg/kg bw per day (rat)
Lowest relevant embryo/fetal NOAEL	200 mg/kg bw per day (rabbit)
Neurotoxicity	
Acute neurotoxicity NOAEL	150 mg/kg bw (decreased motor activity; rat)
Subchronic neurotoxicity NOAEL	976 mg/kg bw per day (highest dose tested; rat)
Developmental neurotoxicity NOAEL	No data
Other toxicological studies	
Immunotoxicity NOAEL	1 760 mg/kg bw per day (highest dose tested; mouse)
Studies on toxicologically relevant metabolites	Quinclorac methyl ester
	Rapidly and extensively absorbed. Initial step in metabolism is demethylation to quinclorac.
	Acute oral LD_{50} > 2 000 mg/kg bw
	LOAEL in 90-day rat study = 128 mg/kg bw per day, based on kidney, liver and thyroid effects
Medical data	
	No adverse effects reported in humans

[a] Unlikely to pose a carcinogenic risk to humans from the diet.

Summary

	Value	Study	Safety factor
ADI	0–0.4 mg/kg bw	One-year toxicity study (dog)	100
ARfD	2 mg/kg bw	Acute neurotoxicity study (rat)	100

RESIDUE AND ANALYTICAL ASPECTS

Quinclorac is a systemic herbicide with uptake through roots and foliage and used to control annual grass and broadleaf weeds. Quinclorac mode of action is similar to phenyl herbicides as it imitates the plant growth hormone auxin. The use of quinclorac results in the rupture of the cell membranes due to overstimulation of the growth of the plant.

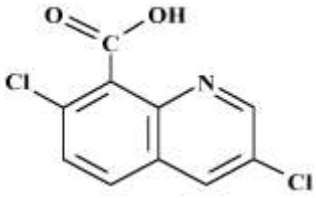
It was scheduled by the Forty-sixth Session of the CCPR (2014) as a new compound for consideration by the 2015 JMPR. The manufacturer submitted studies on metabolism, analytical methods, supervised trials, processing, storage stability, environmental fate in soil and rotational crop studies.

Quinclorac is registered for uses in berries and other small fruits stalk and stem vegetables, cereal grains and rape seed in Australia, Canada, China, Republic of Korea, South America and USA. Information on GAP with supporting labels from Canada and USA was provided to the Meeting.

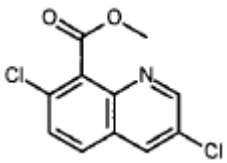
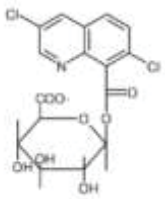
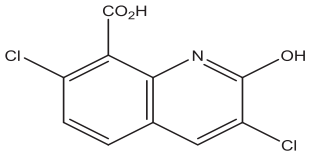
Chemical name

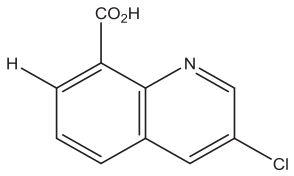
Quinclorac: 3,7-dichloroquinoline-8-carboxylic acid

Structural formula:



Metabolites referred to in the appraisal with codes:

BH 514-Me Quinclorac methyl ester SES218	 methyl-3,7-dichloroquinoline-8-carboxylate
BAS 514 H M1 glucuronide (glucuronic acid) conjugate	
BH 514-2-OH 2 -hydroxyquinclorac	 3,7-dichloro-2-hydroxyquinoline-8-carboxylic acid

BH 514-1 3-chloroquinoline-8-carboxylic acid	 3-chloroquinoline-8-carboxylic acid

Animal metabolism

The Meeting received metabolism studies on laboratory animals, poultry and lactating goats using 2, 3, 4-[^{14}C]-quinclorac (quinoline label).

In rats quinclorac is widely distributed in the body, with highest concentrations of radiolabel present in the blood, kidney and plasma. The labelled material was excreted primarily via urine (50-90% in 24 hours). Absorbed quinclorac was metabolized to only a limited extent, with unchanged parent compound representing approximately 80% of the excreted radiolabel. The major bio-transformation product was quinclorac glucuronide conjugate at approximate 5% of the administrated dose.

One lactating goat received five daily doses of ^{14}C- quinclorac at a rate equivalent to 800 ppm in the diet (34 mg/kg bw). The animal was sacrificed approximately 6 h after the last dose.

A total 67% of the applied radioactivity was recovered. Excretion of radioactivity in urine and faeces accounted for 63 and 3.7% respectively of the total dose. In milk 0.003%, in liver 0.12% and kidney 0.1% of the administrated dose was recovered. The extraction efficiency using 1 M HCl) was generally > 80% TRR in muscle and liver. In milk and kidney it was above 95% TRR.

In milk the TRR levels reached a plateau after 48 hrs. Residues found in tissues at sacrifice were 0.16 to 0.19 mg eq/kg in muscle, 0.14 and 0.78 mg eq/kg in fat (omental and subcutaneous respectively), 10 mg eq/kg in kidney and 2.1 mg eq/kg in liver. Muscle and fat were not analysed further. In milk, liver and kidney, parent quinclorac was the major residue at 86, 81 and 86% TRR respectively. Metabolite (M1) identified as the glucuronic acid conjugate of the parent was found at 4.0% TRR in milk and at 4.7% TRR in kidney.

Seven laying hens (1.8–2.4 kg) were orally dosed once daily for five days with 33–44 mg radiolabelled quinclorac per kg body weight per day corresponding to 800 ppm in the diet. The animals were sacrificed after 6 hours after the last dose. The major part of the radioactivity was recovered in the excreta (93%).

Extraction efficiency (including 1 M HCl) was generally above 80% for excreta, liver, breast muscle and skin. In eggs the TRR levels increased from < 0.06 mg eq/kg one day after first administration up to a plateau of 1.2 mg eq/kg after three days; however levels of TRR showed wide variation in eggs. TRR levels in tissues were 1.1–1.8 mg eq/kg in muscle (breast and leg respectively), 2.0 mg eq/kg in skin/fat, 3.7 mg eq/kg in kidney and 20 mg eq/kg in liver. The unextracted residues were from 2.0–21.1% of TTR.

Parent quinclorac was the major residue in poultry tissues and eggs (78–92% of the TRR). The only metabolite identified was M1, present up to 3% TRR in a combined concentration with two other fractions.

In summary from data presented quinclorac is not significantly metabolised in animals. Parent quinclorac is the major residue found in tissues, milk and eggs, making up from 78–92% TRRs, with the only identified metabolite being M1 present at low levels (< 5% TRR) and also identified in the rat. Since the extraction methods used for lactating goat and poultry tissues included 1 M HCl, it is not clear whether parent compound represents parent only or includes parent released from conjugates and whether the M1 is the fraction of conjugates that remained uncleaved.

Plant metabolism

The Meeting received plant metabolism studies for quinclorac following pre- and/or post-emergent foliar application of 2,3,4-^{14}C-quinclorac to rice, or with 3-^{14}C-quinclorac to wheat, rape seed sorghum and strawberry.

Rice plants were treated in the growth chamber with one foliar application at 1.5 kg ai/ha, and with one application at 0.84 kg ai/ha in the field at the 4 and 3-5 leaf stage, respectively. Samples were collected from whole plant (28 days after application), straw (97 days after application) and grain (97 and 118 days after application from growth chamber and field respectively). Total radioactive residues were 0.49 mg eq/kg from whole plant, 13 mg eq/kg from straw and 1.5 mg eq/kg and 0.12 mg eq/kg from grain in growth chamber and field respectively. Extraction rates were in general above 80% TRR.

Quinclorac was the major residue identified (85–94% TRR) in rice straw, whole plant, and grain in growth chamber and the field. Since rice grain was extracted by reflux with 1 M HCl, the quinclorac detected in rice grain might be released from conjugates. Metabolites present at low levels were not identified.

Wheat plants were treated in the greenhouse with one foliar application of 0.125 kg ai/ha or 0.5 kg ai/ha at the 3–5 leaf stage. Samples were collected of forage (early to late boot stage, 37 days before harvest), straw and grain (92 days after application). Total radioactive residues following the low application rate were 3.3 mg eq/kg (forage), 1.9 mg eq/kg (straw) and 1.1 mg eq/kg (grain) and following the high application rate were 13 mg eq/kg (forage), 8.2 mg eq/kg (straw) and 3.9 mg eq/kg in grain. Extraction with acetone/water and subsequent treatment with NaOH for forage, grain and straw in general was above 80% TRR.

In all plant parts parent quinclorac was the major residue identified at 24% and 45% TRR in forage, 12 and 22% TRR in straw and 62 and 68% TRR in grain from low and high application rate respectively. Metabolites characterized as hydroxyquinclorac conjugates were present in forage at 6.8% TRR (0.22 mg/kg) in the low application rate and 6.4% TRR (0.84 mg/kg) in the high application rate, straw at 14% TRR (0.26 mg eq/kg) and 13% TRR (1.83 mg eq/kg), in grain at 4% TRR (0.05 mg eq/kg) and 4%TRR (0.14 mg eq/kg) in low and high rate application respectively. Other metabolites identified in forage and straw were quinclorac conjugates and hydroxyquinclorac, each < 5% TRR.

Sorghum plants were grown outdoor and treated with a pre-emergence spray application to the soil followed by a foliar treatment (post-emergence) when sorghum plants were 15–25 cm tall. The pre-emergence treatment was 0.525 kg ai/ha and the post-emergence at 0.504 kg ai /ha (total 1.03 kg ai/ha. Residue analysis was done on forage (whole plants) collected at 25 days after the last treatment and on mature fodder and grain collected at 95 days after last treatment.

Extraction with acetone/water and subsequent treatment with HCl were in general above 80% TRR for forage, grain and straw. In all plant samples, unchanged parent quinclorac was the major residue being present at levels of 73% TRR (2.9 mg eq/kg) in forage, 22% TRR (0.19 mg eq/kg) and 74% (0.61 mg eq/kg) in grain. This residue included the quinclorac that was released from remaining solids (4% in grains to 9% TRR in forage and fodder) under hydrolysis conditions. The only other metabolite identified was quinclorac methyl ester present at 3.6% TRR in forage, 5.9% in fodder and 1.7% in grain. A large amount of unidentified residues was present in forage and fodder in organic and aqueous fractions, maximum 19% TRR (0.75 mg eq/kg in forage and 52% TRR (0.46 mg eq/kg) in fodder.

Rape seed plants were grown in a growth chamber and treated with one foliar post emergence application of 0.2 kg ai/ha at 30 days after sowing at 5th true leaf stage. Whole plants were sampled 1 and 29 days after treatment. Seed and straw were sampled 60 days after treatment. Extraction with acetone/ phosphate buffer and subsequent treatment with 0.1M NaOH was above 90% TRR in seed and straw.

Residues in seed were identified as parent quinclorac at 37% TRR (0.18 mg eq/kg) and the quinclorac methyl ester 37% TRR (0.18 mg eq/kg). Metabolites characterized as 'aqueous soluble' were present at 8.7% TRR (0.042 mg eq/kg) and those characterized as 'organo soluble' were found at 8.6% TRR (0.041 mg eq/kg). Residues in straw (0.64 mg eq/kg) and forage (0.68 mg eq/kg) were not further identified

Strawberry plants were grown outdoor and treated with one foliar post-emergence application at growth stage BBCH 73 (seeds clearly visible). The treatment rate was 1.12 kg ai/ha. Foliage and fruits were sampled at three harvest times 21, 37 and 61 days after treatment.

In foliage, unchanged parent quinclorac accounted for 67% TRR (10 mg eq/kg) at first harvest 21 DAT and at 57% TRR (4.4 mg eq/kg) at the last harvest 61 DAT. Conjugated quinclorac released by acid hydrolysis ranged from 27%TRR (4.2 mg eq/kg) at first harvest to 29%TRR (2.3 mg eq/kg) in the last harvest. Extraction efficiency was above 90% TRR in fruit and foliage.

In fruit, unchanged parent quinclorac accounted for 79% TRR (9.1 mg eq/kg) at first harvest and at 51% TRR (1.7 mg eq/kg) at third harvest 61 DAT. Conjugated quinclorac released by acid hydrolysis increased from 11%TRR (1.3 mg eq/kg) at first harvest to 47%TRR (1.6 mg eq/kg) in the last harvest. Quinclorac methyl ester accounted for 9.6% TRR (1.1 mg eq/kg) at first harvest, to 4.9% TRR (0.42 mg eq/kg) at second harvest and was not detected at the last harvest.

In summary the Meeting concluded that in cereals (rice, wheat and sorghum), and in strawberry quinclorac is not significantly metabolized and parent quinclorac including conjugates is the major residue > 80% TRR in both food and feed matrices. A number of identified quinclorac conjugates were identified in amounts below 5% TRR in cereals and up to 47% TRR in fruit. Quinclorac levels reported in cereal metabolism studies may already include the quinclorac released from conjugates. Other metabolites were not found in tested crop matrices above 10% TRR except quinclorac methyl ester which was found at 37% TRR (0.18 mg eq/kg) in rape seed. Quinclorac methyl ester was found as a minor metabolite in strawberry fruit at a maximum of 9.6% TRR (1.1 mg eq/kg), in sorghum at a maximum of 1.7% TRR (0.014 mg eq/kg) and in forage at 3.6% TRR (0.14 mg eq/kg).

Environmental fate in soil

The Meeting received studies on hydrolysis, photolysis, terrestrial and aquatic soil metabolism and field dissipation for the investigation of the environmental fate.

In the photolysis study it was shown that quinclorac degraded slowly with a half-life of 162 days. The soil hydrolysis study showed that quinclorac was stable during the testing period 30 days and at the temperature 25 °C.

In aerobic soil metabolism studies in silt loam soils under laboratory conditions and an application rate of 0.375 kg ai/ha, quinclorac degraded slowly; no degradation was indicated 120 days after treatment. In another study at an application rate of 3.9 to 4.1 kg/ha, the half-life (DT_{50}) for quinclorac was estimated at 391 days in loamy sand and 168 days in a clay soil. In this study two major soil metabolites were detected; 2-hydroxyquinclorac, at a maximum of 12% AR and quinclorac methyl ester at a maximum of 7.8% AR. Other metabolites were present at levels below 10% AR.

In one tested aerobic aquatic system (rice field) at an application rate 3.75 kg ai/ha, quinclorac degraded to the metabolite 3-chloro-8-quinolilne carboxylic acid (BH 514-1) up to a maximum of 55.7% AR. Three additional fractions were present (not characterized) but present at less than 10% AR. The half-life of quinclorac in this system was 4.7 months and for the metabolite 3-chloroquinoline-8-carboxylic acid, 7.4 months. Under anaerobic conditions at the same application rates the same metabolites were formed but at a slower rate; there was 50% conversion of quinclorac to 3-chloroquinoline-8-carboxylic acid.

In one field dissipation study using a loamy sand soil, quinclorac was applied to bare soil with two applications of 2.8 kg ai/ha. DT_{50} and DT_{90} values for parent quinclorac were 126 days and > 360 days respectively following the first application (autumn), and DT_{50} and DT_{90} of 8 days and 26 days

respectively following the second application (summer). The maximum of the two metabolites were less than 5% TRR. The results indicate that quinclorac is tightly bound to the loamy sand soil.

One confined rotational metabolism study from crops rotated after flooded and non-flooded rice grown on silty clay was available. Quinclorac [2, 3, 4-^{14}C] was applied to flooded and non-flooded rice (primary crop) at a rate of 0.84 kg ai/ha in Mississippi, USA. After harvest of mature rice, the first rotational crops (wheat, mustard green and turnips) were planted 120 DAT followed by the second crops (sorghum, mustard green, soya beans and turnip) 360 DAT. The extractable radioactive residues were analysed for quinclorac and the metabolite 3-chloroquinoline-8-carboxylic acid (BH 514-1).

For the first rotational crops, maximum TRRs were 0.028 mg eq/kg for mustard plant, wheat seed, 0.025 mg eq/kg and turnip plant, 0.012 mg eq/kg. For the annual rotational crops, maximum TRRs were 0.014 mg eq/kg for mustard top, soya bean seed 0.017 mg eq/kg and for root and turnip root, 0.02 mg eq/kg. The metabolism of quinclorac by soya bean was qualitatively similar, although up to 62% TRR (0.01 mg eq/kg) was not extractable.

Quinclorac was the only major residue (>10% TRR but less than 0.05 mg eq/kg) detected in the examined rotational crops. Furthermore in the first rotational crops as well as the second rotational crops, TRRs were higher from crops grown under non-flooded conditions.

Another confined rotational metabolism study with one interval (120 days) was also available from crops planted after sorghum. Treatment levels to sorghum plants with 3-^{14}C-quinclorac were 0.53 kg ai/ha pre-emergence and 0.50 kg ai/ha post-emergence giving a total of 1.03 kg ai/ha (2 times GAP). The rotational crops mustard green, turnip and barley were planted 120 days after the last treatment of sorghum. The parent quinclorac was the major (up to 0.1 mg/kg) residue in all matrices. Quinclorac methyl ester was a minor metabolite below 5% in mustard green, turnip roots, and barley.

One field rotational crop study with rape seed planted after barley treated at 0.2 kg ai/ha the previous year was available. The application rate was below -25% critical GAP for cereals (0.29 kg ai/ha, wheat). The residues in rape seed at harvest analysed for parent quinclorac were below the LOQ of 0.05 mg/kg.

In the confined rotational studies, uptake of quinclorac and quinclorac methyl ester was observed in both first and second rotational crops. Residues were no more than 0.01 mg/kg (0.012 mg eq/kg) at the GAP rate.

In summary quinclorac is persistent in some soils and the amount, dependent on the season; residues from quinclorac in rotational crops may be found but generally at levels <.05 mg/kg.

Methods of residue analysis

The Meeting received analytical methods for the analysis of quinclorac residues in plant and animal matrices.

The extraction in lactating goat and laying hen was with acetone/0.1M NaOH. After clean-up, residues of parent quinclorac are determined by GC-ECD. The method is suitable for measuring residues of quinclorac in animal commodities with a LOQ of 0.05 mg/kg. It is not clear whether identified quinclorac represents quinclorac only or also includes quinclorac released from conjugates by the alkaline extraction method used.

The extraction in strawberry was with 1% acetic acid, in rice and wheat with acetone/0.1 M NaOH, in rape seed with acetone. After clean-up, residues of parent quinclorac in wheat, sorghum, rape seed, and strawberry were determined by HPLC-MS/MS or GC-ECD. Methods used for analysis of quinclorac in cereals may hydrolyse any quinclorac conjugates present. The LOQ ranged between 0.01–0.05 mg/kg.

The metabolite quinclorac methyl ester identified as a metabolite in rape seed and sorghum matrices is extracted with acetone and after clean-up determined by HPLC-MS/MS. The LOQ was 0.05 mg/kg.

A radiovalidation study showed that extraction with acetone/0.1 M NaOH converts quinclorac methyl ester partly into parent compound. For this reason, the parent is overestimated in samples containing quinclorac methyl ester. Methods D9708/1 (quinclorac) and R0036 (quinclorac) use acetone/0.1 M NaOH and are therefore not suitable of the determination of parent compound in oilseed rape seed and possibly other pulses and oilseeds, where the quinclorac methyl ester can be expected to be present.

In summary analytical methods are available for determining parent quinclorac in plant (cereals and fruit) and animal (lactating goat and hen) matrices and for the quinclorac methyl ester in plant (fruit and sorghum) matrices. However the methods for animal and cereal commodities use a hydrolysis step; indicating that the quinclorac residues measured may actually include quinclorac released from conjugates. Current analytical methods presented for oil seed rape are likely to overestimate quinclorac residues as the determination of quinclorac may also include some of its methyl ester.

Stability of residues in stored analytical samples

The Meeting received information on the storage stability of quinclorac and quinclorac methyl ester in plant matrices. Quinclorac (> 80% of spiked levels remained) was stable in rice and sorghum matrices for 38 months, in wheat grain for 26 months, and in cranberry fruit for 14 months. For quinclorac and quinclorac methyl ester no significant degradation was observed within 22 months in oilseed meal and oil.

For animal matrices no storage stability studies were provided.

Definition of the residue

In wheat and rice the parent quinclorac is the major residue present (above 80% TRR). Glucose conjugates, hydroxylated conjugates of quinclorac and hydroxyquinclorac were identified as minor metabolites (< 10% TRR) in wheat. In sorghum parent was also the major (> 73% TRR) residue present. The metabolite quinclorac methyl ester was also present (< 6% TRR) in sorghum.

In rape seed besides the parent, the metabolite quinclorac methyl ester was found as a significant metabolite (37%TRR).

In strawberry the parent quinclorac was the major residue present (> 98% TRR). Quinclorac methyl ester accounted for 9.6% TRR in fruit at the first harvest and was not detected in the third harvest

In rotational crop studies including mustard, barley and turnip in first rotation, uptake of residues identified as quinclorac (major) and quinclorac methyl ester (minor) was observed when analyzed and resulted in residues near the LOQ at GAP rate.

Thus based on available metabolism data parent quinclorac is the major residue in examined crops. The metabolite quinclorac methyl ester was a significant residue in rape seeds and was a minor residue in other primary and subsequent rotational crops analysed.

Analytical methods are available for determining parent quinclorac in plant (cereals and fruit) and quinclorac methyl ester in fruit and sorghum matrices.

Current analytical methods determining quinclorac and quinclorac methyl ester in rape seed is not suitable as they overestimate the level of parent present.

Taking into account that the methodology measuring quinclorac is also accounting for conjugates derived from hydrolysis during the extraction process, and that quinclorac is the major residue measured in plants, the Meeting decided that the residue definition should be as follows:

Definition of the residue for compliance with MRL for plant commodities: Quinclorac plus quinclorac conjugates

The Meeting noted that quinclorac methyl ester has a toxicological potency up to 10 times that of quinclorac and decided to include it in the residue definition for dietary intake.

Definition of the residue for estimating dietary intake for plant commodities: Quinclorac plus quinclorac conjugate plus quinclorac methyl ester expressed as quinclorac

In calculating residue values for dietary intake estimation the Meeting agreed to use the following formula: residues = (quinclorac +conjugate) + 10 × quinclorac methyl ester.

In lactating goat the major residue was quinclorac and the highest residues were found in liver and kidney with small amounts of other metabolite also found (less than 5% TRR).

For laying hen, the available data show that quinclorac is the only major residue in tissues and eggs.

In both species, measurement of the parent in the metabolism studies probably also includes conjugates of quinclorac as the extraction method used strong acid or alkali. This conclusion is supported by partitioning of residues in the animal feeding studies where quinclorac residues are more than ten times higher in fat tissue compared to muscle tissue.

The Meeting noted however that quinclorac residue was more than ten times higher in fat tissue compared to muscle tissue.

For quinclorac, a log Kow of -0.72 at pH 7 was reported suggesting residues of free quinclorac are water soluble.

The fact that the residue is generally found in the fat suggests that the actual tissue residue is not the parent molecule but may be a fatty acid conjugate of quinclorac.

Based on the above the Meeting decided the residue definition for compliance with MRLs and estimating the dietary intake should be as follows:

Definition of the residue for compliance with MRL and estimating the dietary intake for animal commodities: Quinclorac plus quinclorac conjugates.

The residue is fat soluble

Results of supervised residue trials on crops

Quinclorac is registered for use as a herbicide in many countries. The Meeting received supervised trial data for foliar application of quinclorac to rice, wheat, rape seed, sorghum, cranberry and rhubarb. The trials were conducted in USA and Canada. Frozen samples from the trials presented are covered by storage stability studies. The residue trials did not measure the methyl ester required for estimating dietary intakes.

The Meeting noted quinclorac methyl ester in oilseed equal level to quinclorac in the rape metabolism study and for cereals and fruit at levels up to10 percent of the parent, and agreed to use to the following formula to estimate levels for use in dietary intake calculations:

Plants except oilseed:

HR/STMR = (quinclorac + conjugate) + 10 x 0.1 (quinclorac + conjugate) = 2 × (quinclorac + conjugate)

Oil seed:

HR/STMR = (quinclorac + conjugate) + 10 x (quinclorac + conjugate) = 11 × (quinclorac + conjugate)

Cranberry

Data from supervised trials on cranberry from USA were presented to the Meeting. The critical GAP in USA is two foliar post-emergent applications of 0.28 kg ai/ha, with a 30 day interval and a PHI of 60 days.

In four independent trials from USA matching the critical GAP residues of quinclorac in cranberry fruit for MRL estimation were (n=4): 0.16, 0.17, 0.18, 0.67 mg/kg. The highest residue of 0.68 mg/kg was measured in an individual cranberry sample.

Residues for dietary intake estimation in cranberry fruit were (n=4): 0.32, 0.34, 0.36 and 1.34 mg/kg

Based on a data set from USA the Meeting estimated a maximum residue level, an STMR value and an HR value for quinclorac in cranberry fruit of 1.5 mg/kg, 0.35 mg/kg and 1.36 mg/kg, respectively.

Rhubarb

Data from supervised trials on rhubarb from USA were presented to the Meeting. The critical GAP in USA is two foliar post-emergence applications of 0.42 kg ai/ha, with a 30 day interval and a PHI of 30 days.

In three independent trials from USA matching the critical GAP residues in rhubarbs for MRL estimation were (n=3) 0.11, 0.18, 0.21 mg/kg. The highest residue of 0.23 mg/kg was measured in an individual rhubarb sample.

Residues for dietary intake estimation in rhubarbs were (n=3): 0.22, 0.36 and 0.42 mg/kg.

Based on a data set from USA the Meeting estimated a maximum residue level, an STMR value and an HR value for quinclorac in rhubarb of 0.5 mg/kg, 0.36 mg/kg and 0.46 mg/kg, respectively.

Rice

Data from supervised trials on rice from USA were presented to the Meeting. The critical GAP in USA is one application of 0.29-0.54 kg ai/ha and a PHI of 40 days. The use can be soil application, pre-planting or pre-emergence (dryland rice) or post-emergence broadcast application after the 2-leaf stage (but before heading) on dryland and water seeded rice. Only six trials matched the GAP and an estimation of maximum residue level was not made.

Wheat

Data from supervised trials on wheat from USA and Canada were presented to the Meeting. The critical GAP in Canada is one post-emergent foliar application of 0.135 kg ai/ha and a PHI of 80 days. Only six trials matched the GAP and an estimation of maximum residue level was not made.

Sorghum grain

Data from supervised trials from USA were presented to the Meeting. The critical GAP is one application pre- and /or post-emergence (at maximum 12 cm height limit) as long as the seasonal maximum amount of 0.7 kg ai/ha is not exceeded. The maximum post-emergent application rate is 0.56 kg ai/ha. The trials did not match the critical GAP and an estimation of maximum residue level was not made.

Rape seed (canola)

A registered use with a supporting label from Canada was presented with one foliar application at 2-6 leaf stage of 0.1 kg ai/ha and a PHI of 60 days. Data from seventeen independent supervised trials from Canada (16) and USA (1) supporting this GAP were presented to the Meeting.

The analytical method used in the trials method D9708/1 for determining quinclorac and method D9806 for determining quinclorac methyl ester (BH514-Me) overestimates the level of the parent. Therefore the trials cannot be used for estimating the maximum residue level.

Animal feeds

Strawberry and rhubarbs are not used as animal feeds.

Fate of residues during processing

The Meeting received information on the fate of incurred residues of quinclorac during the processing of rice, wheat, rape seed and sorghum. Supporting trials with matching GAPs were not available and therefore the studies were not considered by the current Meeting.

Residues in animal commodities

Farm animal feeding studies

The Meeting received feeding studies on residue levels of quinclorac plus quinclorac conjugates in laying hens and lactating cows.

For lactating cows three groups of were dosed daily at levels of 1, 10, 50, or 500 ppm in the diet (0.002, 0.02, 0.09 and 0.9 mg/kg bw) for 28 consecutive days.

In milk residues were only detected in the 500 ppm group. A plateau level was reached in this group after 4 days (mean: 0.032 mg/kg).

In muscle residues were only detected in the 500 ppm group, 0.01–0.037 mg/kg (mean: 0.027 mg/kg).

In fat two different tissues were analyzed (peritoneal and subcutaneous fat). The highest residues were found in subcutaneous fat with < 0.01–0.013 (mean: 0.005 mg/kg) for the 1 ppm group, < 0.01 mg/kg for the 10 ppm group. In peritoneal fat with < 0.01–0.01 mg/kg for the 1 ppm group, < 0.01–0.023 mg/kg for the 10 ppm group.

In liver residues were < 0.01–0.01 mg/kg for the 1 ppm group, 0.01-0.02 mg/kg for the 10 ppm group.

In kidney residues were < 0.01–0.016 mg/kg for the 1 ppm group, 0.062-0.082 mg/kg for the 10 ppm group.

For laying hens three groups of animals were dosed with rates of 1, 10 and 100 ppm by dry weight in the feed (0.07, 0.7 and 7 mg/kg bw/day) for 28 consecutive days. Eggs were collected throughout the whole study and tissues were collected on day 29 after the last dose.

In eggs a clear plateau level was not reached in any dosing group. For the 1 and 10 ppm the residues were below 0.01 mg/kg during the whole experiment.

In dark and light muscle residues were 0.0–0.005 mg/kg (max mean: 0.002 mg/kg) for the 1 ppm group.

In skin + fat total residues in fat for the 1 ppm group was 0.0–0.018 mg/kg.

In liver residues were: 0.0–0.009 mg/kg for the 1 ppm group. In kidney residues were 0.002–0.059 mg/kg for the 1 ppm group.

Animal commodities residue levels estimation

Strawberry and rhubarbs are not used as animal feed and therefore estimation of residue levels was not made for animal commodities.

RECOMMENDATIONS

On the basis of the data from supervised residue trials the Meeting concluded that the residue levels listed in Annex 1 are suitable for establishing maximum residue limits and for the IEDI and IESTI assessment.

Definition of the residue for compliance with MRL for plant commodities: quinclorac plus quinclorac conjugates

Definition of the residue for estimating dietary intake: quinclorac plus quinclorac conjugate plus quinclorac methyl ester expressed as quinclorac

Definition of the residue for compliance with MRL and estimating the dietary intake for animal commodities: quinclorac plus quinclorac conjugates

The residue is fat soluble.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intake of quinclorac for the 17 GEMS/Food regional diets based on estimated STMRs were 0% of the maximum ADI of 0.4 mg/kg bw for the sum of quinclorac, its conjugates plus 10× quinclorac methyl ester, expressed as quinclorac (see Annex 3 of the 2015 Report). The Meeting concluded that the long-term dietary intake of residues of quinclorac is unlikely to present a public health concern.

Short-term intake

The International Estimated Short Intake (IESTI) for quinclorac was calculated for commodities for which STMRs or HRs were estimated and for which consumption data were available. The results are shown in Annex 4 to the 2015 Report. The ARfD for quinclorac, its conjugates plus 10 × quinclorac methyl ester, expressed as quinclorac is 2 mg/kg bw and the IESTIs varied from 0–1% of the ARfD for children and the general population.

The Meeting concluded that the short-term intake of residues of quinclorac when used in ways that have been considered by the JMPR is unlikely to present a public health concern.