5. EVALUATION OF DATA FOR ACCEPTABLE DAILY INTAKE AND ACUTE REFERENCE DOSE FOR HUMANS, MAXIMUM RESIDUE LEVELS AND SUPERVISED TRIALS MEDIAN RESIDUE VALUES

5.1 ABAMECTIN (177)

TOXICOLOGY

Abamectin is the International Organization for Standardization (ISO)–approved common name for a mixture of the components avermectin B_{1a} (≥ 80%) [(2a*E*,4*E*,8*E*)-(5′*S*,6*S*,6′*R*,7*S*,11*R*,13*S*,15*S*,17a*R*,20*R*,20a*R*,20b*S*)-6′-[(*S*)-*sec*-butyl]-5′,6,6′,7,10,11,14,15,17a,20,20a,20b-dodecahydro-20,20b-dihydroxy-5′,6,8,19-tetramethyl-17-oxospiro[11,15-methano-2*H*,13*H*,17*H*-furo[4,3,2-pq][2,6]benzodioxacyclooctadecin-13,2′-[2*H*]pyran]-7-yl 2,6-dideoxy-4-*O*-(2,6-dideoxy-3-*O*-methyl-α-L-arabino-hexopyranosyl)-3-*O*-methyl-α-L-arabino-hexopyranoside] and avermectin B_{1b} (≤ 20%) [(2a*E*,4*E*,8*E*)-(5′*S*,6*S*,6′*R*,7*S*,11*R*,13*S*,15*S*,17a*R*,20*R*,20a*R*,20b*S*)-5′,6,6′,7,10,11,14,15,17a,20,20a,20b-dodecahydro-20,20b-dihydroxy-6′-isopropyl-5′,6,8,19-tetramethyl-17-oxospiro[11,15-methano-2*H*,13*H*,17*H*-furo[4,3,2-pq][2,6]benzodioxacyclooctadecin-13,2′-[2*H*]pyran]-7-yl 2,6-dideoxy-4-*O*-(2,6-dideoxy-3-*O*-methyl-α-L-arabino-hexopyranosyl)-3-*O*-methyl-α-L-arabino-hexopyranoside] (International Union of Pure and Applied Chemistry [IUPAC]), which has the Chemical Abstracts Service (CAS) number 71751-41-2. Abamectin is a macrocyclic lactone product derived from the soil microorganism *Streptomyces avermitilis*. Because of the very similar biological and toxicological properties of the B_{1a} and B_{1b} components, they can be considered to be equivalent. Abamectin is used as an insecticide and acaricide.

Abamectin was previously evaluated by JMPR in 1992, 1994, 1995 and 1997. In 1997, an ADI of 0–0.002 mg/kg bw was established based on the NOAEL of 0.12 mg/kg bw per day for offspring toxicity in a two-generation reproductive toxicity study in rats, with the application of a reduced safety factor of 50 to account for the higher sensitivity of neonatal rats to abamectin, and the NOAEL of 0.24 mg/kg bw per day from the 1-year toxicity study in dogs, with the application of a safety factor of 100. The ADI was deemed to be appropriate for the sum of abamectin and its 8,9-*Z* isomer (a photodegraded product of abamectin), as the isomer was not expected to be of higher toxicity than abamectin. An ARfD was not established when abamectin was last evaluated by JMPR, as that evaluation pre-dated current JMPR guidance for the establishment of ARfDs for pesticides.

In 1996, the forty-seventh meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) established an ADI of 0–0.001 mg/kg bw for abamectin used as a veterinary drug, based on the NOAEL of 0.12 mg/kg bw per day in the study on reproductive toxicity in rats and application of a safety factor of 100.

Abamectin was reviewed by the present Meeting as part of the periodic review programme of CCPR.

The majority of the toxicology studies were conducted with abamectin technical, which is a mixture of avermectin B_{1a} and avermectin B_{1b} (approximately 90:10). Some studies (mainly those requiring radiolabel) were conducted with either avermectin B_{1a} or avermectin B_{1b}.

All critical studies were conducted in compliance with good laboratory practice (GLP), unless otherwise specified.

Susceptibility of CF-1 mice and neonatal rats to abamectin

In mammals, abamectin is a substrate for P-glycoprotein, which is a member of the adenosine triphosphate (ATP)–binding cassette subfamily B (ABCB1), also known as multidrug resistance protein 1 (MDR1). P-glycoprotein is extensively expressed in the intestinal epithelium, liver cells, cells of the proximal tubule of the kidney and capillary endothelial cells of the brain (blood–brain

barrier), placenta, ovaries and testes. As an efflux transporter, P-glycoprotein acts as a protective barrier to keep xenobiotics out of the body by excreting them into bile, urine and intestinal lumen and prevents the accumulation of these compounds in the brain and gonads, as well as the fetus. Therefore, some test animals (e.g. CF-1 mice) in which genetic polymorphisms compromise P-glycoprotein expression are particularly susceptible to abamectin-induced toxicity. As a result, studies on CF-1 mice were not considered relevant for the human risk assessment.

In rats, P-glycoprotein was undetectable in the embryo and early stages of postnatal development. In the brush border of intestinal epithelial cells, expression of P-glycoprotein was absent to minimal on postnatal day (PND) 8 and was more intense but did not reach adult levels by PND 20. In the brain capillaries, expression of P-glycoprotein was minimal in fetuses on gestation day (GD) 20 and in younger pups until PND 11, with subsequent increases to a plateau at adult levels by PNDs 20–28. In humans, P-glycoprotein expression in fetal intestinal epithelium and brain capillaries is at the adult level at week 28 of gestation, and therefore results of reproductive toxicity studies in neonatal rats should be interpreted accordingly.

Biochemical aspects

In rats, orally administered radiolabelled avermectin B_{1a} was rapidly and almost completely absorbed, based on a comparison with urinary excretion after intravenous administration. Maximum concentrations in blood were achieved within 4–8 hours after administration. Radiolabel was widely distributed. Elimination of radiolabel occurred predominantly by non-biliary excretion into the gastrointestinal tract and excretion in the faeces, whereas urinary excretion accounted for only 0.5–1.4% of the dose. Elimination accounted for 80–101% of the administered dose within 96 hours. Rate of oral absorption, tissue distribution and excretion were independent of the dose level, treatment regimen and/or sex; however, the depletion of tissue residues was approximately 2-fold more rapid in males than in females. There was no evidence for tissue accumulation on repeated administration.

In toxicokinetic studies in genotyped subpopulations of CF-1 mice (i.e. mdr1a P-glycoprotein–deficient mice and mice with normal expression of mdr1a P-glycoprotein), plasma levels of avermectin B_{1a} were higher in mdr1a P-glycoprotein–deficient mice than in mice with normal expression of mdr1a P-glycoprotein. Distribution and elimination appeared to be slower in mdr1a P-glycoprotein–deficient mice, with concentrations in the brain tissue of mdr1a P-glycoprotein–deficient mice up to 150 times higher than in mice with normal expression of mdr1a P-glycoprotein. The primary route of excretion was via faeces.

Metabolism of avermectin B_{1a} in the rat was moderate to extensive and proceeded predominantly via demethylation, hydroxylation, cleavage of the oleandrosyl ring and oxidation reactions. The metabolite pattern in urine, faeces and bile was complex but qualitatively independent of the sex and dose, with some quantitative variations. Eleven metabolites were isolated. Unchanged avermectin B_{1a} and the metabolites 3″-*O*-desmethyl abamectin B_{1a} [3″DM], 24-hydroxymethyl abamectin B_{1a} [24aOH], 27-hydroxymethyl abamectin B_{1a} [27OH], 3″-*O*-desmethyl-24-hydroxymethyl abamectin B_{1a} [3″DM,24aOH] and 3″-*O*-desmethyl-27-hydroxymethyl abamectin B_{1a} [3″DM,27OH] represented the majority of the faecal radioactivity.

Toxicological data

Abamectin was of high acute oral toxicity, with a median lethal dose (LD_{50}) of 8.7 mg/kg bw in rats with sesame oil as the vehicle and an LD_{50} of 214 mg/kg bw in rats with water as the vehicle. The acute inhalation toxicity of abamectin was also high, with a median lethal concentration (LC_{50}) of > 0.034 and < 0.21 mg/L in rats. The dermal LD_{50} in both rats and rabbits was greater than 2000 mg/kg bw. Abamectin was not irritating to the eye or the skin of rabbits. It was not a dermal sensitizer in guinea-pigs.

In short- and long-term toxicity studies performed in rats and dogs, clinical signs observed as a response to treatment were tremors in rats and dogs and mydriasis or absent pupil reflex in dogs. There were no histopathological changes in the tissues of the central and peripheral nervous systems. The clinical signs are considered to be an exaggerated pharmacological response to the interaction of

abamectin with the gamma-aminobutyric acid (GABA)–benzodiazepine receptor chloride channel complex. Treatment-related histopathological alterations in dogs were confined to the hepatobiliary system. Based on the severity of clinical signs of neurotoxicity and mydriasis and the doses at which death occurs, the dog was more sensitive than the rat to abamectin.

In an 8-week dietary toxicity study in rats with mean achieved dose levels of 0, 0.5, 1.2, 1.9, 2.2 and 5.0 mg/kg bw per day, death occurred at a dose level of 5.0 mg/kg bw per day. The NOAEL was 1.2 mg/kg bw per day, based on the occurrence of clinical signs and reduced body weight gain at 1.9 mg/kg bw per day and above. No 90-day toxicity study in rats was provided.

In 12-week, 18-week and 53-week toxicity studies in dogs, a very steep dose–response curve for abamectin was noted. In the 12-week feeding study in dogs with dietary concentrations of abamectin adjusted to provide dose levels of 0, 0.25, 0.5, 1.0 and 4.0/2.0 mg/kg bw per day, the NOAEL was 0.5 mg/kg bw per day, based on the occurrence of mydriasis starting in week 1 of treatment at 1.0 mg/kg bw per day. Markedly reduced feed consumption, body weight loss and clinical signs of intoxication were observed at 2.0 mg/kg bw per day and above.

In the 18-week gavage study in dogs administered abamectin at a dose of 0, 0.25, 0.5, 2.0 or 8.0 mg/kg bw per day, the NOAEL was 0.25 mg/kg bw per day, based on mortality, clinical signs of toxicity, reduced body weight gain or body weight loss and histopathological changes in the liver at 0.5 mg/kg bw per day. Signs of toxicity were observed starting on day 7 at 0.5 mg/kg bw per day, on day 3 at 2.0 mg/kg bw per day and on day 1 (within 3 hours after dosing) at 8.0 mg/kg bw per day.

In the 53-week feeding study in dogs with dietary concentrations of abamectin adjusted to provide dose levels of 0, 0.25, 0.5 and 1.0 mg/kg bw per day, the NOAEL was 0.25 mg/kg bw per day, based on mydriasis at 0.5 mg/kg bw per day. Signs of toxicity were observed starting in the first week at 0.5 and 1.0 mg/kg bw per day.

The overall NOAEL for the three dog studies was 0.25 mg/kg bw per day, based on mortality (one animal), clinical signs of toxicity (including mydriasis) and reduced body weight gain or body weight loss at 0.5 mg/kg bw per day.

In a 93-week toxicity and carcinogenicity study in mice, with dietary concentrations of abamectin adjusted to provide dose levels of 0, 2.0, 4.0 and 8.0 mg/kg bw per day, the NOAEL was 4.0 mg/kg bw per day, based on the increased mortality in males and reduced body weight gain in females at 8.0 mg/kg bw per day. There was no increase in tumour incidence.

In a 104-week chronic toxicity and carcinogenicity study in rats, with dietary concentrations of abamectin adjusted to provide dose levels of 0, 0.75, 1.5 and 2.0 mg/kg bw per day, the NOAEL was 1.5 mg/kg bw per day, based on the occurrence of clinical signs of toxicity at 2.0 mg/kg bw per day. There was no increase in tumour incidence.

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

Abamectin has been tested for genotoxicity in an adequate range of assays, both in vitro and in vivo. There was no evidence of genotoxicity.

The Meeting concluded that abamectin is unlikely to be genotoxic.

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

In a two-generation reproductive toxicity study in rats, abamectin (in sesame oil) was administered orally by gavage at a dose level of 0, 0.05, 0.12 or 0.40 mg/kg bw per day. The NOAEL for parental toxicity and reproductive toxicity was 0.40 mg/kg bw per day, the highest dose tested. For offspring toxicity, the NOAEL was 0.12 mg/kg bw per day, based on increased pup mortality, retarded weight gain in both F_1 and F_2 generation progeny and increased incidence of transient retinal folds in the eyes of F_2 generation weanlings at 0.40 mg/kg bw per day.

In a developmental toxicity study in rats, abamectin (in sesame oil) was administered orally by gavage at a dose level of 0, 0.4, 0.8 or 1.6 mg/kg bw per day. The NOAEL for maternal toxicity and embryo/fetal toxicity was 1.6 mg/kg bw per day, the highest dose tested.

In a developmental toxicity study in rabbits, abamectin (in sesame oil) was administered orally by gavage at a dose level of 0, 0.5, 1.0 or 2.0 mg/kg bw per day. The NOAEL for maternal toxicity was 1.0 mg/kg bw per day, based on the occurrence of severe maternal toxicity and body weight loss during gestation at 2.0 mg/kg bw per day. The NOAEL for embryo and fetal toxicity was 1.0 mg/kg bw per day, based on increased incidences of external malformations (cleft palate, omphalocele, clubbed forefeet) and incomplete ossification of sternebrae and metacarpals at 2.0 mg/kg bw per day.

The Meeting concluded that abamectin is teratogenic in rabbits, but not in rats.

In an acute neurotoxicity study in rats, abamectin (in sesame oil) was administered orally by gavage at a dose level of 0, 0.5, 1.5 or 6 mg/kg bw. The NOAEL for acute neurotoxicity was 0.5 mg/kg bw, based on a reduced splay reflex at 1.5 mg/kg bw. This change was seen at 6–7 hours after dosing on day 1 and was consistent with the neurotoxic effects observed at higher doses. No neuropathological changes were observed at dose levels up to 6 mg/kg bw.

In a 90-day neurotoxicity study in rats, abamectin (in sesame oil) was administered orally by gavage at a dose level of 0, 0.4, 1.6 or 4.0 mg/kg bw per day. The NOAEL for systemic toxicity and neurotoxicity was 1.6 mg/kg bw per day, based on reduced body weights in females, clinical signs in both sexes (irregular breathing, upward curvature of the spine, reduced righting reflex, reduced splay reflex) and changes in hindlimb grip strength in females at 4.0 mg/kg bw per day.

In a developmental neurotoxicity study in rats, abamectin (in sesame oil) was administered orally by gavage to parent females once daily from day 7 of gestation until day 22 postpartum at a dose level of 0.12, 0.20 or 0.40 mg/kg bw per day. In parental females, body weights and feed consumption were slightly increased at all dose levels. In offspring, lower body weights post-weaning and hence a delay in time of vaginal opening were observed at 0.20 mg/kg bw per day and above. The NOAEL was 0.12 mg/kg bw per day. There was no effect on function or morphology of the nervous system at dose levels up to 0.40 mg/kg bw per day, the highest dose tested.

In a supplementary developmental neurotoxicity study in rats performed to provide brain morphometry data, abamectin (in sesame oil) was administered orally by gavage to parent females once daily from day 7 of gestation until day 22 postpartum at a dose level of 0.12, 0.20 or 0.40 mg/kg bw per day. In parental females, body weights and feed consumption were slightly increased at all dose levels during gestation. In offspring at 0.40 mg/kg bw per day, clinical signs and increased mortality were observed in the pre-weaning period, and therefore all dams and pups in this group were removed from the study on days 15–38 postpartum. At 0.20 mg/kg bw per day, body weights of pups post-weaning were statistically significantly lower and the time of vaginal opening was statistically significantly later compared with the control group. The NOAEL for offspring toxicity was 0.12 mg/kg bw per day. There was no effect on function or morphology of the nervous system at dose levels up to 0.40 mg/kg bw per day, the highest dose tested.

In a gavage study in Rhesus monkeys, the most sensitive indicator of abamectin toxicity was emesis, as clinical signs of toxicity seen in mice and rats (tremors and convulsions) did not occur. The minimum toxic dose of abamectin was 2.0 mg/kg bw, and the NOAEL was 1.0 mg/kg bw.

The Meeting concluded that abamectin is neurotoxic.

Toxicological data on metabolites and/or degradates

The 8,9-*Z* isomer of abamectin (also referred to as the Δ-8,9-isomer, NOA 427011 and L-652,280) is a photodegraded product of abamectin.

An exploratory acute oral toxicity study with the 8,9-*Z* isomer of abamectin B_{1a} in CD-1 mice and CF-1 mice gave LD_{50} values of 217 and 20 mg/kg bw, respectively.

The 8,9-*Z* isomer of abamectin B_{1a} did not induce gene mutations in bacteria, with or without metabolic activation.

In a one-generation reproductive toxicity study with the 8,9-*Z* isomer of abamectin B_{1a} in rats using dose levels of 0, 0.06, 0.12 and 0.40 mg/kg bw per day, the NOAEL for maternal toxicity, reproductive effects and effects on offspring was 0.40 mg/kg bw per day, the highest dose tested.

In a developmental toxicity study with the 8,9-*Z* isomer of abamectin B_{1a} in CD-1 mice using dose levels of 0, 0.75, 1.5 and 3.0 mg/kg bw per day, the NOAEL for maternal effects and embryo/fetal toxicity, including teratogenicity, was 3.0 mg/kg bw per day, the highest dose tested.

In a developmental toxicity study with the 8,9-*Z* isomer of abamectin B_{1a} in rats using dose levels of 0, 0.25, 0.5 and 1.0 mg/kg bw per day, the NOAEL for maternal effects and embryo/fetal toxicity, including teratogenicity, was 1.0 mg/kg bw per day, the highest dose tested.

The Meeting concluded that the 8,9-*Z* isomer of abamectin B_{1a} is of no greater toxicity than the parent abamectin B_{1a}.

A metabolite, 24-hydroxymethyl abamectin, was found in liver and milk in smaller proportions than the parent. The Meeting concluded that 24-hydroxymethyl abamectin is of no greater toxicity than the parent, because it has been found in amounts of more than 10% in excreta and therefore has been tested in studies with the parent.

Human data

From reports on health records of manufacturing plant personnel, no adverse health effects were noted. A number of reports on intentional poisoning in humans available in the literature showed low susceptibility of humans to abamectin, with variable dose-related neurological signs and symptoms.

Although administration of abamectin to mice, rats and dogs at relatively low dose levels was associated with clinical signs of central nervous system toxicity (including mydriasis, tremors, convulsions, ataxia and bradycardia), it was shown that Rhesus monkeys and humans are less sensitive to abamectin, at least following acute exposure.

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

Toxicological evaluation

The Meeting established a new ADI of 0–0.001 mg/kg bw, based on the NOAEL of 0.12 mg/kg bw per day for lower body weights and delayed time of vaginal opening observed at 0.20 mg/kg bw per day in post-weaning pups in the two developmental neurotoxicity studies in rats, using a safety factor of 100. The Meeting withdrew the existing ADI of 0–0.002 and also concluded that the additional information available to this Meeting regarding the critical period in development and species differences does not justify the application of a reduced safety factor to the NOAEL.

The ADI also applies to the 8,9-*Z* isomer and the 24-hydroxymethyl metabolite of abamectin.

The Meeting established an ARfD of 0.003 mg/kg bw, based on the overall NOAEL of 0.25 mg/kg bw per day for clinical signs in dogs (mydriasis) observed in the first week of treatment at 0.5 mg/kg bw per day. This ARfD also applies to the 8,9-*Z* isomer and the 24-hydroxymethyl metabolite of abamectin.

A toxicological monograph was prepared.

Levels relevant to risk assessment of abamectin and 8,9-Z isomer of abamectin

Species	Study	Effect	NOAEL	LOAEL
Abamectin				
Mouse	Ninety-three-week study of toxicity and carcinogenicity[a]	Toxicity	4.0 mg/kg bw per day	8.0 mg/kg bw per day
		Carcinogenicity	8.0 mg/kg bw per day[b]	–

Species	Study	Effect	NOAEL	LOAEL
Rat	Two-year study of toxicity and carcinogenicity[a]	Toxicity	1.5 mg/kg bw per day	2.0 mg/kg bw per day
		Carcinogenicity	2.0 mg/kg bw per day[b]	–
	Two-generation reproductive toxicity study[c]	Reproductive toxicity	0.40 mg/kg bw per day[b]	–
		Parental toxicity	0.40 mg/kg bw per day[b]	–
		Offspring toxicity	0.12 mg/kg bw per day	0.40 mg/kg bw per day
	Developmental toxicity study[c]	Maternal toxicity	1.6 mg/kg bw per day[b]	–
		Embryo and fetal toxicity	1.6 mg/kg bw per day[b]	–
	Acute neurotoxicity study[a]	Neurotoxicity	0.5 mg/kg bw	1.5 mg/kg bw
	Developmental neurotoxicity studies[a,d]	Developmental neurotoxicity	0.40 mg/kg bw[b]	–
		Toxicity	0.12 mg/kg bw	0.20 mg/kg bw
Rabbit	Developmental toxicity study[c]	Maternal toxicity	1.0 mg/kg bw per day	2.0 mg/kg bw per day
		Embryo and fetal toxicity	1.0 mg/kg bw per day	2.0 mg/kg bw per day
Dog	Twelve-week,[a] 18-week[c] and 53-week[a] studies of toxicity[d]	Toxicity	0.25 mg/kg bw per day	0.5 mg/kg bw per day
8,9-*Z* isomer of abamectin				
CD-1 mice	Developmental toxicity study[c]	Maternal toxicity	3.0 mg/kg bw per day[b]	–
		Embryo and fetal toxicity	3.0 mg/kg bw per day[b]	–
Rat	One-generation study of reproductive toxicity[a]	Reproductive toxicity	0.40 mg/kg bw per day[b]	–
		Parental toxicity	0.40 mg/kg bw per day[b]	–
		Offspring toxicity	0.40 mg/kg bw per day[b]	–
Rat	Developmental toxicity study[c]	Maternal toxicity	1.0 mg/kg bw per day[b]	–
		Embryo and fetal toxicity	1.0 mg/kg bw per day[b]	–

[a] Dietary administration.

[b] Highest dose tested.

[c] Gavage administration.

[d] Two or more studies combined.

Estimate of acceptable daily intake (ADI)

0–0.001 mg/kg bw

Estimate of acute reference dose (ARfD)

0.003 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 abamectin

Rate and extent of oral absorption	Rapid, absorption almost complete, T_{max} 4–8 h
Dermal absorption	No data
Distribution	Widely distributed
Potential for accumulation	None
Rate and extent of excretion	> 80% within 96 h, almost exclusively in faeces
Metabolism in animals	Moderate to extensive; by demethylation, hydroxylation, cleavage of the oleandrosyl ring and oxidation reactions
Toxicologically significant compounds in animals and plants	Abamectin, 8,9-*Z* isomer, 24-hydroxymethyl abamectin
Acute toxicity	
Rat, LD_{50}, oral	8.7 mg/kg bw
Rat, LD_{50}, dermal	> 2 000 mg/kg bw
Rat, LC_{50}, inhalation	> 0.034 and < 0.21 mg/L
Rabbit, dermal irritation	Not irritating
Rabbit, ocular irritation	Not irritating
Guinea-pig, dermal sensitization	Not sensitizing (Magnusson and Kligman test)
Short-term studies of toxicity	
Target/critical effect	Nervous system/clinical signs, mortality
Lowest relevant oral NOAEL	0.25 mg/kg bw (dog)
Lowest relevant dermal NOAEL	No data
Lowest relevant inhalation NOAEC	0.5 µg/L (30-day rat study)
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	Increased mortality in males and reduced weight gain (mouse), clinical signs (rat)
Lowest relevant NOAEL	1.5 mg/kg bw per day (rat)
Carcinogenicity	Not carcinogenic in mice or rats[a]
Genotoxicity	
	No evidence of genotoxicity[a]
Reproductive toxicity	
Target/critical effect	No reproductive effects

Lowest relevant parental NOAEL	0.4 mg/kg bw per day (highest dose tested; rat)
Lowest relevant offspring NOAEL	0.12 mg/kg bw per day (rat)
Lowest relevant reproductive NOAEL	0.4 mg/kg bw per day (highest dose tested; rat)
Developmental toxicity	
Target/critical effect	External malformations at maternally toxic dose (rabbit)
Lowest relevant maternal NOAEL	1.0 mg/kg bw per day (rabbit)
Lowest relevant embryo/fetal NOAEL	1.0 mg/kg bw per day (rabbit)
Neurotoxicity	
Acute neurotoxicity NOAEL	0.5 mg/kg bw (rat)
Subchronic neurotoxicity NOAEL	1.6 mg/kg bw per day (rat)
Developmental neurotoxicity NOAEL	0.40 mg/kg bw per day (highest dose tested; rat)
Studies on 8,9-*Z* isomer (photodegraded product)	
Developmental toxicity	
Target/critical effect	No developmental effects
Lowest relevant maternal NOAEL	3.0 mg/kg bw per day (highest dose tested; CD-1 mouse)
Lowest relevant embryo/fetal NOAEL	3.0 mg/kg bw per day (highest dose tested; CD-1 mouse)
Lowest relevant maternal NOAEL	1.0 mg/kg bw per day (highest dose tested; rat)
Lowest relevant embryo/fetal NOAEL	1.0 mg/kg bw per day (highest dose tested; rat)
Reproductive toxicity	
Target/critical effect	No reproductive effects
Lowest relevant parental NOAEL	0.4 mg/kg bw per day (highest dose tested; rat)
Lowest relevant offspring NOAEL	0.4 mg/kg bw per day (highest dose tested; rat)
Lowest relevant reproductive NOAEL	0.4 mg/kg bw per day (highest dose tested; rat)

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

Summary

	Value	Study	Safety factor
ADI	0–0.001 mg/kg bw	Developmental neurotoxicity studies (rat)	100
ARfD	0.003 mg/kg bw	Twelve-, 18- and 53-week toxicity studies (dog)	100

RESIDUE AND ANALYTICAL ASPECTS

Abamectin is a broad-spectrum acaricide with additional insecticidal action on a limited number of insects. Abamectin was firstly evaluated by JMPR in 1992 (T,R), and was scheduled at the Forty-sixth Session of the CCPR (2014) for the periodic re-evaluation of toxicology and residues by the 2015 JMPR. For the residue evaluation, data were submitted on physical and chemical properties, environmental fate, metabolism on plants and lactating goats, analytical methods, GAP, supervised trials on fruits, vegetables, nuts, beans, coffee, cotton and cereals, processing studies and cow feeding studies.

Abamectin is a mixture containing ≥ 80% avermectin B_{1a} and ≤ 20% avermectin B_{1b}. The absolute stereochemistry of both compounds is known and defined at each chiral centre and stereogenic carbon-carbon double bond by their IUPAC nomenclature. Abamectin (> 98% purity) has a low solubility in water (1.2 mg/L at 7.6 pH and 25 °C), is soluble in most organic solvents (23 g/L in toluene up to 470 g/L in ethyl acetate) and has a log K_{ow} of 4.4.

Abamectin is also used as an anthelmintic drug in veterinary medicine. The JECFA residue definition for the compound is avermectin B_{1a}.

The abamectin structures and the main metabolites and degradates found in water, soil, plants and animals are shown below.

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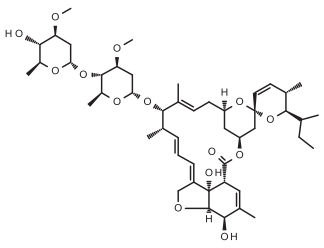
<td> 
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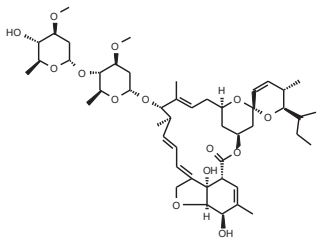
<td> 
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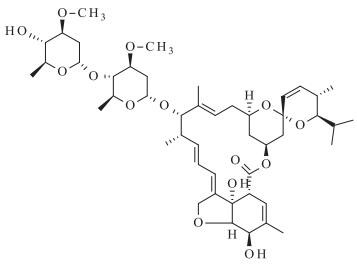
<td> 
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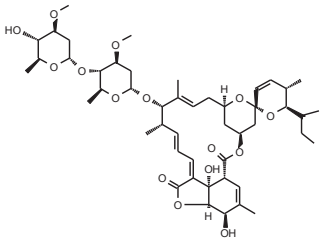
<td> 
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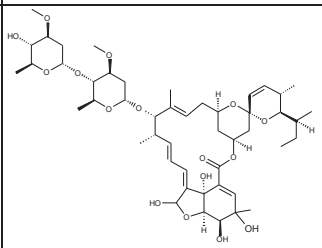
<td> 
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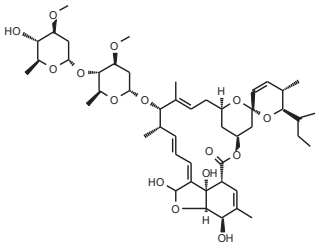
<td> 
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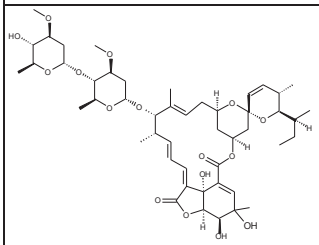
<td> 
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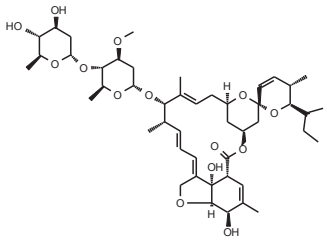
<td> 
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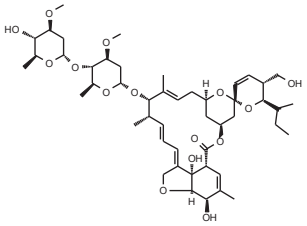
<td> 
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Environmental fate

Various studies were conducted to evaluate the aerobic degradation of [^{14}C- an/or ^{3}H-] avermectin B_{1a} in different non-sterile soils in the dark under various conditions (application rate, temperature and water capacity) over a period of up to 196 days. Avermectin B_{1a} degraded in soils with a half-life ranging from 12 to 52 days, and a mean of 29 ± 14 days (n=14). The degradation pathway occurs via hydroxylation or oxidation in the C-8α position, with 8α-hydroxy-avermectin B_{1a} being the major metabolite (up to 18% of the applied radioactivity, AR), present as an equilibrium mixture between the hemiacetal and the ring cleaved aldehyde form. The oxidation product 8α-oxo-avermectin B_{1a} was found at a maximum of 14% AR. Further hydroxylation in the C-4 position resulted in two additional identified metabolites, 4,8α-dihydroxy-avermectin B_{1a} and 8α-oxo-4-hydroxy-avermectin B_{1a}, each at < 10% AR. 4,8α-dihydroxy-avermectin B_{1a} is also present in an equilibrium mixture as the hemiacetal and the aldehyde forms. At least 25 other residues were also formed at low levels, each representing < 10%. The non-extracted residues and volatile fractions (CO_2), reached their maximum at the end of

the incubation period (44 and 28% AR, respectively). About 6% AR was released by harsh extraction of non-extracted residues, mostly humic, fulvic and humin acids, with only minor amounts identified as avermectin B_{1a}.

Soil photolysis studies demonstrated a similar degradation pattern, except that under the influence of light, avermectin B_{1a} initially isomerises to the 8,9-Z isomer before degrading, mainly to 8α-hydroxy-avermectin B_{1a} and 8α-oxo-avermectin B_{1a} (up to 4.7% AR). The half-life in these studies were 21–22 days. Photolysis significantly increases the rate of degradation of avermectin B_{1a}, as the dark controls showed a half-life of 119 days.

[^{3}H-avermectin B_{1a}] was stable to hydrolysis at pH 4 to 7 under sterile conditions, minimal hydrolysis was observed at pH 9 (DT_{50} of 380 days at 20 °C), with one major transient non-polar degradate 2-epi-avermectin B_{1a} being observed. At 60 °C, this degradate reached a maximum of 25%AR by Day 11 and then degraded with a DT_{50} of 1.5 days. [23-^{14}C-avermectin B_{1a}] degraded in water under light to 8,9-Z avermectin B_{1a} and 8α-oxo-avermectin B_{1a} (half-lives < 6 days).

In summary, avermectin B_{1a} degrades relatively fast in soils, with half-life < 60 days, and 8α-hydroxy- and 8α-oxo- avermectin B_{1a} being the major products. Light accelerates the degradation in water and soil, and isomerises the compound to its 8,9-Z isomer. Aqueous hydrolysis is not a significant degradation route for avermectin B_{1a} at environmentally relevant pHs and temperatures.

Plant metabolism

The metabolism of [^{14}C]avermectin B_{1a} was investigated in citrus plants kept under an open wooden frame with a fibreglass roof and treated at 18 to 40 µg ai/kg on a whole fruit basis. The [^{14}C]avermectin B_{1a} solutions, prepared in a EC formulation blank, was brushed on each fruit (0.5 mL). After 12 weeks of treatment, residues ranged from 33.3% (grapefruit) to 49.8% (lemons) of the AR. On the day of application, at least 98.4%AR was removed from the surface with methanol, and by week 12, surface residues corresponded to up to 41%TRR in oranges. No residues were detected in the pulp without the peel/pulp interface for all fruits; when the interface was included, residues reached 12–13%TRR after 8 weeks. At day 0, at least 85% TRR of the methanol rinse and acetone peel extract was avermectin B_{1a}, the level then decreased rapidly after one week (to 4.4 to 17.4%TRR) and ≤ 7.7% TRR after 12 weeks, when polar residues accounted for at least 46% TRR. The 8,9-Z isomer of avermectin B_{1a} was present in all sample extracts (0.7–4.7%TRR). Non extracted residues ranged from 40–62% TRR at week 12, but were reduced to < 10%TRR after successive treatments (Bligh-Dyer procedure, soxhlet with methanol and acid or enzyme hydrolysis). Most of the non-extracted residues were polar degradates, with avermectin B_{1a} representing 9–12% TRR, and a fraction identified as a mixture of linoleic fatty esters.

The metabolism of avermectin B_{1a} was investigated in celery in three field experiments:

1) plants treated with ^{3}H-avermectin B_{1a} at 11.2 g ai/ha

2) at 112 g ai/ha, with immature plants harvested from 0 to 43 days after the 4th application and mature plants harvested at 0 to 22 days after the 10th application

3) plants treated with [^{14}C]avermectin B_{1a} at 16.8 g ai/ha, with immature plants harvested at 0 and 14 days after the 4th application and mature plants harvested at 0 to 7 days after the 10th application.

In general, residues in immature or mature leaves and stalks decreased significantly during the study period. For example, after the 4th application at 11.2 g ai/ha, residues in immature leaves were 2.74 mg/kg eq, decreasing to 11.5 µg/kg eq 43 days later. Acetone extracts accounted for over 95% TRR in immature leaves after the 4th application at all rates, with avermectin B_{1a} accounting for 65–75% of the extracted residue. After 14 days, leaf acetone extracts were about 80%TRR, with avermectin B_{1a} accounting for 16–26% of the residues and the 8,9-Z isomer for about 5%. In general, stalks and mature leaves showed similar profiles. The 8-hydroxy avermectin B_{1a} and at least ten other unidentified minor components were also detected in the samples. Residual solids from the leaf acetone extract were mostly extracted with methanol/water and hot DMSO, being mostly polar

degradates of avermectin B_{1a}. About 15% of the acetone non-extracted residues in the leaves were incorporated into glucose.

The metabolism of [^{14}C]avermectin B_{1a} was investigated in cotton in four field experiments:

1) individual leaves treated with 100 µg of [^{14}C]avermectin B_{1a} and analysed 8 days after treatment (DAT)

2) cotton plants received two foliar applications at 20 g ai/ha (100 L/ha) and mature bolls harvested at 8 DAT

3) cotton plants were grown in buckets under normal field conditions and treated three times by foliar spray at 22.4 g ai/ha

4) 3× 224 g ai/ha (467 L/ha), and the bolls harvested at 20 DAT.

Over 99.7%AR in the leaves from Experiment 1 were extracted with methanol at day 0, decreasing to 19.3% at Day 8. Avermectin B_{1a} accounted for 99.2%AR at Day 0 and 1.7% AR after 8 days. Non-extracted residues reached 26.1%AR at Day 4. Leaves from Experiments 2 to 4 contained the highest residues (up to 400 µg/kg). Seeds contained up to 85 µg/kg and lint up to 750 µg/kg; this very high level was probably due to the last application in Experiment 4, when approximately 50% of the bolls were open. Avermectin B_{1a} represented most of residues in the leaves methanol rinse from the Experiment 3, accounting for 36% AR at day 1, which decreased to 1% AR by Day 8. The 8,9-Z isomer accounted for 7% AR at 0.25 day, decreasing to 0.1% AR at Day 8. From 26 to 35% TRR in the cotton seed (Experiments 2 to 4) was extracted with hexane, and characterized as triglycerides (linoleic and palmitic acid). Methanol extracts accounted for 50 to 65% TRR and non-extracted material for up to 25% TRR (Experiment 2).

One study was conducted to compare the profile of the residues of [^{14}C]avermectin B_{1a} *in vivo* (citrus, celery and cotton) and *in vitro* photolysis conditions. In this study, a [^{14}C]avermectin B_{1a} methanol solution was dried at room temperature and placed under a 275W Suntanner bulb. Most of the residues in the cotton leaf and citrus fruit surface were of a polar nature, with avermectin B1a accounting for 5–11% TRR after 7–8 days. In stalk and leaf extracts, avermectin B_{1a} accounted for 17 and 10% TRR at 7 DAT, respectively. The *in vitro* study also showed a major decline of avermectin B_{1a} residues with time (from 37% TRR after 19 hours of exposure to light to 7.3% TRR after 30 hours). Re-chromatography of the polar residues from the three treated crops and in the photolysis experiment showed four broad peaks of multiple-oxygenated, hydrated or dehydrated and de-methylated species, which retained little of the macrocyclic characteristics of avermectin B_{1a}.

Metabolism of avermectin B_{1a} was studied in greenhouse-grown tomato plants treated with [^{14}C]avermectin B_{1a} at 5× 26 g ai/ha (sub-study 1) and 3× 281 g ai/ha (sub-study 2). The major metabolite fractions in all of the analysed samples were avermectin B_{1a} and the 8,9-Z isomer of avermectin B_{1a}, in a ratio of approximately 9:1. TRR at 28 DAT in tomato and leaves from sub-study 1 were 0.127 and 6.4 mg/kg eq., respectively, with 51 and 34% as avermectin B_{1a} + its 8,9-Z isomer (9:1), respectively. In sub-study 2, the parent compound and its isomer accounted for 75 and 50% of the residues found in tomato and leaves, respectively. 8α-oxo-avermectin B_{1a}, 8α-hydroxy-avermectin B_{1a}, and 3"-O-desmethyl-avermectin B_{1a} were present at levels < 8% TRR in tomato and leaves samples. The non-extracted radioactivity did not exceed 2% TRR in tomato fruit and 7%TRR in the leaves.

In a field study conducted at 5× 26 g ai/ha or 5× 246 g ai/ha, total residues in tomatoes were 0.017 and 0.108 mg/kg, respectively, with avermectin B_{1a} + its 8,9-Z isomer accounting for 7.1 and 25%TRR, and the 8α-oxo- and 8α-hydroxy- metabolites for less than 3%TRR. In leaves, total residues were 0.71 and 7.8 mg/kg, respectively, with avermectin $B_{1a\ and}$ its isomer accounting for 2.2 and 6.4%TRR and the two metabolites up to 1.2%TRR.

Metabolism of avermectin B_{1a} was investigated in field-grown tomatoes under similar conditions as the greenhouse studies. The major metabolite fraction in all of the analysed samples was avermectin B_{1a} and its 8,9-Z isomer, accounting for about 70–80%TRR at 0 days and decreasing over time (2–6% TRR 28 days after the 5th application). Other identified metabolites were 8α-oxo-

avermectin B_{1a}, 8α-hydroxy-avermectin B_{1a}, and 3"-O-desmethyl-avermectin B_{1a}, present at levels < 7% TRR each in tomatoes and leaves at any sampling time in both experiments.

In a confined rotational crop study conducted in the field, sorghum, lettuce and carrots or turnips were planted in sandy, sandy loam and "muck" (high-organic drained swampland) soils. The soils were filled into large tubes and treated at 135 to 155% of the maximum label rate of 21.3 g ai/ha. The sandy soil received 3× 29.1 g ai/ha and sandy loam and muck soils 12× 33.6 g ai/ha. Sorghum and lettuce were planted in all soil types, turnip in the muck soil and carrot in the sand and sandy loam soils. The plant-back intervals (PBI) were 14, 123 and 365 days for the muck soil, 31, 120 and 365 days for the sandy soil and 29, 123 and 365 days for the sandy loam soil. The highest TRR was found in the lettuces samples from the muck soil (6.9 µg/kg eq.), from which extraction with acetone released only 4.4%TRR. Sorghum leaf-stem TRR ranged from 4 to 12 µg/kg eq. No identification of the residues were performed due to the low TRR levels in all samples.

In summary, the plant metabolism studies conducted in citrus, cotton, celery and tomatoes showed that the residues of avermectin B_{1a} are not significantly translocated into the plants, remaining on the surface, where it is photodegraded to its 8,9-Z isomer. The major proportion of the residues remains parent avermectin B_{1a}. The metabolism pathway include the re-arrangement to the 8,9-Z isomer, hydroxylation to 8α-hydroxy-avermectin B_{1a}, further oxidation to 8α-oxo-avermectin B_{1a}, demethylation to 3"-O-desmethyl-avermectin B_{1a}, and oxidation of the 8α-hydroxy- to form the 4"-oxo-avermectin B_{1a} and 4"-,8α-di-oxo-avermectin B_{1a}. The lack of uptake of radioactive material in succeeding crops indicates the non-systemic behaviour of avermectin B_{1a} and its soil degradates.

Animal metabolism

The metabolism of ^{3}H- and ^{14}C-radiolabelled abamectin B_{1a} in rats was evaluated by the WHO group. In summary, the metabolism of avermectin B_{1a} in the rat proceeded predominantly via demethylation, hydroxylation, cleavage of the oleandrosyl ring, and oxidation reactions. Unchanged avermectin B_{1a} and the metabolites 3"-O-desmethyl, 24-hydroxymethyl, 27-hydroxymethyl, 3"-O-desmethyl-24-hydroxymethyl and 3"-O-desmethyl-27-hydroxymethyl abamectin B1a represented the majority of the faecal radioactivity.

One goat metabolism study was submitted to the meeting. Six lactating goats were dosed daily for ten consecutive days with ^{3}H-avermectin B_{1a} at 0.00125 (D1), 0.0125 (D2) and 0.25 ppm (D3) (two animals per dose) and sacrificed after 24 hours. Urine and faeces were collected daily and goats were milked twice daily. The majority of the radioactivity was found in the faeces (79 to 98% AR). Milk residues plateaued by day 4–6 and were dose dependent (0.34 and 2.6 µg/kg eq. at D2 and D3, respectively). In tissues, highest residues were found in liver (mean of 0.4, 2.8 and 57.2 µg/kg eq. at D1, D2 and D3, respectively), fat (< 0.2, 1.8 and 40.9 µg/kg eq.) and kidney (0.3 to 13.8 µg/kg eq.). In muscle, residues were < 0.2, 0.32 and 5.2 µg/kg eq. Avermectin B_{1a} was the major residue in all tissues, comprising from 41–95%TRR in liver, 40–97%TRR in kidney, 73 to 96%TRR in muscle, 86–99% in fat, and 70–95%TRR in milk. Metabolite 24-hydroxymethyl-avermectin B_{1a} was a major residue in liver of the D1 goats (45.5%TRR) and was present at 2–11% TRR in milk from D3. A second metabolite, 3"-desmethyl-avermectin B_{1a}, was only isolated from Goat 5 liver (≤ 5% TRR). Fat tissue was shown to contain 24-hydroxymethyl avermectin B_{1a} in a conjugated form.

Based on the structures identified, the metabolism of avermectin B_{1a} in the goat proceeds via hydroxylation of the methyl group to 24-hydroxymethyl-avermectin B_{1a} and to a lesser extent demethylation at the 3" position. Avermectin B_{1a} is the major residues in all animal matrices. The metabolic pathway in rats showed a similar profile.

Methods of residue analysis

Abamectin residues in plant materials are analysed by two methods, one by HPLC with fluorescent detector (HPLC-FL; Exc.: 365 nm, Em.: 470 nm) and the other, used in more recent supervised trials, by LC-MS/MS. Transition ions for avermectin B1a and its isomer ($[M+Na]^{+}$) were m/z = 895.5 → 751.5 for quantification and m/z = 895.5 → 449.2 for confirmation.

In the HPLC-FL method, residues are extracted with acetonitrile or methanol and partitioned with hexane, the organic extract is cleaned-up in an aminopropyl solid phase extraction (SPE), and residues eluted with ethyl acetate/methanol. Fluorescent derivatives are formed by reaction with a mixture of triethylamine, trifluoroacetic anhydride and 1-methylimidazole and determined by HPLC-FL. Avermectin B_{1a} and its 8,9-Z isomer results in a single peak, and is determined as the sum of both compounds. It is the same for avermectin B_{1b} and its 8,9-Z isomer. The LOQ for the individual analytes were 0.002 or 0.005 mg/kg for most studies.

The LC-MS/MS methods quantify individually avermectin B_{1a}, avermectin B_{1b} and their 8,9-Z isomers. Residues are extracted with acetonitrile or methanol, partitioned into toluene and cleaned-up using aminopropyl, amino or C8 SPE (LOQ of 0.002 to 0.01 mg/kg), or only extracted with dichloromethane before the analysis (LOQ of 0.02 mg/kg). The method that included the clean-up step was also validated for avermectin B_{1a}, and its 8,9-Z isomer in animal matrices (LOQ of 0.002 mg/kg).

An LC-MS/MS multi-residue QuEChERS method for the determination of residues of avermectin B_{1a}, avermectin B_{1b} and avermectin B_{1a} 8,9-Z isomer in lettuce, sunflower seeds, dried broad beans, wheat grain, oranges and dried hops was validated at the LOQ of 0.002 mg/kg.

Stability of residues during storage

Residues of avermectin B_{1a} in citrus peel samples fortified at levels of 0.005 or 0.025 mg/kg were stable for at least at 52 months when stored at $\leq -10\ ^{o}C$. Residues of avermectin B_{1a} (0.01 or 0.05 mg/kg), avermectin B_{1b} (0.004 mg/kg) and avermectin B_{1a} 8,9-Z isomer (0.009 mg/kg) were shown to be stable in tomato samples for at least 15 months, in celery and strawberry samples for at least 24 months and in pear samples for at least 35 months. Residues of the three analytes at 0.04 mg/kg were shown to be stable for at least 24 months at $\leq -18\ ^{o}C$ when present in orange peel, green beans, sunflower seeds and potatoes. Residues of avermectin B_{1a} and its 8,9-Z isomer (0.02 mg/kg) in grapes and processed commodities were shown to be stable for at least one year under frozen conditions, with the exception of raisins, for which only 28% of avermectin B_{1a} residues remained after 12.5 years.

In summary, avermectin B_{1a} and its 8,9-Z isomer and avermectin B_{1b} were shown to be stable for at least 12 months in a variety of crop samples stored under frozen conditions, except raisins. The storage period of the samples in the residue trials guarantee the stability of the residues, unless it is specified otherwise.

Residue definition

Plant metabolism field studies conducted with ^{14}C and/or ^{3}H-avermectin B_{1a} in citrus, cotton, celery and tomatoes (also glasshouse studies) have shown that the major residue is avermectin B_{1a} (over 20% TRR), which remains on the surface of the crop and isomerizes to the 8,9-Z isomer. When present, the hydroxyl, oxo and desmethyl metabolites each accounted for < 10%TRR. Significant residues in rotational crops are not expected.

Abamectin is a mixture of $\geq$ 80% avermectin B_{1a} and $\leq$ 20% avermectin B_{1b}. In most residue trials, avermectin B_{1b} was found at levels < LOQ, and when present, the levels are significantly lower than avermectin B_{1a}. Hence, avermectin B_{1a} is an adequate marker for the use of abamectin products.

Although the HPLC-FL method used to analyse abamectin residues measure avermectin B_{1a} plus its 8,9-Z isomer together, the isomer is not expected to be a significant part of the residue (one study in tomato estimated a 9:1 ratio of both compounds) and was never detected in trials when the LC-MS/MS method was used. The toxicity of 8,9-*Z* isomer of abamectin B_{1a} is of no greater toxicity than the parent abamectin B_{1a}.

The Meeting agreed for the following residue definition for abamectin in plant commodities for enforcement and dietary risk assessment:

Avermectin B_{1a}

The metabolism of avermectin B_{1a} in lactating goats showed the parent compound as the main residue in all matrices (at least 40%TRR), with only one major metabolite (24-hydroxymethyl-avermectin B_{1a}), which accounted for 45.5%TRR in livers of the low dosed goats (0.00125 ppm) and up to 11% TRR in milk. The toxicity of 24-hydroxymethyl-avermectin B_{1a} is of no greater toxicity than the parent abamectin B_{1a}.

The Meeting agreed for the following residue definition for abamectin in animal commodities for enforcement and dietary risk assessment: Avermectin B_{1a}

Residues of avermectin B_{1a} are five times higher in fat than in muscle and the log K_{OW} is 4.4, which indicates fat solubility.

The residues are fat soluble.

Residues resulting from supervised residue trials on crops

As no trials were submitted on summer squash and watermelon, the Meeting withdraws its previous recommendations for these commodities

Citrus fruits

In the USA, GAP for abamectin in citrus is up to three applications at a maximum rate of 26 g ai/ha (max. of 53 g ai/ha per season), and 7 days PHI. Twenty one trials were conducted in the USA in citrus (grapefruit, orange, tangelo and lemon).

In nine trials conducted in oranges at GAP, abamectin residues at 7 days PHI were < 0.005 (6), 0.008, 0.010 and 0.014 mg/kg. The highest residue in a replicate samples was 0.015 mg/kg.

In two trials conducted at GAP in grapefruit, one in tangelos and one in lemons, residues were < 0.005 (4).

The median residues found in the different crops is the same, which allows the consideration of a group estimation. However, the residue populations are not similar, with residues in oranges being significantly higher than in the other crops.

Based on the residues in oranges, the Meeting estimated a maximum residue level of 0.02 mg/kg, a STMR of 0.005 mg/kg and a HR of 0.015 mg/kg for abamectin in citrus.

This estimation replaces the previous recommendation for abamectin in citrus.

Pome fruit

GAP for abamectin in pome fruit in Italy is up to 2× 22 g ai/ha and 28 days PHI. Various trials were conducted in Europe according to this GAP in apples and pears from 1986 to 2012.

In 26 trials conducted on apples in Europe according to Italian GAP, residues of abamectin were < 0.002 (20), 0.003 (2), 0.004 (2), 0.007 (2) mg/kg. The highest residue in a replicate samples was 0.010 mg/kg.

Two trials conducted in pears at GAP gave abamectin residues of < 0.002 mg/kg (2). Five trials using three applications of the GAP rate also found no residues.

Based on the residue data in apples, the Meeting estimated a maximum residue level of 0.01 mg/kg, a STMR of 0.002 mg/kg and a HR of 0.01 mg/kg for abamectin in pome fruit.

The Meeting withdraws its previous recommendations for apple and pears.

Stone fruit

GAP for abamectin in stone fruit in the USA is 2× 26 g ai/ha and 21 days PHI. Fifteen trials were conducted in cherry in USA according to this GAP, giving abamectin residues of 0.003 (2), 0.004,

0.005, 0.006, 0.007, 0.008, 0.009 (2), 0.010, 0.011, 0.015, 0.016, 0.024, 0.047 mg/kg. The highest residue in a replicate samples was 0.058 mg/kg.

Thirteen trials were conducted in peaches in the USA according to GAP, giving abamectin residues of < 0.002, 0.002 (6), 0.003, 0.004 (2), 0.005, 0.006 (2), 0.008 and 0.024 mg/kg.

Fifteen trials were conducted in plums in the USA according to GAP, giving abamectin residues of < 0.002 (7), 0.002, 0.003 and 0.004 (4) mg/kg. The highest residue in a replicate samples was 0.006 mg/kg

In Italy, GAP for abamectin in peaches is 2× 22 g ai/ha and 14 days PHI. In five trials conducted in France, Italy and Spain according to this GAP, abamectin residues in the whole fruit were < 0.002 (3), 0.004 and 0.006 mg/kg. Residues in the pulp were < 0.002 (3), 0.004 and 0.007 mg/kg

The residue populations in cherries, peaches and plums from the USA gave the highest residues and will be considered for the sub-group estimations.

The Meeting estimated a maximum residue level of 0.07 mg/kg, a STMR of 0.009 mg/kg, and a HR of 0.058 mg/kg for abamectin in cherries.

The Meeting estimated a maximum residue level of 0.03 mg/kg, a STMR of 0.002 mg/kg and a HR of 0.024 mg/kg for abamectin in peaches.

The Meeting estimated a maximum residue level of 0.005 mg/kg, a STMR of 0.004 mg/kg and a HR of 0.006 mg/kg for abamectin in plums.

Raspberry

GAP for abamectin in raspberries and blackberries in Italy is one application at 22 g ai/ha and 7 days PHI. In four trials conducted in Italy at GAP, abamectin residues were < 0.02 (2), 0.02 and 0.03 mg/kg

The Meeting estimated a maximum residue level of 0.05 mg/kg, a STMR of 0.02 mg/kg and a HR of 0.03 mg/kg for abamectin in raspberry, red, black.

The Meeting agreed to extend this estimation to blackberries.

Strawberry

In Denmark, GAP for abamectin in strawberries is greenhouse applications at 3× 22 g ai/ha and 3 days PHI. In eight greenhouse trials conducted in France and Spain according to this GAP, abamectin residues were 0.004, 0.006, 0.014, 0.020, 0.034, 0.042, 0.045 and 0.071 mg/kg. The highest residue in duplicate samples was 0.073 mg/kg.

In the USA, GAP is 4× 21 g ai/ha and 3 days PHI. In five protected trials conducted at GAP, residues were 0.005 (2), 0.006, 0.007 and 0.008 mg/kg. In seventeen field trials, residues were < 0.005 (5), 0.006 (4), 0.009 (2), 0.010 (2), 0.016, 0.020, 0.026, and 0.028 mg/kg.

Based on the protected trials conducted in Europe that gave the highest residues, the Meeting estimated a maximum residue level of 0.15 mg/kg, a STMR of 0.027 mg/kg and a HR of 0.071 mg/kg for abamectin in strawberries.

This estimation replaces the previous recommendation for abamectin in strawberries.

Grapes

GAP for abamectin in grapes in the USA is 2× 21 g ai/ha and 28 days PHI. In nineteen trials conducted in the USA at GAP, residues of abamectin were < 0.002 (10), 0.002 (4), 0.004 (3), and 0.006 (2) mg/kg. The highest residue in a replicate samples was 0.010 mg/kg

The Meeting estimated a maximum residue level of 0.01 mg/kg, a STMR of 0.002 mg/kg and a HR of 0.010 mg/kg for abamectin in grapes.

Avocado

In the USA, GAP for abamectin in avocados is 2× 26 g ai/ha and 14 days PHI. In five trials conducted at GAP in the country, residues were < 0.002, 0.003, 0.004 (2), and 0.007 mg/kg. The highest residue in a replicate samples was 0.009 mg/kg

The Meeting estimated a maximum residue level of 0.015 mg/kg, a STMR of 0.004 mg/kg and a HR of 0.009 mg/kg for abamectin in avocados.

Mango

In Brazil, GAP for abamectin in mangoes is 4× 14 g ai/ha and 7 days PHI. In five trials conducted in the country at GAP, abamectin residues were < 0.002 (3), < 0.004 and 0.004 mg/kg.

The Meeting estimated a maximum residue level of 0.01 mg/kg, a STMR of 0.002 and HR of 0.004 mg/kg for abamectin in mangoes.

Papaya

In Brazil, GAP for abamectin in papaya is 3× 22 g ai/ha and 14 days PHI. In eight trials conducted in the country at GAP, abamectin residues in papaya fruit were < 0.002, 0.002, 0.003 (2), 0.004, 0.005 (2) and 0.008 mg/kg. Residues in the pulp were < 0.002 (6) mg/kg. Six trials conducted at double rate did not show any residues in the pulp (< 0.002 mg/kg), confirming a no residue situation in the pulp when the fruit is treated at GAP.

The Meeting estimated a maximum residue level of 0.015 mg/kg, a STMR and HR of 0 mg/kg for abamectin in papaya.

Onion and shallot

GAP for onion, bulbs (include shallots) in the USA is 2× 21 g ai/ha and 30 days PHI. In eight trials conducted in the country using 3–4 applications at the GAP rate gave residues of < 0.002 (7) and 0.002 mg/kg. The highest residue in a replicate samples was 0.003 mg/kg.

Meeting estimated a maximum residue level of 0.005 mg/kg, a STMR of 0.002 and HR of 0.003 mg/kg for abamectin in onion bulbs. This estimation was extrapolated to shallots and garlic.

Leek

GAP for abamectin in leek in Belgium is 3× 9 g ai/ha and 7 days PHI. Twelve trials conducted in France and the Netherlands within this GAP gave abamectin residues of < 0.002 (10) and 0.002 (2) mg/kg. The highest residue in a replicate samples was 0.003 mg/kg.

The Meeting estimated a maximum residue level of 0.005mg/kg, a STMR of 0.002 mg/kg and HR of 0.003 mg/kg for abamectin in leek.

Cucumber/gherkin

In Denmark, GAP for abamectin in cucumbers and gherkins in four greenhouse applications at 22 g ai/ha and 3 days PHI. Twenty-nine protected trials were conducted in Europe from 1989 to 2013. In twenty five trials (3-5 applications) conducted according to the Denmark GAP, abamectin residues were < 0.002 (6), < 0.005 (5), 0.002 (6), 0.003, 0.004 (2), 0.005, 0.006, 0.007 (2) and 0.025 mg/kg. The highest residue in a replicate samples was 0.029 mg/kg.

The Meeting estimated a maximum residue level of 0.03 mg/kg, a STMR of 0.002 and HR of 0.029 mg/kg for abamectin in cucumbers. This estimation was extrapolated to gherkins.

Melon

In Denmark, GAP for abamectin in melons is three greenhouse applications at 22 g ai/ha and 3 days PHI. Twelve greenhouse trials (3-4 applications) were conducted in Europe from 2000 to 2008

according to this GAP, giving abamectin residues the whole fruit of < 0.002 (6), 0.002 (3), 0.003 (2) and 0.005 mg/kg. Residues in the pulp were < 0.002 (10) mg/kg.

The Meeting estimated a maximum residue level of 0.01 mg/kg, a STMR and HR of 0.002 mg/kg for abamectin in melons, except watermelon.

This estimation replaces the previous recommendation for abamectin in melons, except watermelons.

Pepper

In Denmark, GAP for abamectin in sweet or bell peppers is five greenhouse applications at 22 g ai/ha and 3 days PHI. In eighteen greenhouse trials conducted in Europe within this GAP, abamectin residues were < 0.005 (3), 0.002 (2), 0.004, 0.005, 0.006, 0.008, 0.010, 0.012, 0.015, 0.018, 0.019, 0.02, 0.025, 0.027 and 0.051 mg/kg.

In the USA, GAP for fruiting vegetables, except cucurbits, is 2× 21 g ai/ha and 7 days PHI. Four trials were conducted in chilli pepper using six applications, giving residues < 0.005 mg/kg (4).

The Meeting estimated a maximum residue level of 0.07 mg/kg, a STMR of 0.009 mg/kg and HR of 0.051 mg/kg for abamectin in peppers, sweet.

This estimation replaces the previous recommendation for abamectin in peppers, sweet.

The Meeting estimated a maximum residue level of 0.005* mg/kg, a STMR and a HR of 0.005 mg/kg for abamectin in peppers, chilli.

This estimation replaces the previous recommendation for abamectin in chilli pepper.

The Meeting withdraws its previous recommendation for pepper, chilli, dried.

Tomato and eggplant

GAP for abamectin in tomatoes in Denmark is five greenhouse applications at 22 g ai/ha and in Greece, GAP for tomatoes and eggplants is 4× 22 g ai/ha. In both countries, the PHI is 3 days. Metabolism studies have shown that abamectin degrades rapidly and the Meeting agreed that only the last applications will impact the final residues and decided to use the trials with a lower number of applications for the estimations.

In twenty six greenhouse tomato trials using two to five applications at the GAP rate gave residues of < 0.002 (5), 0.002, 0.003, 0.004 (6), 0.005, 0.006 (2), 0.007 (2), 0.010, 0.011, 0.012, 0.014, 0.24, 0.25 and 0.027 (2) mg/kg.

Nine tomato field trials were conducted in France, Italy and Spain using 3–4 applications of the GAP rate, matching the Greek GAP gave residues of < 0.002 (6) and 0.002 (3) mg/kg.

Based on the greenhouse trials, which gave the highest residues, the Meeting estimated a maximum residue level of 0.05 mg/kg, a STMR of 0.004 mg/kg and HR of 0.027 mg/kg for abamectin in tomato.

This estimation replaces the previous recommendation for abamectin in tomatoes.

In two field trials conducted in eggplants in France using six applications, no abamectin residues were detected at 3 days PHI (< 0.010 mg/kg).

As three trials is not enough for the estimations, the Meeting agreed to extend the estimations for tomatoes to eggplants.

Lettuce

Abamectin can be used in lettuce in Greece at 4× 9 g ai/ha and 14 days and in Italy (includes cos lettuce) at 3× 18 g ai/ha and 7 days PHI.

Nine field trials were conducted in Italy and France according to Italian GAP, giving abamectin residues at 7 days PHI of < 0.002, 0.003 (2) and 0.005 mg/kg in head lettuce, 0.004 and 0.007 mg/kg in leafy lettuce and < 0.002, 0.003, 0.006 and 0.008 mg/kg in cos lettuce.

In protected trials conducted in Europe according to GAP in Greece, residues at 14 days PHI in head lettuce were (n=8) 0.007, 0.011, 0.019, 0.020, 0.035, 0.045, 0.047 and 0.097 mg/kg. Residues from protected trials conducted according to GAP with unidentified lettuce type ranged from 0.003 to 0.012 mg/kg.

Protected trials conducted in head lettuce according to GAP in Greece gave the highest residues. The Meeting estimated a maximum residue level of 0.15 mg/kg, a STMR of 0.0275mg/kg and a HR of 0.097 mg/kg for abamectin in head lettuce.

The Meeting agreed that there are not enough trials to estimate a maximum residue level for abamectin in leafy lettuce and cos lettuce.

The Meeting withdraws its previous recommendation on leafy lettuce.

Corn salad (lambs lettuce)

Abamectin can be used in lambs lettuce in Italy at 3× 18 g ai/ha and 7 days PHI. Two trials were conducted in lambs lettuce in France, but they were not according to GAP.

The Meeting agreed not to estimate a maximum residue level for abamectin in lambs lettuce

Spinach

In the USA, GAP for abamectin in spinach is 2× 21 g ai/ha and 7 days PHI. Six declining trials using six application (7 days interval) and metabolism studies showed a rapid declining of the residues, indicating that the contribution of the early applications does not impact the final residue. In eleven trials conducted with 3–6 applications abamectin residues at 7 days PHI were < 0.002 (2), 0.016, 0.020, 0.021, 0.024, 0.028, 0.042, 0.044, 0.048 and 0.085 mg/kg. The highest residue in a replicate samples was 0.091 mg/kg.

The Meeting agreed to recommend a maximum residue level of 0.15 mg/kg, a STMR of 0.024 mg/kg and a HR of 0.091 mg/kg for abamectin in spinach.

The IESTI from the consumption of spinach represented 140% of the ARfD for abamectin (0.003 mg/kg bw). No alternative GAP was available to the Meeting.

Bean, green with pods

The GAP for abamectin in green beans in Spain is 3× 18 g ai/ha and 3 days PHI. In thirteen greenhouse trials conducted in Italy and Spain according to this GAP, residues in green bean with pods were < 0.002 (4), 0.003, 0.004, 0.007, 0.012, 0.014, 0.016, 0.017, 0.023, and 0.049 mg/kg

The meeting estimated a maximum residue level of 0.08 mg/kg, a STMR of 0.012 mg/kg and a HR of 0.049 mg/kg for abamectin in beans, except broad beans and soya beans (green pods and immature seeds).

Beans, dry

GAP for abamectin in beans, dry, in the USA is 2× 21 g ai/ha and 7 days PHI. In seven trials conducted in the USA using three applications, residues were < 0.002 (6) and 0.003 mg/kg.

As it is unlikely that the first application would impact the final residue, the Meeting agreed to use these trials for estimating a maximum residue level of 0.005 mg/kg and a STMR of 0.002 mg/kg for abamectin in beans, dry.

Celeriac

GAP for abamectin in celeriac in the USA is 2× 21 g ai/ha and 7 days PHI. Two trials were conducted in the country using three applications gave no residues in the root (< 0.002 mg/kg)

The Meeting agreed that two trials are not sufficient to estimate a maximum residue level for abamectin in celeriac.

Potato

In the USA, the GAP for abamectin in tuberous and corm vegetables, which include potatoes, sweet potatoes and yams, is 2× 21 g ai/ha and 14 days PHI. In thirteen potato trials conducted in the country from 1992 to 1998 using from 3-6 applicatons at GAP, no abamectin residues were detected in potato tubers (< 0.005 mg/kg). Trials conducted at 6 × 112 g ai/ha gave the same result.

The Meeting estimated a maximum residue level of 0.005* mg/kg, a STMR and a HR of 0 mg/kg for abamectin in potato. The Meeting agreed to extrapolate this recommendation to sweet potato and yams.

This estimation replaces the previous recommendation for abamectin in potatoes.

Radish

GAP for abamectin in radishes in Belgium is 2× 10 g ai/ha and 14 days PHI. In one protected trial conducted in the Netherlands in 1999 within this GAP, abamectin residues in the root were < 0.002 mg/kg.

The Meeting agreed that one trial is not sufficient to estimate a maximum residue level for abamectin in radishes.

Celery

GAP for abamectin in celery in Greece is 4× 9 g ai/ha and 14 days PHI. In seven trials conducted using three applications, samples were collected at 10 DAT.

In the USA, GAP is 2× 21 g ai/ha and 7 days PHI. Six trials conducted in the country using three applications gave residues of 0.003, 0.005 (2), 0.006 0.01 and 0.016 mg/kg

As it is unlikely that the first application would impact significantly the final residue, the Meeting agreed to use these trials to estimate a maximum residue level of 0.03 mg/kg, a STMR of 0.005 mg/kg and a HR of 0.016 for abamectin in celery.

Rice

In China, GAP for abamectin in rice is 2× 14 g ai/ha and 21 days PHI. In six trials conducted in the country according to GAP, abamectin residues in rice husked were < 0.001 mg/kg (6). Six trials conducted at 2× 20 g ai/ha rate gave residues of < 0.001 (4), 0.001 and 0.002 mg/kg. Applying the proportionally principle to this dataset, residues according to GAP are < 0.001 (5) and 0.0015 mg/kg.

Residues on the 12 trials combined are < 0.001 mg/kg (11) and 0.0015 mg/kg.

The Meeting estimated a maximum residue level of 0.002 mg/kg and a STMR of 0.001 mg/kg for abamectin in rice, husked.

Tree nuts

In the USA, GAP for abamectin in tree nuts is 2× 26 g ai/ha and 21 days PHI. In three trials conducted in almonds according to GAP, residues were <0.005 mg/kg. In another 29trials conducted in almond, pecan and walnut using 3 applications of 28 or 56 g ai/ha, residues at 3 to 14 DAT gave the same result.

As trials conducted at higher GAP or shorter DAT do not give rise to residues in nut meat, the Meeting estimated a maximum residue level of 0.005* mg/kg, a STMR and a HR of 0 mg/kg for abamectin in tree nuts.

The Meeting withdraws its previous recommendation for almonds and walnuts.

Cotton

GAP for abamectin in cotton in Spain is 3× 18 g ai/ha and 3 days PHI. Five trials were conducted in Greece and Spain using two applications, giving abamectin residues at 3 days PHI of < 0.002 mg/kg (5).

In the USA, GAP is 2× 21 g ai/ha and 20 days PHI. In eleven trials conducted in the country according to GAP, residues were < 0.002 (9), 0.005 and 0.01 mg/kg.

The Meeting estimated a maximum residue level of 0.015 mg/kg and a STMR of 0.002 mg/kg for abamectin in cotton seed.

This estimation replaces the previous recommendation for abamectin in cotton.

Peanut

Abamectin is registered in Argentina to be used in peanuts at 1× 2 g ai/ha and 30 days PHI. Four trials were conducted in Brazil using 3× 14 g ai/ha, giving residues < 0.005 mg/kg (4).

Based on the Brazilian trials conducted at high rate and metabolism studies that showed no translocation of abamectin residues in the plant, the Meeting estimated a maximum residue level of 0.005* mg/kg, and a STMR of 0 mg/kg for abamectin in peanuts.

Coffee

Critical GAP for abamectin in coffee in Brazil is one application at 27 g ai/ha and 14 days PHI. Five trials were conducted in the country using 7–9 g ai/ha, giving residues < 0.002 mg/kg (5).

As no trials were conducted according to GAP, the Meeting could not estimate a maximum residue level for abamectin in coffee.

Hops

Abamectin is registered in hops in Slovenia and the USA to be used at 2× 21–22 g ai/ha and 28 days PHI. In seven trials conducted in Germany according to this GAP, abamectin residues in dried cones were < 0.005 (2), 0.010, 0.012 0.02, 0.021 and 0.028 mg/kg. In four trials conducted in the USA at GAP, residues were 0.012, 0.020, 0.056 and 0.061 mg/kg.

Trials conducted in the USA gave the highest residues, and the Meeting estimated a maximum residue level of 0.15 mg/kg and a STMR of 0.038 mg/kg for abamectin in hops, dry.

This estimation replaces the previous recommendation for abamectin in hops, dry.

Feed commodities

Rice husks

In six trials conducted with abamectin in rice in China according to GAP (2× 14 g ai/ha), abamectin residues in rice husks (hulls) at 21 days PHI were < 0.001 (5) mg/kg and 0.006 mg/kg.

The Meeting estimated a median residue of 0.001 mg/kg for abamectin in rice hulls.

Residues in paddy rice plant (including grain with husks) in trials according to GAP were < 0.001 mg/kg (6). Trials conducted at 20 g ai/ha gave the same results.

As no residues were found in rice plant, the Meeting estimated a maximum residue level of 0.001 mg/kg, a median and highest residue of 0.001 mg/kg for abamectin in rice straw.

Green beans

In four European trials conducted in green beans according to GAP in Spain (3× 18 g ai/ha, 3 days PHI), abamectin residues in the vines were 0.329, 0.349, 0.354, and 0.581 mg/kg.

The Meeting estimated a median residue of 0.352 mg/kg and highest residue of 0.581 mg/kg for abamectin in green bean vines.

Almond hulls

In six trials conducted in almonds in the USA at the GAP, residues in the hulls at 21 days PHI were < 0.002, 0.012, 0.035, 0.037, 0.102 and 0.11 mg/kg.

The Meeting estimated a maximum residue level of 0.2 mg/kg and a median residue of 0.036 mg/kg for abamectin in almond hulls.

Cotton hulls

As no trials were conducted in cotton according to GAP that analysed the hulls, the Meeting could not make any estimation for abamectin in cotton hulls.

Fate of residues in processing

Three processing studies were conducted in grapes, with abamectin residues in grapes of 0.012, 0.007 and 0.048 mg/kg. Although the stability study on grape processed commodities have shown that abamectin residues were not stable after 12 months in raisins, in the processed study the samples were analysed within a month after being generated, and the results are evaluated. Eleven studies were conducted in cotton, all in the context of the residue trials described before. The estimated processing factors with the respective recommendations of STMR-P, based on the recommended maximum residue level, are shown in the Table.

RAC	Processed product	PF (median or best estimate)	STMR-P, mg/kg	HR-P, mg/kg	MRL, mg/kg
Grapes	Dried grape	1, 2.8, 3.1	0.0056	0.028	0.03
MRL = 0.01 mg/kg	Grape juice	< 0.25, < 0.57, 1.4	0.0028		0.015
STMR = 0.002 mg/kg	Wet pomace	4.75	0.009		
HR = 0.01 mg/kg	dry pomace	15.8	0.0316		
Plums	Prune	0.8 [a]			
Cotton	Meal	< 0.028, < 0.067	0.000		
STMR = 0.002 mg/kg	Refined oil	< 0.028, < 0.67	0.000		

[a] Recommendation for Plums includes prunes

Residues in animal commodities

A feeding study was conducted in dairy cows (n=3) with abamectin dosed at 0.01, 0.03 and 0.10 ppm levels for 28–30 days. Avermectin B1a residues were determined by HPLC-FL, with an LOQ of 0.001 mg/kg in tissues and 0.0005 mg/kg in milk. Residues in muscle at any feeding level were < 0.01 mg/kg (traces at 0.002 mg/kg at all levels), and in kidney (traces at 0.004–0.005 mg/kg at 0.10 ppm). At this highest dose, maximum residues were 0.014 mg/kg (mean of 0.012 mg/kg) in fat and 0.020 mg/kg in liver (mean of 0.019 mg/kg). In milk, residues were only detected after 2 days dosing at 0.10 ppm (0.001 mg/kg), reaching a maximum of 0.004 mg/kg at day 14, and decreasing to the initial levels at the end of the dosing period. Overall mean was < 0.0005 mg/kg.

Farm animal dietary burden

The Meeting estimated the dietary burden of abamectin in farm animals on the basis of the OECD Animal Feed data published in the 2009 FAO Manual, the STMR, STMR-Ps or highest residue levels estimated at the present JMPR Meetings.

The commodities used to estimate the dietary burden were rice, husked, rice straw, rice hulls, grape pomace dried, bean vines, almond husk, bean dry, and cotton meal. As abamectin is not registered in beans and grapes in Australia, and is unlikely that bean vines and grape pomace would be animal feed in the country, as they are not imported commodities, they were excluded in the calculation for the Australian diet.

Livestock dietary burden for abamectin, ppm of dry matter (DM) diet

	US-Canada		EU		Australia		Japan	
Commodity	Max	Mean	Max	Mean	Max	Mean	Max	Mean
Beef cattle	0.0003	0.0003	0.0007	0.0007	0.004	0.004	0.0006	0.0006
Dairy cattle	0.004	0.004	0.333 [a, b]	0.202 [c, d]	0.004	0.004	0.0003	0.0003
Poultry—broiler	0.0007	0.0007	0.0006	0.0006	0.002 [e]	0.002		
Poultry—layer	0.0007	0.0007	0.0007	0.0006	0.002	0.002 [f]		

[a] Highest maximum beef or dairy cattle dietary burden suitable for maximum residue level estimated for mammalian tissues

[b] Highest maximum dairy cattle dietary burden suitable for maximum residue level estimated for mammalian milk

[c] Highest mean beef or dairy cattle dietary burden suitable for STMR estimated for mammalian tissues.

[d] Highest mean dairy cattle dietary burden suitable for STMR estimated for milk.

[e] Highest maximum poultry dietary burden suitable for maximum residue level estimated for poultry tissues and eggs.

[f] Highest mean poultry dietary burden suitable for STMR estimated for poultry tissues and eggs.

Animal commodity maximum residue level

The calculated maximum cattle dietary burden suitable for the estimation of maximum residue level of tissues and milk is 0.333 ppm. For the estimation of STMRs, the cattle dietary burden was 0.202 ppm.

The feeding level in lactating cows was conducted in a much lower dose (up to 0.10 ppm) than the estimated dietary burden. The Meeting agreed not to make any estimation for abamectin in mammalian commodities.

The Meeting withdraws its previous recommendations for cattle fat, cattle kidney, cattle liver, cattle meat, cattle milk, goat meat, goat milk and goat, edible offal.

Currently, the existing Codex MRLs for abamectin as a veterinary drug only intended to be used in beef cattle are 0.1 mg/kg in cattle liver and cattle fat and 0.05 mg/kg in cattle kidney.

The calculated maximum poultry dietary burden suitable for maximum residue level estimated for poultry tissues and eggs was 0.002 ppm. No feeding study on poultry was submitted to the Meeting.

RECOMMENDATIONS

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

Residue definition for plant commodities for enforcement and dietary risk assessment: *Avermectin B_{1a}*

Residue definition for animal commodities for enforcement and dietary risk assessment: *Avermectin B_{1a}*

The residues are fat soluble.

DIETARY RISK ASSESSMENT

The intake assessments conducted by the Meeting did not include the uses of abamectin as a veterinary drug.

Long-term intake

The International estimated daily intakes (IEDI) of abamectin based on the STMRs estimated by this Meetings for the 17 GEMS/Food regional diets were 1–5% of the maximum ADI of 0.001 mg/kg bw (see Annex 3 to the 2015 Report). The Meeting concluded that the long-term dietary intake of residues of abamectin is unlikely to present a public health concern.

Short-term intake

The ARfD for abamectin is 0.003 mg/kg bw. The International Estimated Short-Term Intake (IESTI) of abamectin for the commodities for which STMR, HR and maximum residue levels were estimated by the current Meeting. The results are shown in Annex 4 to the 2015 Report.

For spinach, the IESTI represented 140% of the ARfD for children. No alternative GAP was available. On the basis of information provided to the Meeting, it was concluded that the short-term intake of abamectin residues from the consumption of spinach may present a public health concern.

The IESTI for the other commodities considered by the Meeting represented a maximum of 70% of the ARfD, and for these commodities, the Meeting concluded that the short-term-intake of abamectin is unlikely to present a public health concern when abamectin is used in ways considered by the Meeting.