5.7 CLOTHIANIDIN (238)

TOXICOLOGY

Clothianidin is the International Organization for Standardization (ISO)–approved name for (*E*)-1-(2-chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine (International Union of Pure and Applied Chemistry [IUPAC]) (Chemical Abstracts Service [CAS] No. 210880-92-5). Clothianidin is a neonicotinoid insecticide that controls insects by acting as an agonist at the nicotinic acetylcholine receptor, affecting the synapses in the insect central nervous system.

Clothianidin has not been evaluated previously by the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) and was reviewed at the present Meeting at the request of the Codex Committee on Pesticide Residues (CCPR).

All pivotal studies with clothianidin were certified to be compliant with good laboratory practice (GLP) and met the basic requirements of the relevant Organisation for Economic Co-operation and Development (OECD) or national test guideline.

Biochemical aspects

Clothianidin was almost completely (90%) absorbed from the gastrointestinal tract within 24 h following oral dosing of rats. The rate and extent of absorption were essentially independent of sex, dose or dose rate.

The compound was widely and homogeneously distributed throughout the tissues (time to maximum concentration = 1.5 h), with a rapid decrease of residues to levels at or near the limit of quantification. There was no evidence of accumulation, although higher levels were detected in kidney and liver up to 4 h post-dosing.

Within 24 h, about 94–96% of the compound was excreted. Urinary excretion was the major elimination route, accounting for about 89–95%, with faecal elimination accounting for about 3–6%. The excretion profile over 72 h after high-dose administration (elimination half-life = 1.9 h) was almost identical to that after low-dose administration (elimination half-life = 1.2 h), although the plasma concentration exhibited biphasic kinetics, suggesting moderate enterohepatic cycling.

Clothianidin metabolism was incomplete, with 56–74% of the dose being excreted unchanged over 72 h. The main metabolic pathways were 1) oxidative demethylation and 2) cleavage of the nitrogen–carbon bond between the thiazolyl-methyl position and the nitroimino moiety. The main urinary metabolites recovered after low-dose testing were thiazolylnitroguanidine (TZNG) (7–11%), *N*-methyl-*N*′-nitroguanidine (MNG) (8–13%) and nitroguanidine (NTG) (1–4%). In the faeces, 2-methylthiothiazole-5-carboxylic acid (MTCA) (9%) and thiazolmethylguanidine (TMG) (2%) were found. Other characterized metabolites were present at less than 2% of the dose.

Based upon the intended uses of clothianidin, representative metabolism studies in farm animals (goat, hen) were evaluated. It was demonstrated that the degradation pathways in farm animals were roughly comparable to those found in the rat (although absorption was probably somewhat lower) and that plant metabolism was less extensive. The major farm animal and plant metabolites (> 5% of the total radioactive residue) were also found in the rat, were structurally related to rat metabolites and/or were of lower toxicity. A notable exception was the plant metabolite methylguanidine (MG), which is similar in toxicity to the parent compound, but which was observed only at low residue levels (maximally 0.25 ppm in sugar beet leaves at harvest).

Toxicological data

Clothianidin is of moderate acute oral toxicity, with a median lethal dose (LD_{50}) between 523 and 1216 mg/kg bw in rats and of 389 mg/kg bw in male mice. The dermal LD_{50} is greater than 2000 mg/kg bw, and the inhalation median lethal concentration (LC_{50}) is greater than 6.14 mg/L (5.54 mg/L by gravimetry). Clothianidin is not irritating to the skin, is practically non-irritating to eyes and is not sensitizing to guinea-pig skin (maximization test).

In repeated-dose studies in mice, rats and dogs, no consistent toxicological profile was evident in any of the species at any of the dose ranges or study durations tested. Effects included lower body weights and body weight gains, decreased food consumption and changes in some clinical chemistry parameters. In the rat, mild induction of hepatic cytochrome P450 enzymes was observed in the 90-day feeding study. Hepatic induction was not assessed in either mouse or dog, although liver effects were also detected in dogs at a high dose.

In a 28-day feeding study in the mouse, atrophic changes in ovaries and uterus were reported at 2000 ppm (equal to 491 mg/kg bw per day). These changes in the reproductive system are considered to reflect the markedly reduced body weight gain.

Reports of increased ovary and uterus weights in a 90-day feeding study in rats at 1250 ppm (equal to 119 mg/kg bw per day for females) and above, accompanied by gross pathological and histopathological findings (uterus fluid distension/uterus luminal dilatation), could not be confirmed in a second study. In the dog, the targets were the haematopoietic system and lymphoid organs (anaemia and leukopenia). The findings in the 30-day study were consistent with those found in the 90-day and 1-year study, with a peak effect around 5 weeks and a time-related adaptation at later times. The overall no-observed-adverse-effect level (NOAEL) for these effects was 1500 ppm (equal to 36.3 mg/kg bw per day).

The lowest relevant NOAEL for short-term studies was 500 ppm (equal to 27.9 mg/kg bw per day) from a 90-day study in the rat, on the basis of reduced body weight and body weight gain at 3000 ppm (equal to 202 mg/kg bw per day). A 90-day study in the mouse was considered unreliable due to deficiencies in the study conduct.

In an 18-month carcinogenicity study in mice with dietary concentrations of up to 2000 ppm, the onset of mortality in females occurred early in the study, and the overall mortality in females was increased. This was most likely due to exceedance of the maximum tolerated dose (MTD) for a few months while the dose was adjusted. Body weight and body weight gain were reduced at 1250 ppm, and there was increased vocalization at this and the highest dose. There was an increase in hepatocellular hypertrophy at 1250 ppm and above. Fibromuscular hyperplasia of the cervix at 1250 ppm and above was observed, although such lesions are common in nulliparous ageing females. In males at 1250 ppm, there was increased incidence of myocardial degeneration. There was no statistically significant increase in the incidence of tumours of any site. The NOAEL was 350 ppm (equal to 47.2 mg/kg bw per day), based on body weight effects, clinical signs, and heart and cervical lesions at 1250 ppm.

Clothianidin was not carcinogenic in mice.

In a 24-month feeding study in rats with dietary concentrations up to 3000 ppm, feed consumption was reduced at 1500 ppm in males and at 500 ppm in females. Body weight and body weight gain were reduced in both sexes at 1500 ppm and above, mainly during the first year. Food efficiency was unaffected. At the highest dose, there was clear histological evidence of local effects in the glandular stomach. The NOAEL for non-neoplastic effects in this study was 150 ppm (equal to 9.7 mg/kg bw per day), based on changes in terminal body weight and feed consumption at 500 ppm.

The incidence of hepatocellular carcinoma in male rats was slightly increased at 500 ppm (one at termination, two in unscheduled deaths) and at 3000 ppm (four in unscheduled deaths). As there was no relationship with dose or duration of treatment and as such tumours occur occasionally in untreated rats, it was concluded that these tumours were not compound related. Increases in the

incidence of thyroid T-cell adenomas in the mid- and high-dose groups were not considered to be compound related, as there was no dose–response relationship in the incidence of adenomas plus carcinomas, and the combined incidence was not significantly increased in the top dose group.

The Meeting concluded that clothianidin was not carcinogenic in rats.

The potential genotoxicity of clothianidin was tested in an adequate range of in vitro and in vivo studies. In general, clothianidin showed no evidence of mutagenicity. There was some evidence of clastogenicity in tests with mammalian cells in vitro at cytotoxic doses. Clothianidin was consistently negative in tests for genotoxicity in vivo.

The Meeting concluded that clothianidin was unlikely to be genotoxic in vivo.

On the basis of the absence of genotoxicity in vivo and the absence of carcinogenicity in the rat and the mouse, the Meeting concluded that clothianidin is unlikely to be carcinogenic in humans.

In a two-generation study of reproductive toxicity in rats at dietary concentrations up to 2500 ppm, both maternal and offspring toxicity were observed at 500 ppm and above, with decreased body weight (F_1, F_2) leading to lower body weight gains (F_1). Offspring toxicity was observed at the top dose and included delayed preputial separation and vaginal patency at clearly maternally toxic doses. The NOAEL for both parental and offspring toxicity was 150 ppm (equal to 10.2 mg/kg bw per day), based on decreased body weight at 500 ppm (equal to 32.7 mg/kg bw per day) for parental animals and on decreased body weight and subsequent effects on preputial separation at 500 ppm (equal to 32.7 mg/kg bw per day) for offspring. The NOAEL for reproductive toxicity was 2500 ppm (equal to 179.6 mg/kg bw per day), the highest dose tested.

In rat developmental studies, the maternal NOAEL was 10 mg/kg bw per day, based on reductions in body weight gain and food consumption. The NOAEL for developmental toxicity was 125 mg/kg bw per day, the highest dose tested.

In the rabbit, fetal and developmental toxicity occurred only at maternally toxic doses. The maternal NOAEL was 10 mg/kg bw per day, based on clinical signs (starting at gestation day 13) at 25 mg/kg bw per day, and the developmental NOAEL was 75 mg/kg bw per day, based on increased post-implantation loss, reduced fetal body weight and retarded sternal ossification at 100 mg/kg bw per day.

The Meeting concluded that clothianidin induced developmental toxicity only in the presence of maternal toxicity and that it was not teratogenic.

The acute neurotoxicity of clothianidin was investigated in three gavage studies in rats at doses up to 400 mg/kg bw. Clinical signs, including behavioural effects, were observed at the top dose on the day of treatment. Dose-dependent effects on arousal were observed at 100 mg/kg bw and above in males and at 200 mg/kg bw and above in females. There were no compound-related histopathological effects on neuronal tissue. The NOAEL for acute neurotoxicity was 60 mg/kg bw, on the basis of reduced locomotor activity in males at 100 mg/kg bw.

In a 13-week rat feeding study of neurotoxicity with dietary concentrations up to 3000 ppm, animals were assessed on weeks 4, 8 and 13 of clothianidin intake. No effects were observed on motor activity, learning or memory capacity. There were no histopathological changes in neuronal tissue. Thus, the NOAEL for neurotoxicity was 177 mg/kg bw per day, the highest dose tested.

A developmental neurotoxicity study was undertaken with clothianidin administered in the diet to rats at concentrations up to 1750 ppm (equal to 142 mg/kg bw per day during gestation and 299 mg/kg bw per day during lactation). The NOAEL for fetal and maternal toxicity was 42.9 mg/kg bw per day, based on changes in body weight at higher doses. At the top dose, subtle modification of acoustic startle habituation and motor activity observed in the pups immediately after weaning were considered secondary to nonspecific toxicity. No biologically significant effects on the central nervous system were observed histomorphometrically or histologically.

The Meeting concluded that clothianidin is not a developmental neurotoxicant. At relatively high doses, it can cause transient, acute neurobehavioural effects.

In a 28-day feeding study of the immunotoxicity of clothianidin in rats at doses up to 3000 ppm, body weights and food consumption were significantly reduced in the high dose group. Based on these changes, the NOAEL for systemic toxicity was 500 ppm (equal to 45.8 mg/kg bw per day). Clothianidin had no effect on the immunoglobulin M antibody-forming cell response to the T cell–dependent antigen (sheep erythrocytes). The NOAEL for immunotoxicity was 3000 ppm (equal to 252.8 mg/kg bw per day), the highest dose tested.

In a developmental immunotoxicity study in rats, pregnant animals were offered diets containing up to 2000 ppm clothianidin from day 6 of gestation. The maternal NOAEL for systemic toxicity was 500 ppm (equal to 35 mg/kg bw per day during gestation and 68.3 mg/kg bw per day during lactation), based on reductions in body weight and food consumption and an increased incidence of ptosis at 3000 ppm. In the F_1 generation, the NOAEL for systemic toxicity was 150 ppm (equal to 26.4 mg/kg bw per day), based on reductions in body weight in females at weaning at 500 ppm. There were no immunologically relevant adverse effects on humoral immunity or cell-mediated immunity in male and female F_1 generation rats following exposure to clothianidin in the uterus during gestation, via maternal milk and maternal feed during the postpartum period or via the diet during the post-weaning period.

The Meeting concluded that clothianidin is not immunotoxic to adults or during development.

Some major (TZNG, > 5% of dose) and minor (thiazolylmethylurea [TZMU], TMG, MG, < 5% of dose) metabolites of clothianidin in the rat are also detected in the hen, goat, plants and environment. They all have oral LD_{50} values less than 2000 mg/kg bw and should thus be considered intrinsically harmful by ingestion.

Other compounds, such as NTG (rat metabolite, 1–4% of the administered dose), *N*′-[amino(2-chlorothiazol-5-ylmethylamino)methylene] acetohydrazide (ATG-Ac) (hen metabolite) and *N*′-[(2-chlorothiazol-5-ylmethylamino)(methylamino)methylene]-2-oxopropanohydrazide (ATMG-Pyr) (goat metabolite) were less toxic, with LD_{50}s above 2000 mg/kg bw.

Metabolite MG may be considered a potential plant residue of concern (known neurotoxicant, like most guanidino compounds), but it is a rat metabolite and it occurred at very low residue levels in plant commodities used for animal feeding only. Thus, further testing on MG is not necessary.

Metabolite MNG was not tested for acute oral toxicity. However, as it was a rat metabolite accounting for about 13% of the dose, it was considered to be covered by the toxicological assessment of clothianidin.

Metabolites TZNG, TZMU, TMG, MG, MNG, ATG-Ac, ATGM-Pyr and 3-methylamino-1H-imidazo[1,5-c]imidazole (MAI) were tested in the *Salmonella typhimurium* reverse gene mutation assay, and all were negative.

In conclusion, metabolic activity in mammals and plants and hydrolytic activity in the environment result in the transformation of clothianidin to breakdown products, which are relatively more toxic than or of the same order of toxicity as the parent compound. As many of these products are also rat metabolites, occur at very low residue levels and are not genotoxic, further testing is not warranted.

The Meeting concluded that the existing database on clothianidin was adequate to characterize the potential hazard to fetuses, infants and children.

Toxicological evaluation

An acceptable daily intake (ADI) of 0–0.1 mg/kg bw was established on the basis of the NOAEL in the chronic study in the rat of 9.7 mg/kg bw per day for decreased body weight and food consumption. A safety factor of 100 was applied.

An acute reference dose (ARfD) of 0.6 mg/kg bw was established on the basis of the NOAEL of 60 mg/kg bw in the acute neurotoxicity study in the rat, based on reduced locomotor activity at 100 mg/kg bw. A safety factor of 100 was applied.

The Meeting considered that the effects seen in mice at 50 mg/kg bw per day in pharmacological studies were marginal and transient (less than 0.5–1 h) at this dose level, whereas at the next dose level, 100 mg/kg bw per day, several effects were evident simultaneously in the same animals for longer times (3 h).

A toxicological monograph was prepared.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Mouse	Eighteen-month study of toxicity and carcinogenicity[a]	Toxicity	350 ppm, equal to 47.2 mg/kg bw per day	1250 ppm, equal to 171.4 mg/kg bw per day
		Carcinogenicity	2000 ppm, equal to 251.9 mg/kg bw per day[b]	—
Rat	Ninety-day studies of toxicity[a]	Toxicity	500 ppm, equal to 27.9 mg/kg bw per day	1250 ppm, equal to 96 mg/kg bw per day
	Two-year studies of toxicity and carcinogenicity[a]	Toxicity	150 ppm, equal to 9.7 mg/kg bw per day	500 ppm, equal to 32.5 mg/kg bw per day
		Carcinogenicity	3000 ppm, equal to 157 mg/kg bw per day[b]	—
	Two-generation study of reproductive toxicity[a]	Parental toxicity	150 ppm, equal to 10.2 mg/kg bw per day	500 ppm, equal to 32.7 mg/kg bw per day
		Offspring toxicity	150 ppm, equal to 10.2 mg/kg bw per day	500 ppm, equal to 32.7 mg/kg bw per day
		Reproductive toxicity	2500 ppm, equal to 179.6 mg/kg bw per day[b]	—
	Developmental toxicity study[c]	Maternal toxicity	10 mg/kg bw per day	40 mg/kg bw per day
		Embryo and fetal toxicity	125 mg/kg bw per day[b]	—
	Acute neurotoxicity study [c]	Neurotoxicity	60 mg/kg bw	100 mg/kg bw
	Developmental neurotoxicity study[a]	Maternal toxicity	500 ppm, equal to 42.9 mg/kg bw per day	1750 ppm, equal to 142 mg/kg bw per day
		Offspring toxicity	500 ppm, equal to 42.9 mg/kg bw per day	1750 ppm, equal to 142 mg/kg bw per day
		Developmental neurotoxicity	1750 ppm, equal to 142 mg/kg bw per day[b]	—

Species	Study	Effect	NOAEL	LOAEL
	Immunotoxicity study[a]	General toxicity	500 ppm, equal to 45.8 mg/kg bw per day	3000 ppm, equal to 252.8 mg/kg bw per day
		Immunotoxicity	3000 ppm, equal to 252.8 mg/kg bw per day[b]	—
	Developmental immunotoxicity study[a]	Maternal toxicity	500 ppm, equal to 35–68.3 mg/kg bw per day	2000 ppm, equal to 120.6–249.7 mg/kg bw per day
		Offspring toxicity	150 ppm, equal to 26.4 mg/kg bw per day	500 ppm, equal to 88.9 mg/kg bw per day
		Developmental immunotoxicity	2000 ppm, equal to 337.7 mg/kg bw per day[b]	—
Rabbit	Developmental toxicity study[c]	Maternal toxicity	10 mg/kg bw per day	25 mg/kg bw per day
		Embryo and fetal toxicity	75 mg/kg bw per day	100 mg/kg bw per day
Dog	Thirteen-week and 1-year studies of toxicity[a,d]	Toxicity	1500 ppm, equal to 36.3 mg/kg bw per day	2000 ppm, equal to 46.4 mg/kg bw per day

[a] Dietary administration.

[b] Highest dose tested.

[c] Gavage administration.

[d] Two or more studies combined.

Estimate of acceptable daily intake for humans

0–0.1 mg/kg bw

Estimate of acute reference dose

0.6 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 clothianidin

Absorption, distribution, excretion and metabolism in mammals	
Rate and extent of oral absorption	Rapid; 90% within 24 h
Distribution	Wide; highest concentrations in kidney and liver
Potential for accumulation	None
Rate and extent of excretion	Largely complete within 72 h
Metabolism in animals	Moderately metabolized; excreted unchanged at 56–74% at 72 h; main pathway was oxidative demethylation and cleavage of the nitrogen–carbon bond between the thiazolyl-methyl position and the nitroimino moiety

Toxicologically significant compounds in animals, plants and the environment	Parent compound and animal metabolites TZNG, MNG, NTG, MTCA and TMG; main plant metabolite is MG
Acute toxicity	
Rat, LD_{50}, oral	523–1216 mg/kg bw
Mouse, LD_{50}, oral	389 mg/kg bw
Rat, LD_{50}, dermal	> 2000 mg/kg bw
Rat, LC_{50}, inhalation	> 5.54 mg/L (4.5 h, nose-only exposure)
Rabbit, dermal irritation	Non-irritating
Rabbit, ocular irritation	Practically non-irritating
Guinea-pig, dermal sensitization	Not sensitizing (Magnusson and Kligman test)
Short-term studies of toxicity	
Target/critical effect	Decreased body weights and body weight gain, decreased kidney weights, decreased food consumption, clinical chemistry changes
Lowest relevant oral NOAEL	27.9 mg/kg bw per day (90-day study in rats)
Lowest relevant dermal NOAEL	1000 mg/kg bw per day (28-day study in rats)
Lowest relevant inhalation NOAEC	No data
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	Decreased food consumption and body weights
Lowest relevant NOAEL	9.7 mg/kg bw per day (rat carcinogenicity study)
Carcinogenicity	Not carcinogenic
Genotoxicity	
	Clothianidin unlikely to be genotoxic in vivo; metabolites not genotoxic (Ames test)
Reproductive toxicity	
Reproduction target/critical effect	None
Lowest relevant reproductive NOAEL	179.6 mg/kg bw per day (highest dose tested)
Developmental target/critical effect	Decreased fetal weight, increased post-implantation loss, decreased sternal ossification centres
Lowest relevant developmental NOAEL	75 mg/kg bw per day (rabbit)
Neurotoxicity/delayed neurotoxicity	
Acute neurotoxicity target/critical effect	Decreased locomotor activity
Lowest relevant acute neurotoxic NOAEL	60 mg/kg bw per day
Short-term neurotoxicity target/critical effect	Decreased body weight and feed consumption
Lowest relevant subchronic neurotoxic NOAEL	60 mg/kg bw per day
Developmental neurotoxicity target/critical effect	No biologically significant effects
Lowest relevant developmental neurotoxic NOAEL	142 mg/kg bw per day (highest dose tested)
Other toxicological studies	
Twenty-eight-day immunotoxicity	No effects on the immune system

Developmental immunotoxicity	No effects on the immune system
Medical data	
	No data

Summary

	Value	Study	Safety factor
ADI	0–0.1 mg/kg bw	Rat, 2-year study	100
ARfD	0.6 mg/kg bw	Rat, acute neurotoxicity study	100

RESIDUE AND ANALYTICAL ASPECTS

Residue and analytical aspects of clothianidin were considered for the first time by the present Meeting. The residue evaluation was scheduled for the 2010 JMPR by the Forty-first Session of the CCPR (ALINORM 09/32/24).

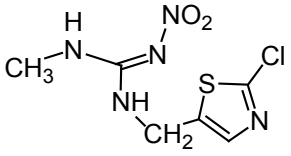
Clothianidin is an insecticide that can be used for soil, foliar and seed treatment belonging to the chemical class of nitromethylenes or neonicotinoids and acts as an agonist of the nicotinic acetylcholine receptor, affecting the synapses in the insect central nervous system of sucking and chewing insects. It has registered uses in many countries on soya beans, cereals, sugar cane, oilseeds, tea and a range of fruits and vegetables.

The Meeting received information from the manufacturer on identity, metabolism, storage stability, residue analysis, use pattern, residues resulting from supervised trials on pome fruit, stone fruit, cranberries, grapes, persimmon, bananas, Brassica vegetables, fruiting vegetables, lettuce, dry soya beans, root and tuber vegetables, cereal grains, sugar cane, oilseeds, animal feeds and teas, fate of residue during processing, and livestock feeding studies. In addition, the Meeting received information from the Netherlands and Japan on use pattern.

Chemical name

Clothianidin or (E)-1-(2-chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine

Structural formula:



Clothianidin exists predominantly in the E-form. This has been confirmed by NMR analysis. Quantum chemical calculations revealed that in water the E-isomer is more stable than the Z-isomer. At room temperature the theoretical ratio between E/Z isomers is estimated as 65:1.

The compound clothianidin is equivalent to the E form of CGA 322704, a metabolite arising from thiamethoxam use. Thiamethoxam is described as an E/Z mixture and the situation is similar for metabolite CGA 322704. No information is given on the actual ratio between E and Z isomers, nor which of these isomers is the active one. Information on the activation energy to convert Z-isomers to E-isomers is not available. If the activation energy for conversion is high, it is likely that the CGA 322704 appears as E/Z mixture in crops, soil, water and animal commodities. HPLC chromatograms of CGA 322704 from supervised trials show a single peak, so it is not clear whether E/Z mixtures cannot be separated by HPLC or whether there is only one isomer present in plant and animal commodities. As a consequence both isomers need to be considered.

Metabolites referred to in the appraisal by codes:

ACT	2-chlorothiazolyl-5-ylmethylamine
ATG	N'-[amino(2-chlorothiazol-5-ylmethyl)guanidine
ATMG	N'-[amino(2-chlorothiazol-5-ylmethyl)-N"-methylguanidine
ATMT	3-amino-4-(2-chlorothiazolyl-5-yl)methyl-5-methyl-4H-1,2,4-triazole
MG	methylguanidine
MNG	methylnitroguanidine
MU	methylurea
TMG	thiazolylmethylguanidine
TMT	3-(2-chlorothiazolyl-5-yl)methylamino-5-methyl-1H-1,2,4-triazole
TZG	thiazolylguanidine
TZMU	thiazolylmethylurea
TZNG	thiazolylnitroguanidine
TZU	thiazolylurea

Animal metabolism

The Meeting received results of animal metabolism studies in a lactating goat and in laying hens. Experiments were carried out using clothianidin ^{14}C labelled at the nitroimino position.

Metabolism in laboratory animals was summarized and evaluated by the WHO panel of the JMPR in 2010.

A lactating goat, orally treated once daily for three consecutive days with nitroimino-[^{14}C]clothianidin at an actual dose rate of 201 ppm in the dry weight feed (equivalent to 9.8 mg ai/kg bw/d), was sacrificed 5 hours after the last dose. Of the administered dose 70.4% was recovered: 13.5% in faeces, 48.8% in urine, 6.6% in tissues and 6.6% in milk. The radioactivity in the gastrointestinal tract or in breathed air was not measured. The radioactivity in the tissues ranged from 16 mg/kg in liver and 9.3 mg/kg in kidney to 4.3 mg/kg in muscle and 2.1 mg/kg clothianidin equivalents in fat. Maximum residue levels in milk were found within 24 hours: 6.0–6.6 mg/kg was found at 8 hours after the 1st, 2nd and 3rd doses and decreased to 0.92–0.97 mg/kg clothianidin equivalents at 24 hours after the 1st and 2nd doses.

Radioactivity was characterized in all tissues and milk. A total of 51%, 67%, 81%, 89% and 94% of the total radioactivity could be identified in liver, kidney, muscle, fat and milk, respectively. Parent was the major compound found at 51%, 25% and 37% of the total radioactivity in milk, muscle and fat, respectively. The major metabolites were TZNG at 14% in milk, TZMU at 13% in fat, and TZU at 11% in milk, 13% in muscle and 12% in fat. In liver and kidney, the parent compound was not found. The major metabolite in liver was TMG and conjugates at 13%. The major metabolites in kidney were TZU at 15%, TZG at 12%, TZMU at 11% and an ATMG-pyruvate at 10%. Other minor metabolites identified were below 8% of the total radioactivity. Part of the extractable residue in tissues and milk remained unidentified (7.3%–42% of the total radioactivity). The non-identified part of the radioactivity consisted mainly of polar compounds. Up to 14% of the total radioactivity remained unextracted.

Six laying hens, orally treated once daily for three consecutive days with nitroimino-[^{14}C]clothianidin at an actual dose rate of 134 ppm in the dry weight feed (equivalent to 10.4 mg ai/kg bw/d), were sacrificed 5 hours after the last dose. Of the administered doses 98% was recovered: 95% in excreta, 3.1% in tissues and 0.15% in eggs. The radioactivity in the tissues ranged from 7.9 mg/kg in kidney and 5.1 mg/kg in liver to 1.4–1.7 mg/kg in muscle, 1.1 mg/kg in skin and 0.19 mg/kg clothianidin equivalents in fat. Residue levels in eggs increased from 0.38–0.94 mg/kg clothianidin equivalents at 24 to 53 hours after the 1st dose.

Radioactivity was characterized in liver, muscle, fat and eggs. At least 65% of the total radioactivity could be identified. Parent was only a minor compound and was found at levels of up to 5.3% of the total radioactivity in tissues and at 21% in eggs. Major metabolites were TZNG at 88% in eggs, 46% in liver and 24% in fat, TZG at 22% in liver and ATG conjugates at 35% in muscle and 38% in fat. Other minor metabolites identified were below 4% of the total radioactivity. Part of the extractable residue in tissues and eggs remained unidentified (0.7%–31% of the total radioactivity). Up to 11% of the total radioactivity remained unextracted.

Clothianidin is efficiently degraded in goats and hens into a large number of metabolites reflecting the existence of numerous degradation pathways such as denitrification, hydrolysis, oxidative methylation and C-N bond cleavage to form TMG, TZMU, TZNG, or MNG, respectively, followed by further transformation to form ATMG conjugates, TZU, TZG and ATG conjugates.

The metabolic pathway proposed for ruminants and poultry is consistent with that for rats. Some poultry specific metabolites such as the ATG conjugates (35–38% in muscle and fat), TMT (2.4% in muscle) and ATMT (3.0% in muscle) and some ruminant specific metabolites like THMG (1.6% in milk) and ATMG-pyruvate (2.5–10.4% in liver, kidney, muscle, fat) were not present in rat metabolism.

Plant metabolism

The Meeting received plant metabolism studies for clothianidin seed treatments on sugar beets or maize, foliar spray treatment of apple trees or tomatoes and granular soil treatment of tomatoes. Experiments were carried out using clothianidin ^{14}C labelled at the nitroimino or the thiazolyl moiety.

Sugar beet seeds were treated with nitroimino-[^{14}C]clothianidin at a rate of 190 g ai/ha. Sugar beets were grown outdoors. Total radioactive residues in the roots harvested 48, 55 and 144 days following last application were 0.86, 0.20, and 0.034 mg/kg clothianidin equivalents. Total radioactive residues in the leaves harvested 48, 55 and 144 days following last application were 1.8, 0.52 and 0.89 mg/kg clothianidin equivalents. At harvest (144 days) a total of 46% and 75% of the total radioactivity could be identified in respectively roots and leaves. At harvest, sugar beet roots contained predominantly the parent compound at 24% of the total radioactivity, whereas the leaves showed a predominant amount of TMG and MG metabolites at 27–29% of the radioactivity and only a low level of parent (4.3%). Other minor metabolites identified were below 10% of the total radioactivity. Part of the extractable residue in roots and leaves at harvest remained unidentified (19–41% of the total radioactivity). Up to 13% of the total radioactivity remained unextracted. At earlier harvest times (48 and 55 days) parent was the major compound in both roots and leaves (49–68%).

Maize seeds were treated with nitroimino-[^{14}C]clothianidin at a rate of 1.06 mg ai/seed. Maize was grown outdoors. Total radioactive residues in the forage harvested 60 days following last application was 0.130 mg/kg clothianidin equivalents. Total radioactive residues in the stover and kernels harvested 145 days following last application were 0.170 and 0.006 mg/kg clothianidin equivalents. A total of 70%, 56% and 53% of the total radioactivity could be identified in forage, stover and kernels, respectively. The parent was the major compound recovered in forage, stover and kernels and accounted for 43%, 20% and 14% of the total radioactivity, respectively. A major metabolite found in stover and kernels was MG at 15% and 22% of the total radioactivity. Other minor metabolites identified were below 10% of the total radioactivity. Part of the extractable residue in forage, stover and kernels remained unidentified (27–36% of the total radioactivity). Up to 12% of the total radioactivity remained unextracted.

Maize seeds were treated with thiazolyl-2-[^{14}C]clothianidin at a rate of 2.52 mg ai/seed. Maize was grown indoors. Total radioactive residues in the forage harvested 63 days following last application was 0.89 mg/kg clothianidin equivalents. Total radioactive residues in the stover and kernels harvested 160 days following last application were 3.1 and 0.063 mg/kg clothianidin equivalents. A total of 80%, 65%, and 62% of the total radioactivity could be identified in respectively forage, stover and kernels. The parent was the major compound recovered in forage,

stover and kernels and accounted for 64%, 40% and 58% of the total radioactivity, respectively. Minor metabolites identified were below 10% of the total radioactivity. Part of the extractable residue in forage, stover and kernels remained unidentified (14–33% of the total radioactivity). Up to 8.5% of the total radioactivity remained unextracted.

Outdoors grown apple trees were sprayed two times with nitroimino-[^{14}C]clothianidin at a dose rate of 150 g ai/ha each and an interval of 85 days. Total radioactive residues in the apple fruits and leaves harvested 14 days following last application were 0.076 and 6.45 mg/kg clothianidin equivalents. The radioactivity was distributed within the fruit and leaves: 33% and 70% of the total radioactivity could be removed from fruits and leaves by a methanolic surface wash respectively, while 63% and 24% could be extracted from fruits and leaves, respectively. A total of 80% and 84% of the total radioactivity could be identified in fruits and leaves, respectively. Parent was the major compound both in the surface washed phase and in the solvent extract accounting for 61% and 54% and of the total radioactivity in fruits and leaves, respectively. The major metabolite found in fruits was TZMU at 11% of the total radioactivity. Minor metabolites identified in fruits and leaves were below 10% of the total radioactivity. Part of the extractable residue remained unidentified (10–16% of the total radioactivity). Up to 5.6% of the total radioactivity remained unextracted.

Indoors grown tomato plants were sprayed two times with nitroimino-[^{14}C]clothianidin at a dose rate of 158 g ai/ha each and an interval of 14 days. Total radioactive residues in the tomato fruits harvested 3 days following last application were 0.57 mg/kg clothianidin equivalents. The major part of the radioactivity was located on the surface: 97% of the radioactivity could be removed by a methanolic surface wash. A total of 97% of the total radioactivity could be identified, which was allocated solely to the parent compound. Only a small part of the extractable residue remained unidentified (3.3% of the total radioactivity), while only 0.1% of the total radioactivity remained unextracted.

Planting holes were treated with nitroimino-[^{14}C]clothianidin at a dose rate of 15 mg ai/hole and 33 day old tomato plants were transplanted in the holes. Tomato plants were grown indoors. Total radioactive residues in the tomato fruits harvested 97 days following the application were 0.014 mg/kg clothianidin equivalents. A total of 92% of the total radioactivity could be identified. Parent was the predominant residue at 66% of the total radioactivity. The major metabolite found was MNG at 18% TRR. Other minor metabolites were below 10% of the radioactivity. Only a small part of the extractable residue remained unidentified (6.0% of the total radioactivity), while only 1.9% of the total radioactivity remained unextracted.

In each commodity tested, except sugar beet leaves at harvest, clothianidin was found to be the major residue (14–97% of the total radioactivity). Major metabolites found were TMG (27% in mature sugar beet leaves), MG (29% in mature sugar beet leaves, 15% in maize stover, 22% in maize kernels), TZMU (11% in apple fruit), and MNG (18% in tomato fruit).

In crops, clothianidin is degraded into a large number of metabolites reflecting the existence of numerous degradation pathways. The major pathways are denitrification, hydrolysis, and C-N bond cleavage to form TMG, TZMU, and MNG, followed by further transformation to MG. Degradation occurred at a relatively low to medium level, leaving the parent compound as the predominant component.

All plant metabolites identified were also found in rats.

Environmental fate in soil

The Meeting received information on the fate of clothianidin after aerobic degradation in soil and after photolysis on the soil surface. In addition, the Meeting received information on the uptake of clothianidin soil residues by rotational crops. Experiments were carried out using clothianidin ^{14}C labelled at the nitroimino or the thiazolyl moiety.

An aerobic soil degradation study was conducted with three different soils. Soils were mixed with nitroimino-[^{14}C]clothianidin at 0.133 mg ai/kg, equivalent to 300 g ai/ha. Soils were incubated for 120 days in the dark at 20 °C at 40% of maximum water holding capacity (silt loam and silt), or for 365 days at 75% of 333 mbar moisture (sandy loam). Calculated half lives (DT_{50}) were 143, 227, and 490 days for silt, silt loam, and loamy sand, respectively. Parent was the predominant residue at the end of the study (54–69% of the total applied radioactivity). The major metabolites were TZNG at 9.1% and MNG at 11% of the total applied radioactivity.

A second aerobic soil degradation study was conducted with two silt loam soils. Soils were mixed with thiazolyl-2-[^{14}C]clothianidin at 0.133 mg ai/kg, equivalent to 300 g ai/ha. Soils were incubated for 181 or 379 days in the dark at 20 ºC at 75% of 333 mbar moisture. Calculated half lives (DT_{50}) for the silt loam soils were 541 and 808 days. Parent was the predominant residue at the end of the study (60–78% of the total applied radioactivity). Only minor metabolites were found (less than 2% of total applied radioactivity).

A photolysis study was conducted on a soil surface. Nitroimino-[^{14}C]clothianidin was applied uniformly on a sandy loam soil surface, equivalent to a rate of 300 g ai/ha. Samples were exposed to artificial sunlight for 17 days, equivalent to 42 days of natural sunlight. The half live was calculated as 8.2 days. Parent was the predominant residue at the end of the study (22% of the total applied radioactivity). Only minor metabolites were found (less than 5% of the applied radioactivity).

In a confined rotational crop study, nitroimino-[^{14}C]clothianidin was sprayed on a sandy loam soil at a rate of 328 g ai/ha under greenhouse conditions. Rotational crops were sown 29, 153 and 314 days after the application, representing first, second and third rotations. Wheat forage was harvested at 41–50 days after sowing, wheat hay 77–106 days after sowing and wheat straw/grain, Swiss chard and turnip leaves/roots at 123–161 and 41–61, 75–84 days after sowing, i.e., at maturity. Total radioactivity was 0.016, 0.011 and 0.007 mg/kg clothianidin equivalents in turnip roots after the first, second and third rotations respectively, 0.11, 0.052 and 0.044 mg/kg in the wheat grain, 0.15, 0.25 and 0.12 mg/kg in the Swiss chard, 0.36, 0.22 and 0.11 mg/kg in the turnip leaves, 0.30, 0.39 and 0.34 mg/kg in wheat forage, 0.53, 0.36 and 0.37 mg/kg in wheat hay and 2.6, 1.2 and 1.2 mg/kg in wheat straw. Parent was the major compound in turnip roots at 27–40% of total radioactivity. The metabolite TZNG was the major compound in wheat grain at 10–23% of total radioactivity. Parent, TZNG and MNG were the major compounds at 12–46%, 3.9–16% and 11–37% of total radioactivity in green crop parts including wheat hay. Parent, TZNG, MG and MNG were the major compounds in wheat straw at 7.2–12%, 7.3–11%, 9.3–18% and 9.1–13% of total radioactivity, respectively.

In a field rotational crop study, maize seeds were treated at a rate of 2 mg ai/seed and sown in the field, corresponding to a rate of 162–192 g ai/ha. Maize plants were tilled into the soil and rotational crops were sown 1, 4, 8 and 12 months after sowing the maize seeds. Turnips (roots, tops), wheat (forage, hay, straw, grain) and mustard greens were harvested at earliest crop maturity. Clothianidin levels in green crop parts including wheat hay ranged from < 0.01–0.025 mg/kg, < 0.01–0.017 mg/kg, and < 0.01–0.023 mg/kg at the 1, 4 and 8 month plant back intervals, respectively. Clothianidin was not found at the 12 month plant back intervals (< 0.01 mg/kg). Clothianidin was not found in turnip roots, wheat grain and wheat straw at any of the plant back intervals (< 0.01 mg/kg). TZNG was only quantified at the 1 month plant back interval and was not found in any of the commodities (< 0.01 mg/kg).

The proposed degradation pathway in soil proceeds via two main routes with clothianidin being transformed in TZNG by oxidative methylation and to MNG by C-N bond cleavage. These soil metabolites could then be taken up by plants and further metabolised.

Environmental fate in water-sediment systems

The Meeting received information on the hydrolysis and photolysis of clothianidin in sterile water. Experiments were carried out using clothianidin ^{14}C labelled at the nitroimino or the thiazolyl moiety.

Clothianidin is regarded as hydrolytically stable at pH 4 and 7 at 50 °C, but is unstable at pH 9 at this high temperature. At ambient temperature, clothianidin is stable at pH 4, 7 and 9. The experimental half-life for clothianidin at pH 9 was 14.4 days at 50 °C, 3.7 days at 62 °C and 0.68 days at 74 °C. After 33 days there is a clothianidin decrease of 6% at 25 °C. Clothianidin is degraded to a low extent by hydrolysis to form mainly TZMU and ACT.

A photolysis study was conducted in sterile water with artificial sunlight for 18 days, equivalent to 22.5 days of natural sunlight. The half-life for clothianidin was 3.3 hours for artificial sunlight, equivalent to 4.1 hours in natural sunlight. When the study was repeated with non-sterile water, a half-life for clothianidin of 35–37 minutes was found. Photo-degradation therefore contributes significantly to the elimination of clothianidin in aquatic systems. Clothianidin is degraded by hydrolysis, denitrification and complex cyclisation reactions to form mainly TZMU, MU and MG.

Methods of analysis

The Meeting received description and validation data for analytical methods for clothianidin, TZNG, TMG, TZMU and MNG in plant commodities or for clothianidin, TZG, TZU and the pyruvate conjugate of ATMG in animal commodities.

Three single residue analytical methods were proposed to the Meeting as post-registration monitoring and enforcement method for parent clothianidin in plant and animal commodities. Compatibility of clothianidin in an existing multi-residue HPLC-MS method (e.g., DFG S19) was not tested.

The Meeting considers the HPLC-MS-MS single residue method 00552 and modifications thereof and the HPLC-UV single residue method 00657 and modifications thereof sufficiently validated for the determination of parent clothianidin in plant commodities with high water content, plant commodities with high acid content, plant commodities with high fat content, and dry plant commodities. The use of deuterated standards in HPLC-MS-MS method 00552 makes the method very expensive and therefore less suitable as enforcement-monitoring method for world-wide use. The Meeting considers the HPLC-UV single-residue method 00656 and modifications thereof sufficiently validated for the determination of parent clothianidin in animal tissues, milk and eggs. The LOQs for these three methods were in the range of 0.01–0.02 mg/kg, depending on the matrix.

The methods reported to the Meeting and used in the supervised residue trials, processing studies, storage stability studies and feeding studies determined parent clothianidin and in some cases also the metabolites TZNG, TMG, TZMU and MNG (in plant commodities) or TZG, TZU and the pyruvate conjugate of ATMG (in animal commodities). Macerated samples were generally extracted with acetonitrile/water. The extract was cleaned up by solvent partition and/or column chromatography and/or solid phase extraction, if necessary. The final residue could then be determined by HPLC-UV or HPLC-MS-MS. The Meeting considers validation sufficient for all commodities and all analytes analysed in the supervised residue trials and feeding studies. LOQs were in the 0.01–0.05 mg/kg range for clothianidin and its metabolites in plant and animal commodities. LOQs for milk were in the 0.002–0.01 mg/kg range for clothianidin.

Extraction efficiencies for acetonitrile/water (2:1) including clean-up steps as used in HPLC-MS-MS method 00552 for plant commodities were verified using samples with incurred radioactive residues from metabolism studies on apple (14 day surface washed fruit sample) and maize (63 day forage, 160 day stover and 160 day kernel sample). Extraction efficiency for acetonitrile/water (2:1) for clothianidin was 85%, 81%, 74%, 61% respectively in surface washed apple fruit, maize forage, maize stover and maize kernels. The Meeting considers the extraction efficiencies for the extraction and clean-up steps as used in the analytical methods generally sufficient for plant commodities. However the study is not conclusive on grains, since the recovery of 61% might be within analytical errors at such low residue levels.

Extraction efficiencies for acetonitrile/water (2:1) including clean-up steps as used in HPLC-MS-MS method 00624 for animal commodities were verified using samples with incurred radioactive residues from metabolism studies on goat (milk, muscle, fat and liver). Extraction efficiency was 100%, 75%, 73% in milk, muscle and fat for clothianidin, 72%, 46%, 106% in muscle, fat and liver for the pyruvate conjugate of ATMG, 62%, 69%, 67% in muscle, fat and liver for TZG, and 87%, 73%, 94% and 68% for milk, muscle, fat and liver for TZU. The Meeting considers the extraction efficiencies for the extraction and clean-up steps as used in the analytical methods for clothianidin sufficient for animal commodities. However, extractions efficiencies for metabolites TZG, the pyruvate conjugate of ATMG and TZU are considered insufficient (less than 70% for some or all commodities).

Stability of pesticide residues in stored analytical samples

The Meeting received information on the stability of clothianidin and TMG in plant commodities stored frozen. No storage stability studies were provided for animal commodities. Since the samples from the animal feeding study were analysed within 30 days after slaughter, there is no need to have storage stability studies on animal commodities.

Parent clothianidin was stable when stored at –10 °C or lower for at least 24 months in crops with high water content (apple, Japanese pear, apricot, peach, cauliflower, head cabbage, cucumber, tomato, lettuce, maize and forage), for at least 18 months in crops with high acid content (cranberries and grapes), for at least 24 months in crops with high oil content (dry soya beans, cottonseed, rape and seed), for at least 24 months in crops with high starch content (maize grain, rice grain, sugar beet roots and potatoes), for at least 10 months in dry tea leaves, for at least 24 months in maize straw, for at least 2 months in tomato paste, for at least 4 months in cotton meal, and for at least 4 months in cotton oil.

Metabolite TMG was stable when stored at –10 °C or lower for at least 25 months in crops with high water content (cauliflower, lettuce and sugar beet leaves), at least 162 days in crops with high acid content (grapes), at least 25 months in crops with high starch content (potatoes) and at least 25 months in processed potato commodities (flakes and chips).

All crop commodities from supervised residue trials were analysed within this period, although storage temperatures varied. Since clothianidin is shown to be stable for a long period of time, trials where samples were stored for a few days at + 5 °C before being frozen and trials where temperatures of frozen samples increased to –1 °C were not rejected.

Definition of the residue

The composition of the residue was investigated for livestock, plant commodities, soil and water.

Based on the available livestock studies, parent clothianidin was the major component in ruminant muscle, ruminant fat and milk (21–51% of the total radioactivity TRR), but was metabolised further in ruminant liver, ruminant kidney, poultry tissues and eggs. The major residue in ruminant liver consists of TMG including conjugates (13%); the major residue in ruminant kidney consists of TZU (15%), TZG (12%), TZMU (11%) and ATMG-pyruvate (10%) and parent was not found in liver and kidney. Because the lactating goat was sacrificed only 5 hours after dosing, parent levels might decrease further, while metabolite levels might rise in time. However the metabolite study on goats shows that maximum levels in milk are reached within 24 hours, showing that the residue disappears very quickly. The major residue in poultry consists of ATG conjugates (35%) in muscle; TZNG (24%) and ATG conjugates (38%) in fat; and TZNG (46%) and TZG (22%) in liver. Parent was only found at low levels (up to 5.2%). The major residue in poultry eggs consists of TZNG (88%), parent was found at 21% of the total radioactivity. Of these metabolites, ATMG (conjugates) and ATG (conjugates) were not found in rats. Additional toxicity studies with ATMG-pyruvate and ATG-acetate indicated no toxicological concern, (LD_{50} > 2000 mg/kg, negative mutagenicity test). Because of this and because the conjugates of ATMG and ATG are expected to be

excreted readily, these metabolites are not included in the residue definition. Since TZNG forms a major part of the residue in poultry fat (24%), poultry liver (46%) and poultry eggs (88%), and TZNG may be significant in ruminants, TZNG is considered for inclusion in the residue definition.

No poultry feeding study has been conducted, therefore actual residue levels in poultry tissues and eggs are not available. Since poultry dietary burden is very low compared to dose levels in the metabolism study (0.25 ppm versus 134 ppm), no residues are anticipated in poultry tissues and eggs. A feeding study on dairy cows was conducted at a maximum level of 2.6 ppm dry feed which is in the same order of magnitude as the dietary burden (0.75 ppm). At this level, the parent compound was only found in milk at levels of up to 0.012 mg/kg. TZNG was not tested. Metabolites TZG, TZU and ATMG-pyruvate were not found in tissues or in milk (< 0.01 mg/kg). Based on these results it is not expected that metabolites will be found in ruminant tissues and milk, nor in poultry tissues and eggs. Therefore the Meeting concluded that the residue definition should only include the parent compound.

Fat solubility of clothianidin in milk has not been investigated in metabolism studies or in feeding studies. The log K_{ow} for clothianidin of approximately 0.7–0.9 does not suggest fat solubility. Fat solubility of TZNG has not been investigated, but based on its molecular structure it is expected to be in the same order of magnitude as the parent compound. The Meeting considers the residue in animal commodities (clothianidin and TZNG) not to be fat-soluble.

Based on the available comparative plant metabolism studies, parent clothianidin is the major component (14–97% of the total radioactivity TRR) of the crops tested, except in mature sugar beet leaves (27% TMG, 29% MG). TMG, MNG, TZMU and TZNG have been analysed in some supervised field trials. TMG was not found in grapes, persimmons, potatoes, sugar beet roots (< 0.01 or < 0.01 mg/kg), but was found in leafy crops like head cabbage (< 0.01–0.013 mg/kg), head lettuce (< 0.01–0.078 mg/kg), cotton gin trash (0.048–0.14 mg/kg), sugar beet tops (< 0.01–0.026 mg/kg). MNG was not found in persimmons (< 0.01 mg/kg). TZMU and TZNG were found in persimmon at 0.02–0.03 mg/kg. In rotational crops, clothianidin was metabolised further and metabolites TZNG, MNG, and MG were found at quantifiable levels. TZNG is found as a minor metabolite in primary crops (< 10% TRR) and as a major metabolite in rotational crops (10–23% in grain, 3.9–16% in green crop parts and 7.3–11% in wheat straw). However in a field rotational crop study, TZNG could not be found (< 0.01 mg/kg) at the earliest 1 month plant back interval. All plant metabolites identified were also found in rats. Therefore, metabolites are not included in the residue definition.

Clothianidin exists predominantly in the E-form. The compound clothianidin is equivalent to the E form of CGA 322704, a metabolite arising from thiamethoxam use. No information is given on the actual ratio between E and Z isomers, nor which of these isomers is the active one. Information on the activation energy to convert Z-isomers to E-isomers is not available. If the activation energy for conversion is high, it is likely that the CGA 322704 appears as E/Z mixture in crops, soil, water and animal commodities. HPLC chromatograms of CGA 322704 from supervised trials show a single peak, so it is not clear whether E/Z mixtures cannot be separated by HPLC or whether there is only one isomer present in plant and animal commodities. Therefore, both isomers should be included in the residue definition. Clothianidin and the CGA 322704 metabolite of thiamethoxam will appear the same as clothianidin in the analytical methods. The Z-isomer may result from use of thiamethoxam.

The Meeting recommended the following as residue definitions for clothianidin:

Definition of the residue for compliance with the MRL or for estimation of the dietary intake for plant commodities: *sum of clothianidin and its Z-isomers*

Definition of the residue for compliance with the MRL or for estimation of the dietary intake for animal commodities: *sum of clothianidin and its Z-isomers.*

The Meeting considers the residue in animal commodities not fat soluble.

Results of supervised trials on crops

The Meeting received supervised trials data for clothianidin on apples, pears, apricots, cherries, nectarines, peaches, plums, cranberries, grapes, persimmons, bananas, head cabbages, broccoli, cucumber, summer squash, egg plants, sweet corn, tomatoes, head lettuce, leaf lettuce, dry soya beans, carrots, chicory roots, potatoes, sugar beet roots, barley, maize, popcorn, rice, sorghum, wheat, sugarcane, cotton seed, rape seed, sunflower seed and tea.

The Meeting noted that clothianidin residues may arise from use of clothianidin as well as from use of thiamethoxam. The compound clothianidin is equivalent to the E form of CGA 322704, a metabolite arising from thiamethoxam use. Residues of CGA 322704 occurring in food are included in the clothianidin MRLs. In the present appraisal first the maximum residue levels, STMRs and HRs for clothianidin use are evaluated. The same is done for the CGA 322704 metabolite in the thiamethoxam appraisal. In the present appraisal an overview table is given, where a recommendation is given for both uses.

Pome fruits

Field trials involving apples were performed in Australia, Germany, Hungary, the UK, France, Italy, Spain, Japan and the USA.

GAP for apples and pears in Australia is for two foliar spray applications (interval 14 days) at 20 g ai/hL with a PHI of 21 days, either with or without adjuvant. In trials from Australia matching this GAP (2 × 20 g ai/hL, interval 15 days and PHI 21 days, with adjuvant) clothianidin residues in apple whole fruit were 0.24 mg/kg (n = 1).

GAP for apples in Australia is for one soil drench application at 2.5 g ai/tree with a PHI of 21 days. Field trials performed in Australia did not match this GAP.

GAP for pome fruit in Hungary is for one foliar spray application at 75 g ai/ha with a PHI of 28 days. Field trials performed in Germany, the UK and France did not match this GAP. In trials in Hungary matching this GAP (1 × 72 g ai/ha and PHI 28 days) clothianidin residues in apple whole fruit were < 0.02 mg/kg (n = 1).

GAP for apples and pears in Italy is for one foliar spray application at 7.5 g ai/hL with a PHI of 14 days). Field trials performed in Italy, France and Spain did not match this GAP. However trials performed with two applications can be taken into account, since results from samples taken prior to the 2nd application showed residues to be < 0.01–0.011 mg/kg. In trials in France and Italy with two applications (2 × 7.5–7.6 g ai/hL, interval 7 days and PHI 14 days) clothianidin residues in apple whole fruit were < 0.01 (3) and 0.014 mg/kg (n = 4).

GAP for apples in Romania is for an unstated number of foliar spray applications at 10 g ai/hL, unstated interval and unstated PHI. In trials in France, Italy and Spain matching this GAP (1–2 × 7.5–13 g ai/hL, interval 7 days, PHI of 0–21 days) clothianidin residues in apple whole fruit were < 0.01, < 0.01, 0.013, 0.014, 0.049, 0.058 0.067 and 0.12 mg/kg (n = 8) without adjuvant and 0.012 and 0.085 mg/kg (n = 2) with adjuvant on the same location. Since an adjuvant is not indicated in the label only the dataset without adjuvant is taken into account.

GAP for apples in Japan is for three spray applications at 8.0 g ai/hL, unstated interval and PHI 1 day. In trials from Japan matching this GAP (3 × 8.0 g ai/hL, interval 7 days and PHI 1 day) clothianidin residues in apple whole fruit were 0.06 and 0.15 mg/kg (n = 2). The Meeting noted that trial plots consisted of only three trees with a height of 3 m. As the trial design complied with official Japanese guidelines with sampling done randomly and of sufficient size, the Meeting decided to accept the residue results.

GAP for Pome fruit in the USA is for one foliar spray application at 224 g ai/ha (maximum of 224 g ai/ha per season, interval 10 days and a PHI of 7 days. In trials from the USA matching this

GAP (1 × 219–225 g ai/ha and PHI 6–7 days) clothianidin residues in apple whole fruit were < 0.01, 0.010, 0.019, 0.025, 0.052, 0.087, 0.094, 0.10, 0.10, 0.12, 0.15, 0.16 and 0.20 mg/kg (n = 13).

The datasets corresponding to the GAPs for Australia, Hungary, Italy and Japan were considered insufficient to support a recommendation. The Meeting noted that the GAP for Romania resulted in a similar dataset when compared to the GAP for USA (Mann-Whitney U test). However, as the GAPs are different the data cannot be combined. Since the highest residue is found in the USA dataset, the Meeting decided to use only the apple data corresponding to the GAP of the USA.

Field trials involving pears were performed in Australia, Germany, France, Italy, Spain, Japan and the USA.

GAP for apples and pears in Australia is for two foliar spray applications at 20 g ai/hL (interval 14 days) and PHI 21 days, either with or without adjuvant. In trials from Australia matching this GAP (2 × 20 g ai/hL, interval 15 days and PHI 21 days, with adjuvant) clothianidin residues in pear whole fruit were 0.13 mg/kg (n = 1).

GAP for Pome fruit in Hungary is for one foliar spray application at 75 g ai/ha and PHI 28 days. Field trials performed in Germany and France did not match this GAP.

GAP for apples and pears in Italy is for one foliar spray application at 7.5 g ai/hL (PHI 14 days). Field trials performed in Italy, France and Spain did not match this GAP.

GAP for pears in Japan is for three spray applications at 8.0 g ai/hL, unstated interval and PHI 1 day. In trials from Japan matching this GAP (3 × 8.0 g ai/hL; interval 7 days and PHI 1 day) clothianidin residues in pear minus stylar scar, core and peduncle base were 0.18 and 0.39 mg/kg (n = 2). The Meeting noted that there was only one tree/plot with tree height 2 m. Since the trial design complied with Japanese guidelines and sampling was random with sufficient size, the Meeting decided to accept the residue results

GAP for Pome fruit in the USA is for one foliar spray application at 224 g ai/ha (max 224 g ai/ha per season, interval 10 days and PHI 7 days. In trials from the USA matching this GAP (1 × 221–224 g ai/ha and PHI 6–7 days) clothianidin residues in pear whole fruit were 0.042, 0.071, 0.10, 0.14, 0.15, 0.15 and 0.18 mg/kg (n = 7).

The datasets corresponding to the GAPs for Australia, Hungary, Italy and Japan were considered insufficient to support a recommendation. The Meeting decided to use only the pear data corresponding to the GAP of the USA.

The Meeting noted that the USA datasets for apples and pears were from similar populations (Mann-Whitney U test). Since residue behaviour within the pome fruit group is expected to be similar, the Meeting agreed that they could be combined. Clothianidin residues in pome fruit (whole fruit) were:< 0.01, 0.010, 0.019, 0.025, 0.042, 0.052, 0.071, 0.087, 0.094, 0.10, 0.10, 0.10, 0.12, 0.14, 0.15, 0.15, 0.15, 0.16, 0.18 and 0.20 mg/kg (n = 20).

The Meeting agreed that the USA data for apples and pears could be used to support a pome fruit commodity maximum residue level recommendation and estimated a maximum residue level of 0.4 mg/kg for clothianidin on pome fruit and estimated an STMR of 0.10 mg/kg and an HR of 0.20 mg/kg.

The maximum residue level estimate derived from use of the NAFTA statistical calculator (mean + 3 SD) was 0.27 mg/kg, which differed from the estimate made by the Meeting. The chosen level was higher in recognition of the ratio between the median and the highest residue.

Stone fruits

Field trials involving apricots were performed in Japan.

GAP for Ume (Japanese apricot) in Japan is for three spray applications at 8.0 g ai/hL at unstated interval and PHI 3 days. In field trials on apricots and Japanese apricots from Japan

matching this GAP (3 × 8.0 ai g/hL; interval 6–7 days, PHI 3 days) clothianidin residues in Japanese apricot pitted fruit were 0.50 and 1.1 mg/kg (n = 2). The Meeting noted that there were only 1–2 trees/plot with tree heights of 5 m. Since the trial design complied with Japanese guidelines and sampling was random with sufficient size, the Meeting decided to accept the residue results.

Field trials involving cherries were performed in Japan.

GAP for cherries in Japan is for two spray applications at 8.0 g ai/hL, unstated interval with a PHI 1 day. In indoor trials from Japan matching this GAP (2 × 8.0 g/hL, interval 7 days and PHI 1 day) clothianidin residues in cherry pitted fruit were 1.1 and 2.0 mg/kg (n = 2). The Meeting noted that there was only one tree/plot with tree height of 4 m. Since the trial design complied with Japanese guidelines and sampling was random with sufficient size, the Meeting decided to accept the residue results.

Field trials involving nectarines were performed in Australia and Japan.

GAP for peaches and nectarines in Australia is for two foliar spray applications at 20 g ai/hL, 14 day interval, and PHI 21 days. Field trials performed in Australia did not match this GAP.

GAP for nectarines in Japan is for three spray applications at 8.0 g ai/hL, unstated interval and PHI 3 days. In trials from Japan matching this GAP (3 × 8.0 g ai/hL, interval 7 days and PHI 3 days) clothianidin residues in nectarine pitted fruit were 0.58 and 0.64 mg/kg (n = 2). The Meeting noted that there were only 1–2 trees/plot with tree height of 2 m. Since the trial design complied with Japanese guidelines and sampling was random with sufficient size, the Meeting decided to accept the residue results.

Field trials involving peaches were performed in Australia, Hungary, Japan, USA and Canada.

GAP for peaches and nectarines in Australia is for two foliar spray applications at 20 g ai/hL, 14 day interval and PHI 21 days. Field trials performed in Australia did not match this GAP.

GAP for peaches in Hungary is for one foliar spray application at 8.8 g ai/hL and PHI 14 days. In field trials performed in Hungary matching this GAP (1 × 10 g ai/hL and PHI 14 days) clothianidin residues in peach whole fruit were < 0.02 mg/kg (n = 1).

GAP for peaches in Japan is for three spray applications at 8.0 g ai/hL, unstated interval and PHI 7 days. In field trials performed in Japan matching this GAP (3 × 8.0 g ai/hL, interval 7–8 days and PHI 7 days) clothianidin residues in peach pitted fruit were 0.25 mg/kg (n = 1). In indoor trials performed in Japan matching this GAP (3 × 8.0 g ai/hL, interval 6–8 days and PHI 7days) clothianidin residues in peach pitted fruit were 0.33 mg/kg (n = 1). The Meeting noted that there were only 1–3 trees/plot with tree height of 2 m. Since the trial design complied with Japanese guidelines and sampling was random with sufficient size, the Meeting decided to accept the residue results.

GAP for peaches in the USA is for two foliar spray applications at 112 g ai/ha (max 224 g ai/ha per season), 10 day interval and PHI 7 days. Field trials performed in the USA and Canada did not match this GAP.

Field trials involving plums were performed in Japan.

GAP in Japan for Japanese plums is for three spray applications at 8.0 g ai/hL, unstated interval and PHI 3 days. In field trials performed in Japan matching this GAP (3 × 8.0 g ai/hL, interval 7 days and PHI 3 days) clothianidin residues in plums pitted fruit were 0.03 and 0.06 mg/kg (n = 2). The Meeting noted that there was only 1 tree/plot with tree height of 3 m. Since the trial design complied with Japanese guidelines and sampling was random and of sufficient size, the Meeting decided to accept the residue results.

The datasets for apricots, cherries, nectarines, peaches and plums were considered insufficient to support a recommendation. The Meeting could not estimate maximum residue levels for each of these commodities individually or for a stone fruit group.

Berries and other small fruits

Field trials involving cranberries were performed in the USA. GAP for cranberries in the USA is for three foliar spray applications at 75 g ai/ha (max 224 g ai/ha per season), interval 7 days and PHI 21 days. In field trials performed in the USA matching this GAP (3 × 73–80 g ai/ha, interval 6–8 days and PHI 21–22 days) clothianidin residues in cranberry whole fruit (berries) were < 0.01, < 0.01, < 0.01, < 0.01 and < 0.01 mg/kg (n = 5).

GAP for cranberries in the USA is for one soil treatment at 224 g ai/ha (max 224 g ai/ha per season) and PHI 21 days. In field trials performed in the USA matching this GAP (233–243 g ai/ha and PHI 21–22 days) clothianidin residues in cranberry whole fruit (berries) were < 0.01, < 0.01, < 0.01, < 0.01 and < 0.01 mg/kg (n = 5).

The Meeting noted that the foliar spray treatment and the soil treatment according to the USA GAP both showed no residues (< 0.01 mg/kg). The Meeting estimated a maximum residue level of 0.01* mg/kg for clothianidin on cranberries and estimated an STMR of 0.01 mg/kg and an HR of 0.01 mg/kg.

Statistical calculations using the NAFTA calculator were not possible, since all levels are below LOQ.

Field trials involving grapes were performed in Australia, Japan and the USA.

GAP for grapes (table) in Australia is for two foliar spray applications at 20 g ai/hL, interval 21 days and with a PHI 42 days, with or without adjuvant. In field trials performed in Australia matching this GAP (2 × 20–25 g ai/hL, interval 13–22 days and PHI 41–44 days) clothianidin residues in grapes (whole fruit without stems) were $0.28^{SC,\$}$, 0.82^{WG}, $1.6^{SC,\$}$ mg/kg (n = 3) without adjuvant and 0.06^{WG}, 0.17^{WG} and 1.9^{WG} mg/kg (n = 3) with adjuvant. SC and WG mark the use of SC and WG formulations. In those cases where residues at higher PHI were higher, these residues were selected instead. However, figures marked with $ cannot be used for a recommendation, because of sampling deficiencies and poor condition of the fruit. In a single bridging study with a WG formulation with and without adjuvant, residue levels with adjuvant were higher (1.9 mg/kg with versus 0.82 mg/kg without). Therefore only the dataset with adjuvant will be used in the estimation.

GAP for grapes (table and wine) in Australia is for one soil treatment at 300 g ai/ha. In field trials performed in Australia matching this GAP (300 g ai/ha and PHI 96–132 days) clothianidin residues in grapes whole fruit without stems were $< 0.02^{SC,\$}$, $< 0.02^{SC}$ and $< 0.02^{WG}$ mg/kg (n = 3). SC and WG mark the use of SC and WG formulations. However, the figure marked with $ could not be used for a recommendation, due to sampling deficiencies and the poor condition of the fruit.

GAP for grapes in Japan is for three spray applications at 8.0 g ai/hL, unstated interval and PHI 1 day. Indoor trials performed in Japan matching this GAP (2 × 8.0 g ai/hL and interval 7–8 days, in grapes (whole fruit without stems) were $0.66^{\$}$ and $1.0^{\$}$ mg/kg (n = 2). In those cases where residues at higher PHI were higher, these residues were selected instead. However, values marked with $ cannot be used for a recommendation because of sampling deficiencies.

GAP for grapes in the USA is for two foliar spray applications at 112 g ai/ha (maximum of 224 g ai/ha per season), interval 14 days and PHI 0 days. In field trials performed in the USA matching this GAP (2 × 110–116 g ai/ha, interval 13–14 days and PHI 0 days) clothianidin residues in grapes whole fruit with stems were 0.042, 0.053, 0.074, 0.090, 0.098, 0.11, 0.13, 0.13, 0.14, 0.28, 0.33 and 0.41 mg/kg (n = 12).

A second GAP for grapes in the USA is for one soil treatment at 224 g ai/ha (max 224 g ai/ha per season) and a PHI of 30 days. In field trials performed in the USA matching this GAP (1 × 221–223 g ai/ha total and PHI 30 days) clothianidin residues in grapes (whole fruit with stems) were < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02 and < 0.02 mg/kg (n = 10).

The datasets corresponding to the GAPs for Australia and Japan were considered insufficient to support a recommendation. The Meeting noted that the GAP for foliar treatment in the USA

resulted in higher residues when compared to the GAP for soil treatment in the USA. Therefore, the Meeting decided to use only the grape data corresponding to the GAP of the USA for foliar treatment: 0.042, 0.053, 0.074, 0.090, 0.098, 0.11, 0.13, 0.13, 0.14, 0.28, 0.33 and 0.41 mg/kg (n = 12).

The Meeting estimated a maximum residue level of 0.7 mg/kg for clothianidin on grapes and estimated an STMR of 0.12 mg/kg and an HR of 0.41 mg/kg.

The maximum residue level estimate derived from use of the NAFTA calculator (95/99 99th percentile) was 0.64 mg/kg, which was in agreement with the Meetings estimate (after rounding up to one figure).

Assorted tropical and sub-tropical fruits, edible peel

Field trials involving persimmon were performed in Japan and Korea.

GAP for Japanese persimmon in Japan is for three spray applications at 8.0 g ai/hL, unstated interval and PHI 7 days. In field trials performed in Japan matching this GAP (3 × 8.0 g ai/hL, interval 5–9 days and PHI 7 days) clothianidin residues in persimmon whole fruit were 0.11 and 0.14 mg/kg (n = 2). The Meeting noted that there were only 1–2 trees/plot with tree height of 3 m. Since the trial design complied with Japanese guidelines and sampling was random with sufficient size, the Meeting decided to accept the residue results.

GAP for persimmon in Korea is for three foliar applications at 8.0 g ai/hL, interval 7–10 days and PHI 10 days. In field trials performed in Korea matching this GAP (3 × 8.0 g ai/hL, interval 10 days and PHI 10 days) clothianidin residues in persimmon whole fruit were 0.047$ mg/kg (n = 1). However, the values marked with $ cannot be used for a recommendation because of sampling deficiencies.

The datasets for persimmon were considered insufficient to support a recommendation. The Meeting could not estimate maximum residue levels for persimmon.

Assorted tropical and sub-tropical fruits, inedible peel

Field trials involving bananas were performed in Australia.

GAP for bananas in Australia is for one stem spray application at 0.9 g ai/stem. In field trials performed in Australia matching this GAP (0.9 g ai/stem and PHI 256–553 days) clothianidin residues in banana whole fruit (including peel) were < 0.02, < 0.02, < 0.02, < 0.02, < 0.02 and < 0.02 mg/kg (n = 6).

GAP for bananas in Australia is for one stem injection application at 0.6 g ai/stem. In field trials performed in Australia matching this GAP (0.6 g ai/stem and PHI 256–553 days) clothianidin residues in banana whole fruit (including peel) were < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02 and 0.02 mg/kg (n = 8).

The Meeting noted that the stem injection application according to the Australian GAP showed residues below or at LOQ (< 0.02–0.02 mg/kg). The Meeting estimated a maximum residue level of 0.02 mg/kg for clothianidin on banana whole fruit and estimated an STMR of 0.02 mg/kg and an HR of 0.02 mg/kg.

Statistical calculations using the NAFTA calculator were not possible, as all levels were at or below the LOQ.

Brassica vegetables

Field trials involving head cabbage were performed in Belgium, Germany, the UK, France, Italy, Spain, Japan and the USA.

GAPs for seed treatments in Belgium, Germany, the UK, France, Italy and Spain are not available. GAP for New Zealand cannot be matched to European trials because the New Zealand GAP is only for forage Brassicas, not meant for human consumption.

GAP for head cabbage in Japan is for one application, soil incorporated, at 10 mg ai/plant (at seeding up to transplanting) combined with two foliar applications at 8.0 g ai/hL, unstated interval and PHI 3 days. In field trials performed in Japan matching this GAP (1 × 10 mg ai/plant plus two foliar applications at 8.0 g ai/hL, interval 6–8 days and PHI 3 days) clothianidin residues in cabbage (head only without core) were $0.16^{\$}$ and $0.18^{\$}$ mg/kg (n = 2). However, values marked with $ cannot be used for a recommendation because of sampling deficiencies.

GAP for Brassica (cole) leafy vegetables in the USA is for three foliar spray applications at 74 g ai/ha (max 224 g ai/ha per season), interval 10 days and PHI 7 days. Field trials performed in the USA did not match this GAP.

GAP for Brassica (cole) leafy vegetables in the USA is for one soil treatment at 224 g ai/ha (max 224 g ai/ha per season) at planting. In trials performed in the USA matching this GAP (1 × 224 g ai/ha and PHI 77 days) clothianidin residue levels were 0.015 mg/kg (n = 1).

The datasets for head cabbages were considered insufficient to support a recommendation. The Meeting could not estimate maximum residue levels for head cabbages.

Field trials involving broccoli were performed in Japan.

GAP for broccoli in Japan is for one soil incorporated treatment at 10 mg ai/plant (at seeding up to transplanting) combined with three foliar applications at 8.0 g ai/hL, unstated interval and PHI 3 days. In field trials performed in Japan matching this GAP (1 × 10 mg ai/plant plus three foliar applications at 8.0 g ai/hL, interval 6–7 days and PHI 3 days) clothianidin residues in broccoli (buds without leaves) were $0.07^{\$}$ and $0.33^{\$}$ mg/kg (n = 2). However, values marked with $ cannot be used for a recommendation because of sampling deficiencies.

GAP for broccoli in Japan is for one soil incorporation at 10 mg ai/plant (at seeding up to transplanting). In field trials performed in Japan matching this GAP (1 × 10 mg ai/plant and PHI 71–151 days), clothianidin residues in broccoli (buds without leaves) were $< 0.01^{\$}$ and $0.04^{\$}$ mg/kg (n = 2). However, values marked with $ cannot be used for a recommendation because of sampling deficiencies.

The datasets for broccoli were considered insufficient to support a recommendation. The Meeting could not estimate maximum residue levels for broccoli.

Fruiting vegetables, Cucurbits

Field trials involving cucumbers were performed in Brazil, Japan and the USA.

GAP for cucumber in Brazil is for four foliar treatments at 10 g ai/hL, unstated interval and PHI 1 day. Field trials performed in Brazil did not match this GAP.

GAP for cucumber in Japan is for one soil incorporation at 10 mg ai/plant (at transplanting) combined with three foliar sprays at 8.0 g ai/hL, unstated interval and PHI 1 day. In indoor trials performed in Japan matching this GAP (1 × 10 mg ai/plant at planting + 3 × foliar spray at 8.0 g ai/hL, interval 7 days and PHI 1 day) clothianidin residues in cucumber were: 0.2 and, 0.70 mg/kg (n = 2).

GAP for cucurbit vegetables in the USA is for three foliar spray applications at 74 g ai/ha (max 224 g ai/ha per season), interval 10 days and PHI 7 days. Field trials performed in the USA did not match this GAP.

GAP for cucurbit vegetables in the USA is for one soil treatment at 224 g ai/ha (max 224 g ai/ha per season) at planting. In field trials performed in the USA matching this GAP (1 ×

232 g ai/ha and PHI 21 days) clothianidin residue levels in cucumber whole fruit were 0.014 mg/kg (n = 1).

Field trials involving summer squash were performed in the USA.

GAP for cucurbit vegetables in the USA is for three foliar spray applications at 74 g ai/ha (max 224 g ai/ha per season), interval 10 days and PHI 7 days. Field trials performed in the USA did not match this GAP.

GAP for cucurbit vegetables in the USA is for one soil treatment at 224 g ai/ha (max 224 g ai/ha per season) at planting. In field trials performed in the USA matching this GAP (1 × 231 g ai/ha and PHI 73 days) clothianidin residue levels in summer squash whole fruit were < 0.01 mg/kg (n = 1).

The datasets for cucumbers and summer squash were considered insufficient to support a recommendation. The Meeting could not estimate maximum residue levels for each of these commodities individually or for a cucurbit fruiting vegetable group.

Fruiting vegetables, other than Cucurbits

Field trials involving egg plants were performed in Japan.

GAP for egg plants in Japan is for one soil incorporation at 5 mg ai/plant (at transplanting) combined with three foliar sprays at 8.0 g ai/hL, unstated interval and PHI 1 day. In indoor trials performed in Japan matching this GAP (1 × 10 mg ai/plant at planting + 3 × foliar spray at 8.0 g ai/hL, interval 7 days and PHI 1 day) clothianidin residues in egg plants were: 0.29 and 0.38 mg/kg (n = 2). Where residue levels at higher PHIs were higher, these were selected instead.

The dataset for egg plant was considered insufficient to support a recommendation. The Meeting could not estimate maximum residue levels for egg plant.

Field trials involving sweet corn were performed in the USA and Canada.

GAP for maize (field corn, popcorn and sweet corn) in the USA and Canada is for one seed treatment at 1.25 mg ai/seed. Seed treatment with subsequent field trials performed in the USA and Canada did not match this GAP. However, seed treatments performed at an exaggerated rate of 2.0 mg ai/seed and subsequent field trials performed in the USA and Canada (PHI 72–113) showed no residues in sweet corn (kernels plus cobs with husks removed): < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01 and < 0.01 mg/kg (n = 17).

The Meeting decided that the trials performed at an exaggerated rate could be used for a recommendation. The Meeting estimated a maximum residue level of 0.01* mg/kg for clothianidin on sweet corn and estimated an STMR of 0.01 mg/kg and an HR of 0.01 mg/kg.

Statistical calculations using the NAFTA calculator were not possible, as all residue levels were below the LOQ.

Field trials involving tomatoes were performed in Japan and the USA.

GAP for tomatoes in Japan is for one soil incorporation at 10 mg ai/plant (at transplanting) combined with three foliar sprays at 8.0 g ai/hL, unstated interval and PHI 1 day. In indoor trials performed in Japan matching this GAP (1 × 10 mg ai/plant at planting + 3 × foliar spray at 8.0 g ai/hL, interval 7 days and PHI 1 day) clothianidin residues in tomatoes were: 0.66 and 0.90 mg/kg (n = 2) in grape tomatoes and 0.12 and 0.23 mg/kg (n = 2) in regular size tomatoes. Where residue levels at higher PHIs were higher, these were selected instead.

GAP for tomatoes in Japan is for one soil incorporation at 10 mg ai/plant (at transplanting) In indoor trials performed in Japan matching this GAP (1 × 10 mg ai/plant and PHI 77–98 days)

clothianidin residues were < 0.01 and < 0.01 mg/kg (n = 2). The laboratory results with the higher LOQ value of 0.05 mg/kg were not taken into account.

GAP for fruiting vegetables in the USA is for three foliar spray applications at 74 g ai/ha (max 224 g ai/ha per season), interval 7 days and PHI 7 days. Field trials performed in the USA did not match this GAP.

GAP for fruiting vegetables in the USA is for one soil treatment at 224 g ai/ha (max 224 g ai/ha per season) at planting. In field trials performed in the USA matching this GAP (1 × 222–226 g ai/ha and PHI 21–82 days) clothianidin residue levels in tomato whole fruit were < 0.01 and 0.028 mg/kg (n = 2).

The datasets for tomato were considered insufficient to support a recommendation. The Meeting could not estimate maximum residue levels for tomato.

Leafy vegetables

Field trials involving head lettuce were performed in the USA.

GAP for leafy vegetables in the USA is for three foliar spray applications at 74 g ai/ha (max 224 g ai/ha per season), interval 10 days and PHI 7 days. Field trials performed in the USA did not match this GAP.

GAP for leafy vegetables in the USA is for one soil treatment at 224 g ai/ha (max 224 g ai/ha per season) at planting. In field trials performed in the USA matching this GAP (1 × 224 g ai/ha and PHI 32 days) clothianidin residues in head lettuce were 0.044$ mg/kg (n = 1). However, the value marked with $ could not be used for a recommendation because the heads didn't form properly.

Field trials involving leaf lettuce were performed in the USA.

GAP for leafy vegetables in the USA is for three foliar spray applications at 74 g ai/ha (max 224 g ai/ha per season), interval 10 days and PHI 7 days. Field trials performed in the USA did not match this GAP.

GAP for leafy vegetables in the USA is for one soil treatment at 224 g ai/ha (max 224 g ai/ha per season) at planting. In field trials performed in the USA matching this GAP (1 × 227 g ai/ha and PHI 22 days) clothianidin residues in leaf lettuce were 0.046 mg/kg (n = 1).

The datasets for head lettuce and leaf lettuce were considered insufficient to support a recommendation. The Meeting could not estimate maximum residue levels for each of these commodities individually or for a leafy vegetable group.

Pulses

Field trials involving soya bean (dry) were performed in Japan and the USA.

GAP for soya beans in Japan is either for three high volume spray applications at 8.0 g ai/hL or for three aerial spray applications at 833 g ai/hL or for three dusting applications at 200 g ai/ha, unstated interval and PHI 7 days. Trials performed in Japan did not match this GAP.

GAP for soya beans in the USA is for three foliar spray applications at 75 g ai/ha (maximum 224 g ai/ha per season), interval 7 days and PHI 21 days. Field trials performed in the USA did not match this GAP.

Since the datasets for dry soya beans did not match GAP, the Meeting could not estimate a maximum residue level for soya beans.

Root and tuber vegetables

Field trials involving carrots were performed in Belgium, Germany, Netherlands, the UK, France, Italy, Portugal and Spain.

GAPs for seed treatments in Belgium, Germany, Netherlands, the UK, France, Italy and Spain were not available.

Since there was no GAP available, the Meeting could not estimate a maximum residue level for carrots.

Field trials involving chicory roots were performed in Belgium.

GAP for chicory roots in Belgium is for one seed treatment at 0.3 mg ai/seed. In field trials performed in Belgium matching this GAP (1 × 0.265 mg ai/seed and PHI 161 days) clothianidin residue levels in chicory roots were < 0.01 mg/kg (n = 1).

The dataset for chicory roots was considered insufficient to support a recommendation. The Meeting could not estimate a maximum residue level for chicory roots.

Field trials involving potatoes were performed in the USA and Canada.

GAP for tuberous and corm vegetables in the USA is for four foliar spray treatments at 56 g ai/ha (maximum of 224 g ai/ha per season), interval 7 days with a PHI of 14 days. Field trials performed in the USA and Canada did not match this GAP. However, treatments performed in the USA and Canada at an exaggerated rate (3 × 73–77 g ai/ha, interval 5–8 days and PHI 13–14 days) showed no residues: < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02 and < 0.02 mg/kg (n = 17) in potato tubers with peel.

GAP for tuberous and corm vegetables in the USA is for one soil treatment at 224 g ai/ha (maximum of 224 g ai/ha per season) at planting. In field trials performed in the USA and Canada matching this GAP (1 × 217–226 g ai/ha and a PHI of 48–145 days) clothianidin residue levels in potato tubers with peel were: < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, 0.020, 0.020, 0.029 and 0.033 mg/kg (n = 17) using an SG formulation at planting and < 0.02 and < 0.02 mg/kg (n = 2) using a WG formulation at planting (at the same locations). Since only one value is selected per location, only the results for the SG formulation were considered.

The Meeting noted that the GAP for soil treatment in the USA resulted in higher residues when compared to the GAP for foliar treatment in the USA. Therefore, the Meeting decided to use only the potato data corresponding to the GAP of the USA for soil treatment: < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, 0.020, 0.020, 0.029 and 0.033 mg/kg (n = 17).

The Meeting estimated a maximum residue level of 0.05 mg/kg for clothianidin on potatoes with peel and estimated an STMR of 0.02 mg/kg and an HR of 0.033 mg/kg (considering potatoes with peel as edible portion).

The maximum residue level estimate derived from use of the NAFTA statistical calculator was 0.03 mg/kg (mean + 3 SD, no MLE used) differed from the estimate made by the Meeting. The higher level was chosen in recognition of the number of majority of values below LOQ and the small number above.

Field trials involving sugar beet roots were performed in Belgium, Germany, the UK, France, Italy, Spain and the USA.

GAP for sugar beets in Belgium, Denmark, Finland, Germany, Netherlands, Slovakia and the UK is for one seed treatment at 0.6 mg ai/seed. For seed treatments and subsequent field trials performed in the UK, France and Germany matching this GAP (1 × 0.6 mg ai/seed and PHI 92–148 days) clothianidin residues in sugar beet roots were < 0.01, < 0.01 and 0.012 mg/kg (n = 3).

GAP for sugar beets in Italy, Slovenia, and Spain is for one seed treatment at 0.6 mg ai/seed. Trials performed in Spain and Italy did not match this GAP.

GAP for sugar beets in the USA is for one seed treatment at 0.6 mg ai/seed (FS formulation). For seed treatments and subsequent field trials performed in the USA matching this GAP (1 × 0.6 mg ai/seed and PHI 109–179 days SE formulation) clothianidin residues in sugar beet roots were < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, 0.015 and 0.019 mg/kg, n = 12.

The Meeting noted that the GAP for Northern Europe resulted in a similar dataset when compared to the GAP for USA (Mann-Whitney U test). Because the GAPs are identical the data can be combined. The Meeting decided to use the combined dataset for sugar beet roots corresponding to the GAP of Northern Europe and the USA: < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, 0.012, 0.015 and 0.019 (n = 15).

The Meeting estimated a maximum residue level of 0.03 mg/kg for clothianidin on sugar beet roots and estimated an STMR of 0.01 mg/kg and an HR of 0.019 mg/kg.

The maximum residue level estimate derived from use of the NAFTA statistical calculator was 0.02 mg/kg (mean + 3 SD, no MLE used), which differed from the estimate made by the Meeting. The NAFTA calculator value was not considered as it does not give reliable results with large numbers of censored data.

Cereal grains

Field trials involving maize (corn) were performed in the USA and Canada.

GAP for maize (field corn, popcorn and sweet corn) in the USA and Canada is for one seed treatment at 1.25 mg ai/seed. Seed treatment with subsequent field trials performed in the USA and Canada did not match this GAP. However, seed treatments performed at an exaggerated rate of 2.0 mg ai/seed and subsequent field trials performed in the USA and Canada (PHI 119–170 days) showed no residues in maize seed: < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01 < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01 < 0.01, < 0.01, < 0.01, < 0.01, < 0.01 and < 0.01 mg/kg (n = 26).

Field trials involving popcorn were performed in the USA and Canada.

GAP for maize (field corn, popcorn and sweet corn) in the USA and Canada is for one seed treatment at 1.25 mg ai/seed. Seed treatment with subsequent field trials performed in the USA and Canada did not match this GAP. However, seed treatments performed at an exaggerated rate of 2.0 mg ai/seed and subsequent field trials performed in the USA and Canada (PHI 119–170 days) showed no residues: < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01 < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01 < 0.01, < 0.01, < 0.01, < 0.01, < 0.01and < 0.01 mg/kg (n = 26).

Field trials involving rice were performed in Japan.

GAP for rice in Japan is for one application in a seedling box at 0.75 g ai/box and three GR spreading applications at 200 g ai/ha, unstated interval and a 7 day PHI. Since the application in a seedling box is not expected to contribute to the final residue, trials where the spreading applications are according to GAP are considered acceptable. For field trials performed in Japan matching this GAP (seedling treatment at 1.25–1.65 g ai/box + three spreading (GR) applications at 200 g ai/ha, interval 6–29 days and PHI 7 days) clothianidin residues in rice grains were < 0.01, 0.01, 0.02 and 0.04 mg/kg, n = 4. When higher residues were found at later PHIs these residues were selected instead. After harvest, rice was dried and protected from rain for 9–22 days. Residue values are for husked rice grain (brown rice).

GAP for rice in Japan is for one application in a seedling box at 0.75 g ai/box and three DP dust applications at 200 g ai/ha, unstated interval and a 7 day PHI. Since the application in a seedling

box is not expected to contribute to the final residue, trials where dusting applications were according to GAP were considered acceptable. For field trials performed in Japan matching this GAP (seedling treatment at 1.65 g ai/box + three dusting (DP) applications at 200 g ai/ha, interval 7–22 days and a 7 day PHI) clothianidin residues in rice grains were 0.07 and 0.11 mg/kg, n = 2. When higher residues were found at later PHIs these residues were selected instead. After harvest, rice was dried and protected from rain for 9–14 days. Residue values were for husked rice grain.

GAP for rice in Japan is for one application in a seedling box at 0.75 g ai/box and three high volume spray applications at 4 g ai/hL, unstated interval, and PHI 7 days. Since the application in a seedling box is not expected to contribute to the final residue, trials where the spray applications are according to GAP are considered acceptable. For field trials performed in Japan matching the GAP (seedling treatment at 1.65 g ai/box + three high volume spray applications at 4.0 g ai/hL with SC or SP formulations, interval 7–22 days and a 7 day PHI) clothianidin residues in rice grains were 0.12 and 0.14 mg/kg, n = 2 for an SP formulation and 0.12 and 0.16 mg/kg, n = 2 for an SC formulation on the same locations. When higher residues were found at later PHIs these residues were selected instead. After harvest, rice was dried and protected from rain for 9–14 days. Residue values were for husked rice grain.

GAP for rice in Japan is for one application in a seedling box at 0.75 g ai/box and three low volume spray applications at 16 g ai/hL, unstated interval, and PHI 7 days. Since the application in a seedling box is not expected to contribute to the final residue, trials where the spray applications are according to GAP are considered acceptable. For field trials performed in Japan matching the GAP (seedling treatment at 1.25–1.65 g ai/box + three high volume spray applications at 16 g ai/hL with SC or SP formulations, interval 3–21 days and a 7 day PHI) clothianidin residues in rice grains were 0.07 and 0.10 mg/kg, n = 2 for an SP formulation and 0.15 and 0.21 mg/kg, n = 2 for an SC formulation (on different locations). When higher residues were found at later PHIs these residues were selected instead. After harvest, rice was dried and protected from rain for 9–27 days. Residue values were for husked rice grain.

GAP for rice in Japan is for one application in a seedling box at 0.75 g ai/box and three aerial spray applications at 833 g ai/hL, unstated interval and PHI 14 days. Since the application in a seedling box is not expected to contribute to the final residue, trials where the spray applications are according to GAP are considered acceptable. For field trials performed in Japan matching the GAP (seedling treatment at 1.65 g ai/box + three aerial spray applications at 833 g ai/hL with SC formulations, interval 6–21 days and PHI 7 days) clothianidin residues in rice grains were 0.04 and 0.16 mg/kg, n = 2. When higher residues were found at later PHIs these residues were selected instead. After harvest, rice was dried protected from rain for 16–35 days. Residue values were for husked rice.

In all Japanese rice trials, the rice was left to dry after harvest. The Meeting considered this acceptable, since it is normal practice in Japan. Trials conducted at different GAPs generally cannot be combined. However, The Meeting decided that the trials from the three different foliar spray treatments could be combined, since the trials resulted in similar residues. For trials conducted at the same location on the same day, only the maximum value for that location was selected. This resulted in the following dataset: 0.04, 0.07, 0.10, 0.14, 0.15, 0.16, 0.16 and 0.21 mg/kg (n = 8).

The Meeting estimated a maximum residue level of 0.5 mg/kg for clothianidin in husked rice and an STMR of 0.145 mg/kg.

The maximum residue level estimate derived from use of the NAFTA statistical calculator was 0.41 mg/kg (95/99 rule), which was in agreement with the estimate made by the Meeting (after rounding up to one figure).

Field trials involving sorghum were performed in the USA.

The GAP for sorghum in the USA is for one seed treatment at 2.5 kg ai/T seeds. In field trials performed in the USA matching this GAP (1 × 2.5 kg ai/T seeds and PHI 97–167 days) clothianidin

residues in sorghum grain were: < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01 and < 0.01 mg/kg (n = 12).

Field trials involving barley were performed in Germany, the UK, France and Italy.

GAP for winter barley in the UK and Ireland is for one seed treatment at 0.50 kg ai/T seeds. For seed treatments and subsequent trials performed in Germany, the UK and France matching this GAP (1 × 0.44–0.47 kg ai/T seed and PHI 130–147 days, spring barley) clothianidin residue levels in barley grain were < 0.01, < 0.01 and < 0.01 mg/kg (n = 3).

GAP for seed treatments in Italy were not available.

Field trials involving wheat were performed in Germany, the UK, France and the USA.

The GAP for wheat in the UK is for one seed treatment at 0.50 kg ai/T seeds. For seed treatments and subsequent field trials performed in the UK, Germany and France, matching this GAP (1 × 0.38–0.63 kg ai/T seeds and PHI 130–155 days) clothianidin residues in wheat (grain) were: < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01 and < 0.01 mg/kg (n = 8).

GAP for wheat in the USA is for one seed treatment at 0.07 kg ai/T seeds. Trials performed in the USA did not match this GAP.

The Meeting noted that after seed treatment on maize, popcorn and sorghum according to GAP in the USA and after seed treatments on barley and wheat according to GAP in Northern EU, no residues were found in grains (< 0.01 mg/kg). Since GAP and residue levels for rice was different from other cereals, the results for barley, wheat, maize, popcorn and sorghum cannot be extrapolated to rice or vice versa. Although the USA and EU data on barley, wheat, maize, popcorn and sorghum could be used to support a cereal grains commodity group (excluding rice) recommendation, the Meeting decided to recommend maximum residue levels for individual cereals, to be in line with the thiamethoxam evaluation, where quantitative amounts of metabolite CGA 322704 differed in different cereals. The Meeting estimated a maximum residue level of 0.01* mg/kg for clothianidin on barley, maize, popcorn, sorghum and wheat and estimated an STMR of 0.01 mg/kg.

Statistical calculations using the NAFTA calculator were not possible, as all levels were below the LOQ.

Grasses for sugar and syrup production

Field trials involving sugarcane were performed in Australia.

GAP for sugarcane in Australia is for one soil directed spray application at 500 g ai/ha and PHI 147 days. In trials performed in Australia matching this GAP (1 × 500 g ai/ha and PHI 146–175 days) clothianidin residue levels in sugarcane billets were < 0.02, 0.04 and 0.14 mg/kg (n = 3) using an SC formulation and < 0.02 and 0.02 mg/kg (n = 2) using a WG formulation, on partly the same locations. In a single bridging study using a WG and SC formulation, residue levels were identical (both < 0.02 mg/kg). The datasets are too small for a Mann-Whitney U test. The Meeting agreed to combine the datasets and take only the maximum value per location. This resulted in the following dataset for sugarcane billets: < 0.02, 0.02, 0.04 and 0.14 mg/kg (n = 4).

The Meeting estimated a maximum residue level of 0.4 mg/kg for clothianidin on sugarcane and estimated an STMR of 0.03 mg/kg and an HR of 0.14 mg/kg.

The value using the NAFTA calculator (NAFTA UCL/median 95 = 0.31, no MLE used) differed from the estimate of 0.4 mg/kg made by the Meeting. The chosen level was higher to recognize the small dataset.

Oilseeds

Field trials involving undelinted cotton seed were performed in Australia and the USA.

GAP for cotton in Australia is for two foliar aerial or ground spray applications at 50 g ai/ha, with adjuvant, unstated interval and PHI 5 days. Trials performed in Australia did not match this GAP. However, foliar treatments performed at an exaggerated rate in Australia (4 × 50 g ai/ha, with adjuvant, interval 14 days, PHI 5 days) showed no residues: < 0.02$, < 0.02$ and < 0.02$ mg/kg, n = 3. However, values marked with $ cannot be used for a recommendation because of sampling deficiencies.

GAP for cotton in the USA is for one seed treatment at 2.1 kg ai/T seeds. Trials performed in the USA did not match this GAP. However, trials performed at an exaggerated dose rate of 3.5 kg ai/T seeds, showed no residues: < 0.01$, < 0.01$, < 0.01$, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01 and < 0.01 mg/kg (n = 12). However, values marked with $ cannot be used for a recommendation because of sampling deficiencies.

GAP for cotton in the USA is for three foliar spray applications at 75 g ai/ha (max 224 g ai/ha per season), interval 7 days and PHI 21 days. Field trials performed in the USA did not match this GAP.

Since USA foliar treatments at exaggerated dose rates show residues, the seed treatment dataset is considered not representative for cotton GAP. The dataset for cottonseed is considered insufficient to support a recommendation. The Meeting could not estimate maximum residue levels for cottonseed.

Field trials involving rape seed were performed in Germany, Sweden, the UK, France, the USA and Canada.

GAP for rape seed in the Czech Republic, Estonia, Finland, and Germany is for one seed treatment at 10 kg ai/T seeds. In field trials performed in Germany, Sweden and France matching this GAP (1 × 7.4–9.5 kg ai/T seeds and PHI 111–320 days) clothianidin residue levels in rapeseeds were < 0.01$, < 0.01$, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01 and < 0.01 mg/kg (n = 9). However, values marked with $ cannot be used for a recommendation because of sampling deficiencies.

GAP for rapeseed (including canola) in the USA and Canada is for one seed treatment at 4.0 kg ai/T seeds. Field trials performed in the USA and Canada did not match this GAP. Although field trials are available at an exaggerated dose rate, the results of these trials are considered not reliable because of sampling deficiencies.

The Meeting estimated a maximum residue level of 0.01* mg/kg for clothianidin on rape seed and estimated an STMR of 0.01 mg/kg.

Statistical calculations using the NAFTA calculator were not possible, since all levels are below LOQ.

Field trials involving sunflower seed were performed in France, Italy and Spain.

GAP for sunflower seeds in Romania is for one seed treatment at 0.5 mg ai/seed. Trials performed in Italy and Spain did not match this GAP. For seed treatments and subsequent field trials performed in France matching this GAP (1 × 0.50–0.62 mg ai/seed, 115–145 days PHI) clothianidin residues in sunflower seeds were < 0.01, < 0.01 and < 0.01 mg/kg (n = 3).

The dataset for sunflower seed is considered insufficient to support a recommendation. The Meeting could not estimate maximum residue levels for sunflower seed.

Legume animal feeds

Field trials involving soya bean forage and soya bean hay were not available.

Straw, fodder and forage of cereal grains and grasses

Field trials involving field corn forage were performed in the USA and Canada.

GAP for maize (field corn, popcorn and sweet corn) in the USA and Canada is for one seed treatment at 1.25 mg ai/seed. Seed treatment with subsequent field trials performed in the USA and Canada did not match this GAP.

The Meeting could not estimate an STMR or highest residue for field corn forage as there were no trials matching the GAP.

Field trials involving sweet corn forage were performed in the USA and Canada.

GAP for maize (field corn, popcorn and sweet corn) in the USA and Canada is for one seed treatment at 1.25 mg ai/seed. Seed treatment with subsequent field trials performed in the USA and Canada did not match this GAP.

The Meeting could not estimate an STMR or highest residue for sweet corn forage as there were no trials matching the GAP.

Field trials involving field corn stover were performed in the USA and Canada.

GAP for maize (field corn, popcorn and sweet corn) in the USA and Canada is for one seed treatment at 1.25 mg ai/seed. Seed treatment with subsequent field trials performed in the USA and Canada did not match this GAP.

The Meeting could not estimate an STMR or highest residue for field corn stover as there were no trials matching the GAP.

Field trials involving popcorn stover were performed in the USA and Canada.

GAP for maize (field corn, popcorn and sweet corn) in the USA and Canada is for one seed treatment at 1.25 mg ai/seed. Seed treatment with subsequent field trials performed in the USA and Canada did not match this GAP.

The Meeting could not estimate an STMR or highest residue for popcorn stover as there were no trials matching the GAP.

Field trials involving sweet corn stover were performed in the USA and Canada.

GAP for maize (field corn, popcorn and sweet corn) in the USA and Canada is for one seed treatment at 1.25 mg ai/seed. Seed treatment with subsequent field trials performed in the USA and Canada did not match this GAP.

The Meeting could not estimate an STMR or highest residue for sweet corn stover as there were no trials matching the GAP.

Field trials involving rice whole crop silage were not available.

Field trials involving rice straw were not available.

Field trials involving sorghum grain forage were performed in the USA.

GAP for sorghum in the USA is for one seed treatment at 2.5 kg ai/T seeds. In field trials performed in the USA matching this GAP (1 × 2.5 kg ai/T seeds and PHI 42–112 days) clothianidin residues in green sorghum forage were < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01 and < 0.01 mg/kg (n = 12).

The Meeting estimated an STMR of 0.01 mg/kg and a highest residue of 0.01 mg/kg for clothianidin in sorghum grain forage. A maximum residue level is not required, since forage is not traded.

The NAFTA calculator is not needed here, since maximum residue levels are not proposed for livestock forage.

Field trials involving sorghum grain stover were performed in the USA.

GAP in the USA for sorghum is for one seed treatment at 2.5 kg ai/T seeds. In field trials performed in the USA matching this GAP (1 × 2.5 kg ai/T seeds and PHI 97–167 days) clothianidin

residues in dry sorghum grain stover were < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01 and < 0.01 mg/kg (n = 12). After harvest, sorghum stover was left drying in the field for 0–24 days. The Meeting considered this acceptable, since it is normal practice in the USA.

The Meeting estimated a maximum residue level of 0.01* mg/kg for clothianidin in sorghum grain stover, an STMR of 0.01 mg/kg and a highest residue of 0.01 mg/kg. A correction for dry weight is not necessary here since all the values are below LOQ. The dry weight values are considered to be the same.

Statistical calculations using the NAFTA calculator were not possible, since all levels are below LOQ.

Field trials involving green barley forage were performed in Germany, the UK, France and Italy.

GAP for winter barley in the UK and Ireland is for one seed treatment at 0.50 kg ai/T seeds. For seed treatments and subsequent trials performed in Germany, the UK and France matching this GAP (1 × 0.44–0.47 kg ai/T seed and PHI 55–57 days, spring barley) clothianidin residue levels in barley forage were 0.02, 0.02 and 0.05 mg/kg (n = 3).

GAP for seed treatments in Italy are not available.

The dataset for green barley forage is considered insufficient to support a recommendation. The Meeting could not estimate an STMR or highest residue for green barley forage.

Field trials involving green wheat forage were performed in Germany, the UK, France and the USA.

GAP for wheat in the UK is for one seed treatment at 0.50 kg ai/T seeds. For seed treatments and subsequent field trials performed in the UK, Germany and France matching this GAP (1 × 0.38–0.63 kg ai/T seeds and PHI 28–61 days) clothianidin residues in wheat green wheat forage were < 0.02, 0.022$, 0.024$, 0.030$, 0.058, 0.15$, 0.19$ and 0.23 mg/kg (n = 8). However, values marked with $ could not be used for a recommendation because of sampling deficiencies.

GAP for wheat in the USA is for seed treatment at 0.07 kg ai/T seeds. Trials performed in the USA did not match this GAP.

The dataset for green wheat forage is considered insufficient to support a recommendation. The Meeting could not estimate an STMR or highest residue for green wheat forage.

Field trials involving barley hay were not available. However, the Meeting decided that for the purpose of dietary burden calculations, data from barley straw can be used for barley hay.

Field trials involving wheat hay were performed in the USA.

GAP for wheat in the USA is for seed treatment at 0.07 kg ai/T seeds. Trials performed in the USA did not match this GAP.

The Meeting could not estimate an STMR or highest residue for wheat hay as there were no trials matching the GAP. However, the Meeting decided that for the purpose of dietary burden calculations, data from wheat straw can be used for wheat hay.

Field trials involving barley straw were performed in Germany, the UK, France and Italy.

GAP for winter barley in the UK and Ireland is for one seed treatment at 0.50 kg ai/T seeds. For seed treatments and subsequent trials performed in Germany, the UK and France matching this GAP (1 × 0.44–0.47 kg ai/T seed; PHI 130–147 days, spring barley) clothianidin residue levels in barley straw were < 0.02, < 0.02 and < 0.02 mg/kg (n = 3).

GAP for seed treatments in Italy are not available.

Field trials involving wheat straw were performed in Germany, the UK, France and the USA.

GAP for wheat in the UK is for one seed treatment at 0.50 kg ai/T seeds. For seed treatments and subsequent field trials performed in the UK, Germany and France matching this GAP (1 × 0.38–0.63 kg ai/T seeds and PHI 130–155 days) clothianidin residues in wheat straw (dry) were < 0.02$, < 0.02$, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02 and < 0.02 mg/kg (n = 8). However, the values marked with $ cannot be used for a recommendation because of storage deficiencies.

GAP for wheat in the USA is for seed treatment at 0.07 kg ai/T seeds. Field trials performed in the USA did not match this GAP.

Since wheat straw may not always be readily distinguishable from barley straw in trade, (since residues of wheat straw and barley straw are similar and since the GAPs for barley and wheat are similar), residues from wheat straw can be combined with residues from barley straw. This resulted in the following dataset: < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02, < 0.02 and < 0.02 mg/kg (n = 9).

The Meeting estimated a maximum residue level of 0.02* mg/kg for clothianidin in barley and wheat straw, an STMR of 0.02 mg/kg and a highest residue of 0.02 mg/kg. A correction for dry weight is not necessary here since all the values are below LOQ. The dry weight values are considered to be the same.

Statistical calculations using the NAFTA calculator were not possible, since all levels are below LOQ.

Miscellaneous fodder and forage crops

Field trials involving cotton gin by-products were performed in Australia and the USA.

GAP for cotton in Australia is for two foliar aerial or ground spray applications at 50 g ai/ha, unstated interval and PHI 5 days. Trials performed in Australia did not match this GAP.

GAP for cotton in the USA is for one seed treatment at 2.1 kg ai/T seeds. Trials performed in the USA did not match this GAP.

GAP for cotton in the USA is for three foliar spray applications at 75 g ai/ha (max 224 g ai/ha per season), interval 7 days, PHI 21 days. Field trials performed in the USA did not match this GAP.

The Meeting could not estimate an STMR or highest residue for cotton gin by-products as there were no trials matching the GAP.

Field trials involving green rape forage were performed in Germany, Sweden, the UK, and France.

GAP for rape seed in the Czech Republic, Estonia, Finland, and Germany is for one seed treatment at 10 kg ai/T seeds. In field trials performed in Germany, Sweden and France matching this GAP (1 × 7.4–9.5 kg ai/T seeds and PHI 27–191 days) clothianidin residue levels in green rape forage were < 0.02, < 0.02, < 0.02, < 0.02, < 0.02$, < 0.02$, < 0.02$, 0.027, 0.038$ and 0.055$ mg/kg (n = 10). However, values marked with $ cannot be used for a recommendation because of sampling deficiencies.

The meeting estimated an STMR of 0.02 mg/kg and a highest residue of 0.027 mg/kg of clothianidin in green rape forage. A maximum residue level is not required, since forage is not traded.

The NAFTA calculator is not needed here, since maximum residue levels are not proposed for livestock forage.

Field trials involving sugar beet tops were performed in Belgium, Germany, the UK, France, Italy, Spain and the USA.

GAP for sugar beets in Belgium, Denmark, Finland, Germany, Netherlands, Slovakia and the UK is for one seed treatment at 0.6 mg ai/seed. For seed treatments and subsequent field trials

performed in the UK, France and Germany matching this GAP (1 × 0.6 mg ai/seed and PHI 92–148 days) clothianidin residues in sugar beet tops were < 0.02, < 0.02 and < 0.02 mg/kg (n = 3). Residue levels in immature plants were not selected, because sugar beet leaves are normally harvested when roots are mature.

GAP for sugar beet in Italy, Slovenia, and Spain is for one seed treatment at 0.6 mg ai/seed. Trials performed in Spain and Italy did not match this GAP.

GAP for sugar beets in the USA is for one seed treatment at 0.6 mg ai/seed (FS formulation). For seed treatments and subsequent field trials performed in the USA matching this GAP (1 × 0.6 mg ai/seed, PHI 109–179 days, SE formulation) clothianidin residues in sugar beet leaves were < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, < 0.01 and 0.011 mg/kg (n = 12).

The Meeting noted that the GAP for Northern Europe is identical to the GAP for the USA. But because the LOQ of the USA dataset was lower, the Meeting decided to use only the USA dataset for a recommendation. The Meeting estimated an STMR of 0.01 mg/kg and a highest residue of 0.011 mg/kg of clothianidin in sugar beet tops. A maximum residue level is not required, since forage is not traded.

The NAFTA calculator was not used as maximum residue levels are not proposed for livestock forage.

Field trials involving sugarcane tops were performed in Australia.

GAP for sugar cane in Australia is for one soil directed spray application at 500 g ai/ha (PHI 147 days). In field trials performed in Australia matching this GAP (1 × 500 g ai/ha and a PHI 146–175 days) clothianidin residue levels in sugarcane tops were 0.08, 0.21 and 0.27 mg/kg (n = 3), expressed on dry weight (dw) for an SC formulation and 0.15 and 0.17 mg/kg dw (n = 2) for a WG formulation at similar locations. In a single bridging study using a WG and SC formulation, residue levels for the WG formulation were higher (0.15 versus 0.08 mg/kg for WG and SC formulation). The datasets are too small for a Mann-Whitney U test. The Meeting agreed to combine the datasets and take only the maximum value per location. This resulted in the following dataset for sugarcane tops: 0.15, 0.17, 0.21 and 0.27 mg/kg dw (n = 4)

The meeting estimated an STMR of 0.19 mg/kg and a highest residue of 0.27 mg/kg of clothianidin in sugarcane tops, based on dry weight basis. A maximum residue level is not required, since forage is not traded.

The NAFTA calculator is not needed here, since maximum residue levels are not proposed for livestock forage.

Field trials involving sugarcane fodder were not available.

Teas

Field trials involving dry leaves of tea were performed in Japan.

GAP for tea (green, black) in Japan is for one spray application at 12 g ai/hL and PHI 7 days. In field trials performed in Japan matching this GAP (1 × 12 g ai/hL and PHI 7 days) clothianidin residues in tea (dry leaves) were 5.3 and 18 mg/kg (n = 2).

The dataset for tea is considered insufficient to support a recommendation. The Meeting could not estimate maximum residue levels for tea.

Combination of residues from clothianidin use and thiamethoxam use

As indicated before, clothianidin residues may arise from use of clothianidin as well as from use of thiamethoxam (metabolite CGA 322704). The Meeting considered it unlikely that both pesticides are

used on the same crop and therefore the maximum estimated levels, the maximum STMR, and the maximum HR of each use is taken as recommendation.

CCN	Commodity name	Origin	Recommendation mg/kg	STMR mg/kg	HR mg/kg
FC 0001	Citrus fruits	CGA 322704	0.07	0.02	0.02
		clothianidin	no GAP		
		both uses	0.07[b]	0.02	0.02
FP 0009	Pome fruits	CGA 322704	0.1	0.025	0.04
		clothianidin	0.4	0.10	0.20
		both uses	0.4[a,b]	0.10	0.20
FS 0012	Stone fruits	CGA 322704	0.2	0.04	0.12
		clothianidin	insufficient data		
		both uses	0.2[a,b]	0.04	0.12
FB 0018	Berries and other small fruits	CGA 322704	0.07	0.01	0.05
	Cranberries	clothianidin	0.01*	0.01	0.01
	Grapes	clothianidin	0.7	0.12	0.41
	Berries and other small fruits, except grapes	both uses	0.07[a,b]	0.01	0.05
	Grapes	both uses	0.7[a,b]	0.12	0.41
FI 0327	Banana	CGA 322704	0.02*	0.02	0.02
		clothianidin	0.02	0.02	0.02
		both uses	0.02[a,b]	0.02	0.02
FI 0350	Papaya	CGA 322704	0.01*	0	0
		clothianidin	no GAP		
		both uses	0.01*[,b]	0	0
FI 0353	Pineapple	CGA 322704	0.01*	0	0
		clothianidin	no GAP		
		both uses	0.01*[,b]	0	0
VB 0040	Brassica (cole or cabbage) vegetables, Head cabbages, flowerhead Brassicas	CGA 322704	0.2	0.015	0.04
	Cabbages, head	clothianidin	insufficient data		
	Broccoli	clothianidin	insufficient data		
	Brassica (cole or cabbage) vegetables, Head cabbages, flowerhead Brassicas	both uses	0.2[b]	0.015	0.04
	Head cabbage with wrapper leaves (for livestock dietary burden)	CGA 322704	–	0.03	0.08
		clothianidin	insufficient data		
		both uses	–	0.03	0.08
VC 0045	Fruiting vegetables, Cucurbits	CGA 322704	0.02*	0.02	0.02
	Cucumber	clothianidin	insufficient data		
	Squash, summer	clothianidin	insufficient data		
	Fruiting vegetables, Cucurbits	both uses	0.02*[,b]	0.02	0.02
VO 0050	Fruiting vegetables, other than cucurbits (except sweet corn)	CGA 322704	0.05	0.02	0.03
	Egg plant	clothianidin	insufficient data		
	Tomato	clothianidin	insufficient data		
	Fruiting vegetables, other than cucurbits (except sweet corn)	both uses	0.05[b]	0.02	0.03
VO 0447	Sweet corn (corn-on-the-cob)	CGA 322704	0.01*	0.01	0.01
		clothianidin	0.01*	0.01	0.01
		both uses	0.01*[, a,b]	0.01	0.01
HS 0444	Pepper Chilli, dried	CGA 322704	0.5	0.2	0.3
		clothianidin	no GAP		
		both uses	0.5[b]	0.2	0.3
VL 0053	Leafy vegetables	CGA 322704	2	0.52	0.80
	Lettuce, Head	clothianidin	insufficient data		
	Lettuce, Leaf	clothianidin	insufficient data		
	Leafy vegetables	both uses	2[b]	0.52	0.80

CCN	Commodity name	Origin	Recommendation mg/kg	STMR mg/kg	HR mg/kg
VP 0060	Legume vegetables	CGA 322704	0.01*	0.01	0.01
		clothianidin	no GAP		
		both uses	0.01*[,b]	0.01	0.01
VD 0070	Pulses	CGA 322704	0.02	0.02	–
	Soya bean (dry)	clothianidin	insufficient data		
	Pulses	both uses	0.02[b]	0.02	–
VR 0075	Root and tuber vegetables	CGA 322704	0.2	0.01	0.15
	Carrots	clothianidin	insufficient data		
	Chicory roots	clothianidin	insufficient data		
	Potato	clothianidin	0.05	0.02	0.033
	Sugar beet roots	clothianidin	0.03	0.01	0.019
	Root and tuber vegetables	both uses	0.2[a,b]	0.02	0.15
VS 0620	Artichoke, Globe	CGA 322704	0.05	0.024	0.029
		clothianidin	no GAP		
		both uses	0.05[b]	0.024	0.029
VS 0624	Celery	CGA 322704	0.04	0.01	0.02
		clothianidin	no GAP		
		both uses	0.04[b]	0.01	0.02
GC 0640	Barley	CGA 322704	0.04	0.01	–
		clothianidin	0.01*	0.01	–
		both uses	0.04[a,b]	0.01	–
GC 0645	Maize	CGA 322704	0.02	0.02	–
		clothianidin	0.01*	0.01	–
		both uses	0.02[a,b]	0.02	–
GC 0656	Popcorn	CGA 322704	0.01	0.01	–
		clothianidin	0.01*	0.01	–
		both uses	0.01[a,b]	0.01	–
GC 0649	Rice	CGA 322704	insufficient data		
		clothianidin	0.5[a]	0.145	–
		both uses	0.5[a]	0.145	–
GC 0651	Sorghum	CGA 322704	no GAP		
		clothianidin	0.01*	0.01	–
		both uses	0.01*[a]	0.01	–
GC 0654	Wheat	CGA 322704	0.02*	0.02	–
		clothianidin	0.01*	0.01	–
		both uses	0.02*[,a,b]	0.02	–
GS 0659	Sugarcane	CGA 322704	no GAP		
		clothianidin	0.4	0.03	0.14
		both uses	0.4[a]	0.03	0.14
TN 0672	Pecan	CGA 322704	0.01*	0.01	0.01
		clothianidin	no GAP		
		both uses	0.01*[,b]	0.01	0.01
SO 0088	Oilseed	CGA 322704	0.02*	0.02	–
	Cottonseed (undelinted seed)	clothianidin	insufficient data		
	Rape seed	clothianidin	0.01*	0.01	–
	Sunflower seed	clothianidin	insufficient data		
	Oilseed	both uses	0.02*[,a,b]	0.02	–
SB 0715	Cacao beans	CGA 322704	0.02*	0.02	–
		clothianidin	no GAP		
		both uses	0.02*[,b]	0.02	–
SB 0716	Coffee beans	CGA 322704	0.05	0.015	–
		clothianidin	no GAP		
		both uses	0.05[b]	0.015	–
AL 0528	Pea vines	CGA 322704	–	0.05	0.05
		clothianidin	no GAP		
		both uses	–	0.05	0.05

CCN	Commodity name	Origin	Recommendation mg/kg	STMR mg/kg	HR mg/kg
AL 0072	Pea hay or Pea fodder (dry)	CGA 322704	0.2, dw	0.05, dw	0.10, dw
		clothianidin	no GAP		
		both uses	0.2, dw [b]	0.05, dw	0.10, dw
AF ----	Barley forage (green)	CGA 322704	–	0.04	0.05
		clothianidin	insufficient data		
		both uses	–[b]	0.04	0.05
AF 0645	Field corn forage (maize forage)	CGA 322704	–	0.01	0.02
		clothianidin	insufficient data		
		both uses	–[b]	0.01	0.02
AF 0645	Sweet corn forage (maize forage)	CGA 322704	–	0.01	0.02
		clothianidin	insufficient data		
		both uses	–[b]	0.01	0.02
AF 0651	Sorghum grain forage (green)	CGA 322704	no GAP		
		clothianidin	not required	0.01	0.01
		both uses	–[a]	0.01	0.01
AF ----	Wheat forage (green)	CGA 322704	–	0.05	0.06
		clothianidin	insufficient data		
		both uses	–[b]	0.05	0.06
AS 0640	Barley straw and fodder, dry	CGA 322704	0.2, dw	0.05, dw	0.14, dw
		clothianidin	0.02*, dw	0.02, dw	0.02, dw
		both uses	0.2, dw [b,a]	0.05, dw	0.14, dw
AS 0645	Field corn stover (Maize fodder)	CGA 322704	0.01*	0.01	0.01
		clothianidin	insufficient data		
		both uses	0.01*[b], dw	0.01, dw	0.01, dw
AS 0645	Popcorn stover (Maize fodder)	CGA 322704	0.01*, dw	0.01, dw	0.01, dw
		clothianidin	insufficient data		
		both uses	0.01*[b], dw	0.01, dw	0.01, dw
AS 0645	Sweet corn stover (Maize fodder)	CGA 322704	0.01, dw	0.01, dw	0.01, dw
		clothianidin	insufficient data		
		both uses	0.01, dw [b]	0.01, dw	0.01, dw
AS 0651	Sorghum grain stover (sorghum straw and fodder, dry)	CGA 322704	no GAP		
		clothianidin	0.01*, dw	0.01, dw	0.01, dw
		both uses	0.01*, dw [a]	0.01, dw	0.01, dw
AS 0654	Wheat straw and fodder, dry	CGA 322704	0.2, dw	0.05, dw	0.14, dw
		clothianidin	0.02*, dw	0.02, dw	0.02, dw
		both uses	0.2, dw [b,a]	0.05, dw	0.14, dw
AV ----	Rape forage (green)	CGA 322704	–	0.05	0.05
		clothianidin	–	0.02	0.027
		both uses	–[a,b]	0.02[c]	0.027[c]
AV 0596	Sugar beet tops (Sugar beet leaves or tops)	CGA 322704	–	0.02	0.02
		clothianidin	–	0.01	0.011
		both uses	–[b]	0.02	0.02
AV 0659	Sugarcane tops (sugarcane forage)	CGA 322704	no GAP		
		clothianidin	–	0.19, dw	0.27, dw
		both uses	–[a]	0.19, dw	0.27, dw
DT 1114	Tea, Green, Black (black, fermented and dried)	CGA 322704	0.7	0.12	–
		clothianidin	insufficient data		
		both uses	0.7[b]	0.12	–

[a] based on clothianidin use as derived from 2010 clothianidin evaluation

[b] based on thiamethoxam use as derived from 2010 thiamethoxam evaluation (metabolite CGA 322704).

[c] overall residue based on trials with the lower LOQ

– not required to recommend MRL (animal forage) or HR (seeds, grains)

dw = residue value expressed as dry weight (i.e., corrected to 100% dry matter)

Residues from rotational crops

In a field rotational crop study, where the soil was treated with 162–192 g ai/ha, clothianidin levels in green crop parts ranged from < 0.01–0.025 mg/kg, < 0.01–0.017 mg/kg, and < 0.01–0.023 mg/kg at the 1, 4 and 8 month plant back intervals, respectively. Clothianidin was not found at the 12 month plant back intervals (< 0.01 mg/kg). Clothianidin was not found in turnip roots, wheat grain and wheat straw at any of the plant back intervals (< 0.01 mg/kg).

Dose rates used in the field rotational crop study are within the normal GAP ranges; therefore, residues from rotational crops need to be taken into account for the MRL recommendation. The field rotational crop study shows that residues from rotational crops are only expected in leafy crop types like Brassica vegetables (010, VB), leafy vegetables (013, VL), legume vegetables (014, VP), stalk and stem vegetables (017, VS), legume feeds (050, AL), forage of cereal grains and grasses (051, AF), and miscellaneous forage crops (052, AV).

The proposed MRL recommendation for direct treatment of Brassica vegetables, leafy vegetables, legume vegetables with clothianidin or thiamethoxam use covers the residues from rotation. However, for stalk and stem vegetables (017, VS), legume feeds (050, AL), forage of cereal grains and grasses (051, AF) and miscellaneous forage crops (052, AV) only a few of the commodities within the group are covered by the direct treatment recommendations.

At the 1 month plant back interval in the field rotational crop study, the following residues were found in different rotational leafy crops: < 0.01, < 0.01, < 0.01, < 0.01, < 0.01, 0.011, 0.014, 0.014 and 0.025 mg/kg (n = 9). For the commodities in groups 017 VS without a recommendation for direct treatment, the Meeting decided to recommend a maximum residue level of 0.04 mg/kg, an STMR of 0.01 mg/kg, and an HR of 0.025 mg/kg. For the animal forage commodities, a maximum residue level is not appropriate, since these commodities are not traded. The Meeting decided to recommend an STMR of 0.01 mg/kg and a highest residue of 0.025 mg/kg in animal forage crops (050 AL, 051 AF, 052 AV) without a recommendation for direct treatment.

Fate of residues during processing

Information on the fate of residues during processing by radioactivity studies was not available. Processing studies with clothianidin were undertaken for apples, grapes, tomatoes, potatoes, sugar beets, and cottonseed. In the table below, relevant processing factors for these commodities are summarized.

In addition, processing studies for apple, coffee beans, plums and tomatoes were available from the 2010 thiamethoxam evaluation. A hydrolysis study on thiamethoxam showed that thiamethoxam is stable under the hydrolysis conditions used in food processing. Therefore clothianidin levels do not arise from thiamethoxam hydrolysis and processing factors for CGA 322704 from the thiamethoxam evaluation can be used to estimate processing factors for clothianidin.

Processing factors obtained from high level residue levels in the RAC were considered to be more reliable than processing factors obtained from low level residues in the RAC. For this reason, the processing factors for apple pomace and apple juice from the clothianidin evaluation are considered the best estimate, while the processing factors for tomato paste and tomato puree from the thiamethoxam evaluation are considered the best estimate.

Using the $STMR_{RAC}$ obtained from both the thiamethoxam and clothianidin use, the Meeting estimated STMR-Ps for processed commodities as listed below. The Meeting considered the appropriate STMR-P to be used in the livestock dietary burden calculation or dietary intake calculation. An HR-P is not required for processed commodities.

Commodity	Processing factors	Processing factor (median or best estimate)	STMR-P mg/kg ([a,b] use)
Apple pomace (wet)	0.24[a] 1.4, 1.5, 1.5[b]	0.24[a]	0.10 × 0.24 = 0.024 (pome fruits)
Apple juice	0.14[a] 1.0, 1.0, 1.0[b]	0.14[a]	0.10 × 0.14 = 0.014 (pome fruits)
Dried plums, prunes	1.5, 2.0[b]	1.75[b]	0.04 × 1.75 = 0.07 (stone fruits)
Grape raisins	1.6, 3.6[a]	2.6[a]	0.12 × 2.6 = 0.31
Grape juice	1.1, 1.8[a]	1.45[a]	0.12 × 1.45 = 0.18
Grape pomace	1.9[a]	1.9[a]	0.12 × 1.9 = 0.23
Tomato paste	1.2[a] 2.00, 2.38, 3.33, 3.75, 5.50, 5.78, 6.0, 6.0, 6.5, 6.5, 9.7, 11.3[b]	5.9[b]	0.02 × 5.9 = 0.12 (fruiting veg)
Sugar beet dried pulp (85% dm)	1.7[a]	1.7[a]	0.02 × 1.7 = 0.034 (root and tubers)
Sugar beet molasses (62% dm)	3.2[a]	3.2[a]	0.02 × 3.2 = 0.064 (root and tubers)
Cottonseed meal (96% dm)	0.1[a]	0.1[a]	0.02 × 0.1 = 0.002 (oilseeds)
Cottonseed hulls (88% dm)	0.76[a]	0.76[a]	0.02 × 0.76 = 0.015 (oilseeds)
Cottonseed, refined oil	< 0.077[a]	< 0.077	0.02 × < 0.077 = 0.0015 (oilseeds)
Coffee beans, roasted	< 0.33, < 0.33, < 0.33, < 0.33, < 0.33, < 0.50, < 0.50, < 0.50, < 0.50, < 0.50[b]	< 0.33[b]	0.015 × < 0.33 = < 0.005

[a]: based on clothianidin use as derived from 2010 clothianidin evaluation

[b]: based on thiamethoxam use as derived from 2010 thiamethoxam evaluation (metabolite CGA 322704).

Based on a highest residue of 0.12 mg/kg for stone fruits and processing factor of 1.75, The Meeting estimated a maximum residue level of 0.2 mg/kg for dried plums, prunes (based on thiamethoxam and clothianidin use) and an HR of 0.21 mg/kg.

Based on a highest residue of 0.41 mg/kg for grapes and a processing factor of 2.6, The Meeting estimated a maximum residue level of 1 mg/kg for raisins (based on thiamethoxam and clothianidin use) and an HR of 1.066 mg/kg.

Based on an STMR of 0.12 mg/kg for grapes and a processing factor of 1.45, The Meeting estimated a maximum residue level of 0.2 mg/kg for grape juice (based on thiamethoxam and clothianidin use).

Livestock dietary burden

The Meeting estimated the dietary burden of clothianidin residues (both from thiamethoxam and clothianidin use) on the basis of the livestock diets listed in the FAO manual appendix IX (OECD feedstuff table). Calculation from highest residue, STMR (some bulk commodities) and STMR-P values provides the levels in feed suitable for estimating MRLs, while calculation from STMR and STMR-P values from feed is suitable for estimating STMR values for animal commodities.

Forage commodities do not appear in the Recommendations Table (because no maximum residue level is needed) but they are used in estimating livestock dietary burden. Therefore all plant commodities used in the dietary burden calculation are listed below. Also, the terminology for commodities in the OECD feed tables is not always identical to the descriptions in the original studies or Codex description and some clarification is needed. Codex groups have been assigned in the JMPR 2009 and 2010 Meeting. Despite the long list of plant commodities used in dietary burden calculation, data on pea silage, soya bean hay, soya bean silage, barley silage, sorghum grain silage,

wheat silage, barley bran fractions, sugar beet ensiled pulp, brewer's grain, canola meal, citrus dried pulp, maize aspirated grain fractions, maize milled by-products, hominy meal of field corn, sweet corn cannery waste, maize gluten, maize gluten meal, distiller's grain, cotton gin by-products, pineapple process waste, potato process waste, potato dried pulp, rape meal, rice hulls, rice bran, sorghum grain aspirated grain fractions, soya bean aspirated grain fractions, soya bean meal, soya bean hulls, soya bean okara, soya bean pollard, sugarcane molasses, sugarcane bagasse, tomato wet pomace, wheat aspirated grain fractions, wheat gluten meal, wheat milled by-products are not available and are therefore not taken into account in dietary burden calculations. Dietary burden for livestock therefore might be underestimated.

The Meeting decided that residue values for pea vines could be extrapolated to cowpea forage, that residue values for pea hay could be extrapolated to cowpea hay, that residue values for barley straw could be extrapolated to barley hay and that residue values for wheat straw could be extrapolated to wheat hay in the calculation of livestock dietary burden. Residues in cotton meal could not be extrapolated to other oilseed meals, because different processing processes are involved.

Codex Group	Codex commodity description	Crop	Feed Stuff	Highest residue	STMR or STMR-P	Residue Level	DM (%)
		Forages					
AL	Alfalfa forage (green)	Alfalfa	forage	0.025	0.01	HR	35
AF/AS		Barley	forage	0.05	0.04	HR	30
AF/AS	Barley straw and fodder, dry	Barley	hay	0.14	0.05	HR	100
AF/AS	Barley straw and fodder, dry	Barley	straw	0.14	0.05	HR	100
AL	Bean forage (green)	Bean	vines	0.025	0.01	HR	35
AM/AV	Sugar beet leaves or tops	Beet, mangel	fodder	0.02	0.02	HR	15
AM/AV	Sugar beet	Beet, sugar	tops	0.02	0.02	HR	23
AM/AV	Cabbages, head	Cabbage	heads, leaves	0.08	0.03	HR	15
AL	Clover	Clover	forage	0.025	0.01	HR	30
AF/AS	Maize forage	Corn, field	forage/silage	0.02	0.01	HR	40
AF/AS	Maize fodder	Corn, field	stover	0.01	0.01	HR	100
AF/AS		Corn, pop	stover	0.01	0.01	HR	100
AF/AS		Corn, sweet	forage	0.02	0.01	HR	48
AF/AS		Corn, sweet	stover	0.01	0.01	HR	100
AL		Cowpea	forage	0.05	0.05	HR	30
AL		Cowpea	hay	0.1	0.05	HR	100
AL		Crown vetch	forage	0.025	0.01	HR	30
AF/AS		Grass	forage (fresh)	0.025	0.01	HR	25
AM/AV	Kale forage	Kale	leaves	0.025	0.01	HR	15
AL	Lespedeza	Lespedeza	forage	0.025	0.01	HR	22
AF/AS		Millet	forage	0.025	0.01	HR	30
AF/AS	Oat forage	Oat	forage	0.025	0.01	HR	30
AL	Pea vines (green)	Pea	vines	0.05	0.05	HR	25

Codex Group	Codex commodity description	Crop	Feed Stuff	Highest residue	STMR or STMR-P	Residue Level	DM (%)
AL	Pea hay or fodder	Pea	hay	0.1	0.05	HR	100
AM/AV	Rape greens	Rape	forage	0.027	0.02	HR	30
AF/AS		Rice	whole crop silage	0.025	0.01	HR	40
AF/AS	Rye forage (green)	Rye	forage	0.025	0.01	HR	30
AF/AS		Sorghum, grain	forage	0.01	0.01	HR	35
AF/AS		Sorghum, grain	stover	0.01	0.01	HR	100
AL	Soya bean forage (green)	Soya bean	forage	0.025	0.01	HR	56
AM/AV		Sugarcane	tops	0.27	0.19	HR	100
AL		Trefoil	forage	0.025	0.01	HR	30
AF/AS		Triticale	forage	0.025	0.01	HR	30
AM/AV	Turnip leaves or tops	Turnip	tops (leaves)	0.025	0.01	HR	30
AL		Vetch	forage	0.025	0.01	HR	30
AF/AS		Wheat	forage	0.06	0.05	HR	25
AF/AS	Wheat straw and fodder, dry	Wheat	hay	0.14	0.05	HR	100
AF/AS	Wheat straw and fodder, dry	Wheat	straw	0.14	0.05	HR	100
		Roots & Tubers					
VR	Carrot	Carrot	culls	0.15	0.02	HR	12
VR	Cassava	Cassava/tapioca	roots	0.15	0.02	HR	37
VR	Potato culls	Potato	culls	0.15	0.02	HR	20
VR	Swede	Swede	roots	0.15	0.02	HR	10
VR	Turnip, Garden	Turnip	roots	0.15	0.02	HR	15
		Cereal Grains/ Crops Seeds					
GC	Barley	Barley	grain		0.01	STMR	88
VD	Beans, dry	Bean	seed		0.02	STMR	88
GC	Maize	Corn, field	grain		0.02	STMR	88
GC	Popcorn	Corn, pop	grain		0.01	STMR	88
VD	Cowpea	Cowpea	seed		0.02	STMR	88
VD	Lupin	Lupin	seed		0.02	STMR	88
VD	Field pea, (dry)	Pea	seed		0.02	STMR	90
GC	Rice	Rice	grain		0.145	STMR	88
GC	Sorghum	Sorghum, grain	grain		0.01	STMR	86
VD	Soya bean, dry	Soya bean	seed		0.02	STMR	89
VD	Vetch	Vetch	seed		0.02	STMR	89
GC	Wheat	Wheat	grain		0.02	STMR	89
		By-products					
AB	Apple pomace, dry	Apple	pomace, wet		0.024	STMR	40

Codex Group	Codex commodity description	Crop	Feed Stuff	Highest residue	STMR or STMR-P	Residue Level	DM (%)
AB	Sugar beet pulp, dry	Beet, sugar	dried pulp		0.034	STMR	85
DM	Sugar beet molasses	Beet, sugar	molasses		0.064	STMR	62
SM	Cotton meal	Cotton	meal		0.002	STMR	96
SO		Cotton	undelinted seed		0.02	STMR	88
SM	Cotton hulls	Cotton	hulls		0.015	STMR	88
AB	Grape pomace, dry	Grape	pomace, wet		0.23	STMR	15

Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are provided in Annex 6. A mean and maximum dietary burden for livestock, based on thiamethoxam and clothianidin use, is shown in the table below.

Animal dietary burden for clothianidin (from thiamethoxam and clothianidin use), expressed as ppm of dry matter diet

	US	EU	AU	JPN	overall	
	max	max	max	max	max	
beef cattle	0.298	0.795	0.640	0.027	0.795 (EU)	[a]
dairy cattle	0.277	0.586	0.632	0.061	0.632 (AU)	[b]
poultry broiler	0.051	0.209	0.094	0.022	0.209 (EU)	
poultry layer	0.051	0.258	0.094	0.021	0.258 (EU)	[c,d]
	mean	mean	mean	mean	mean	
beef cattle	0.089	0.170	0.465	0.024	0.465 (AU)	[a]
dairy cattle	0.119	0.170	0.459	0.033	0.459 (AU)	[b]
poultry broiler	0.051	0.040	0.094	0.020	0.094 (AU)	
poultry layer	0.051	0.070	0.094	0.021	0.094 (AU)	[c,d]

[a] Highest mean and maximum beef or dairy cattle dietary burden suitable for maximum residue level and STMR estimates for mammalian meat.

[b] Highest mean and maximum dairy cattle dietary burden suitable for maximum residue level and STMR estimates for milk.

[c] Highest mean and maximum poultry broiler or layer dietary burden suitable for maximum residue level and STMR estimates for poultry meat.

[d] Highest mean and maximum poultry layer suitable for maximum residue level and STMR estimates for eggs.

Livestock feeding studies

The Meeting received a feeding study on lactating cows.

Three groups of three lactating Holstein-Friesian cows were dosed once daily via capsules at levels of 0.27, 0.80 and 2.6 ppm dry weight feed for 28 consecutive days. Milk was collected throughout the study and tissues were collected on day 29 within 15–17 hrs after the last dose.

No residues of clothianidin were found in tissues at any dose level (< 0.02 mg/kg). Levels of clothianidin in milk were < 0.002 mg/kg in the 1 × dose group, < 0.002–0.003 mg/kg (mean 0.0020 mg/kg) in the 3 × dose group and < 0.002–0.012 mg/kg (mean 0.0046 mg/kg) in the 10 × dose group.

Residues in animal commodities

Cattle

In a feeding study where lactating cows were dosed with clothianidin at up to 2.6 ppm dry feed, no clothianidin was found in tissues (< 0.02 mg/kg). Therefore, no residues are to be expected in tissues at the mean and maximum calculated dietary burden of 0.465 and 0.795 ppm based on clothianidin dietary burden.

For milk MRL estimation, the highest residues in the milk resulting from dietary burden based on clothianidin were calculated by interpolating the maximum dietary burden for dairy cattle (0.632 ppm) between the relevant feeding levels (0.27 and 0.8 ppm) from the dairy cow feeding study and using the mean milk concentration from those feeding groups.

For milk STMR estimation, the median residues in the milk resulting from dietary burden were calculated by interpolating the mean dietary burden for dairy cattle (0.459 ppm) between the relevant feeding levels (0.27 and 0.80 ppm) from the dairy cow feeding study and using the mean milk concentration from those feeding groups.

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

Dietary burden (ppm) Feeding level [ppm]	Milk (mg/kg residue)
	mean
MRL dairy cattle (0.632 ppm) [0.27–0.80 ppm]	< 0.0020 [< 0.0020–0.0020]
STMR dairy cattle (0.459 ppm) [0.27–0.80 ppm]	< 0.0020 [< 0.0020–0.0020]

Another route for clothianidin residues to end up in animal commodities is from dietary burden resulting from thiamethoxam use. Based on a lactating cow feeding study with thiamethoxam, the CGA 322704 residues in milk were estimated at 0.011 and 0.004 mg/kg resulting from the maximum (5.23 ppm) and mean (1.59 ppm) dietary burden from thiamethoxam use. The CGA 322704 residues in liver were estimated at 0.10 and 0.035 mg/kg resulting from the maximum (5.23 ppm) and mean (1.59 ppm) dietary burden from thiamethoxam use. The CGA 322704 residues in muscle, fat and kidney were below the LOQ of 0.01 mg/kg for the maximum (5.23 ppm) dietary burden from thiamethoxam use. These residues need to be taken into account.

The Meeting estimated a maximum residue level for clothianidin of 0.02* mg/kg in meat from mammals other than marine mammals, mammalian offal, except liver, and mammalian fat (based on clothianidin use). The Meeting estimated a maximum residue level for clothianidin of 0.2 mg/kg in liver of cattle, goats, pigs and sheep (based on thiamethoxam use). The meeting estimated a maximum residue for clothianidin of 0.02 mg/kg in milks (based on thiamethoxam use). The residue in animal commodities is considered not fat-soluble.

The Meeting estimated an STMR and HR of 0.02 mg/kg in meat from mammals other than marine mammals, mammalian offal, except liver and mammalian fat (based on clothianidin use). The Meeting estimated an STMR of 0.035 mg/kg and HR of 0.10 mg/kg in liver (based on thiamethoxam use). The Meeting estimated an STMR of 0.004 mg/kg in milks (based on thiamethoxam use).

Poultry

No poultry feeding study is available for clothianidin, but the metabolism studies in laying hens can be used to estimate residue levels resulting from dietary burden based on clothianidin in poultry

tissues or eggs from a mean and maximum dietary burden of 0.070 and 0.258 ppm. When extrapolating from a dose rate of 134 ppm in the laying hen metabolism study to 0.258 ppm as maximum dietary burden for poultry, and using the maximum total residues in liver of 5.1 mg/kg, residue levels in tissues and eggs are expected to be well below the LOQ of 0.01 mg/kg.

Another route for clothianidin residues to end up in animal commodities is from dietary burden resulting from thiamethoxam use. Based on a poultry metabolism study with thiamethoxam, CGA 322704 residues in poultry meat, fat and eggs from a thiamethoxam dietary burden of 1.59 ppm are also well below the LOQ of 0.01 mg/kg. However, CGA 322704 residues in poultry offal from thiamethoxam dietary burden of 1.59 ppm are higher than from clothianidin dietary burden. These residues need to be taken into account. Maximum residue levels from thiamethoxam dietary burden in poultry liver are 0.050 mg/kg clothianidin; mean residue levels in poultry liver are 0.018 mg/kg clothianidin.

The Meeting estimated a maximum residue level for clothianidin of 0.01* mg/kg in poultry meat, poultry fats, and eggs (based on clothianidin use). The Meeting estimated a maximum residue level for clothianidin of 0.1 mg/kg in poultry offal (based on thiamethoxam use). The residue in animal commodities is considered not fat-soluble.

The Meeting estimated an STMR and HR of 0.01 mg/kg in poultry meat, poultry fats, and eggs (based on clothianidin use). The Meeting estimated an STMR of 0.018 mg/kg in poultry offal and an HR of 0.050 mg/kg in poultry offal (based on thiamethoxam use).

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes (IEDI) of for clothianidin was calculated from recommendations for STMRs for raw and processed commodities in combination with consumption data for corresponding food commodities. The results are shown in Annex 3.

The IEDI of in the 13 GEMS/Food cluster diets, based on the estimated STMRs were in the range 1%–2% of the maximum ADI of 0.1 mg/kg bw. The Meeting concluded that the long-term intake of residues of clothianidin from uses considered by the Meeting is unlikely to present a public health concern.

Short-term intake

The International Estimated Short Term Intake (IESTI) for clothianidin was calculated from recommendations for STMRs and HRs for raw and processed commodities in combination with consumption data for corresponding food commodities. The results are shown in Annex 4.