

**CLOTHIANIDIN (238)**

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**APPRAISAL**

Clothianidin is reconsidered by the Meeting because new data for thiamethoxam became available and clothianidin is a metabolite (sometimes referred to as CGA322704) of thiamethoxam.

Clothianidin was evaluated for toxicology and residues as a new compound in 2010, resulting in a number of MRL recommendations. Additional residue data were evaluated in 2011 and 2012. The residue definition for clothianidin in plant commodities for enforcement and dietary risk assessment is clothianidin.

The 2010 Meeting established an acceptable daily intake (ADI) of 0–0.1 mg/kg bw per day and established the acute reference dose (ARfD) as 0.6 mg/kg bw for clothianidin. Clothianidin residues can also arise from thiamethoxam use (metabolite CGA322704). Therefore, both compounds need to be considered if residue data in support of new uses are submitted. The residue definition in plant commodities for enforcement is thiamethoxam, while the residue definition for dietary risk assessment is thiamethoxam and the metabolite CGA322704 (clothianidin), considered separately.

At the 2014 JMPR Meeting residue data were submitted to support the use of thiamethoxam on use avocado, mango, beans, mint, hops, and persimmon.

The Meeting received analytical methods and supervised trials data for the use of thiamethoxam on avocado, mango, beans, mint, hops and persimmon as well as processing data on mango and mint. The resulting CGA322704 data relevant for maximum residue level recommendations of clothianidin are summarized below.

*Combination of residues from clothianidin use and thiamethoxam use*

Clothianidin residues may arise from use of clothianidin as well as from use of thiamethoxam (metabolite CGA322704).

The Meeting considered it unlikely that both pesticides are used on the same crop and therefore the maximum estimated residue levels, the maximum STMR, and the maximum HR of each use is taken as recommendation.

Summary of residue data of clothianidin following use of thiamethoxam in relation to clothianidin use reviewed by the 2014 Meeting.

CCN	Commodity name	Origin of use	MRL mg/kg	STMR or STMR-P mg/kg	HR or HR-P mg/kg
FI 0326	Avocado	thiamethoxam	0.03 T	0.01 T	0.02 T
FI 0345	Mango	thiamethoxam	0.04 T	0.02 T	0.02 T
DH 1100	Hops	thiamethoxam	0.07 T	0.026 T	0.028 T
HH 0738 <sup>e</sup>	Mints	thiamethoxam	0.3 T	0.11 T	0.12 T
VP 0061	Beans with pods	thiamethoxam	0.2 T	0.07 T	0.10 T
	Bean forage	thiamethoxam		0.075 T	0.11 T

T = Thiamethoxam use

*Fate of residues during processing*

Processing studies were undertaken for the use of thiamethoxam on mango and mint (no known use of clothianidin). Processing factors based on the residue for the metabolite clothianidin are listed in the table below. Using the STMR<sub>RAC</sub> obtained from the thiamethoxam use, the Meeting estimated STMR-Ps for processed commodities to be used in dietary intake calculations.

Commodity	PFs	PF (median or best estimate)	STMR-P = STMR <sub>RAC</sub> x PF (mg/kg)	HR-P = HR <sub>RAC</sub> x PF (mg/kg)
	Metabolite CGA322704 (clothianidin) (STMR <sub>pulp+peel</sub> = 0.02 mg/kg, HR <sub>pulp+peel</sub> = 0.02 mg/kg)			
Mango, dried flesh	5.67, 8.40, 7.00, 4.00	6.3	0.13	0.13
Mint, oil	< 0.22, < 0.19	< 0.20	n.a.	n.a.

### *Livestock dietary burden*

The additional data on residue levels of clothianidin in bean forage from thiamethoxam use (JMPR 2014) warranted new dietary burden calculations for clothianidin.

The Meeting estimated the dietary burden of clothianidin on the basis of the livestock diets listed in the FAO manual appendix IX (OECD feedstuff table) using the OECD\_Feed\_Calculator\_V1\_4. 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. The 2014 JMPR Meeting recalculated the livestock dietary burden of clothianidin through clothianidin and thiamethoxam use based on the uses presented by the 2010 Meeting and including the residue values for fresh bean forage from the 2014 JMPR Meeting on thiamethoxam.

The new dietary burdens calculations of clothianidin for beef cattle, dairy cattle, broilers and laying poultry are provided in Annex 6. The calculations were made according to the livestock diets from US/CAN, EU, Australia and Japan in the OECD Feed Table 2009.

#### Livestock dietary burden, clothianidin, ppm of dry matter

	US	EU	AU	JP	overall	
	Max	Max	Max	Max	max	
Beef cattle	0.30	0.80	1.1	0.027	1.1	<sup>a</sup>
Dairy cattle	0.28	0.61	0.87	0.051	0.87	<sup>b</sup>
Poultry – broiler	0.050	0.21	0.094	0.022	0.21	
Poultry – layer	0.050	0.26	0.094	0.018	0.26	<sup>c</sup>
	Mean	Mean	Mean	Mean	Mean	
Beef cattle	0.088	0.17	0.75	0.024	0.75	<sup>a</sup>
Dairy cattle	0.12	0.17	0.61	0.033	0.61	<sup>b</sup>
Poultry – broiler	0.050	0.040	0.094	0.017	0.094	
Poultry – layer	0.050	0.070	0.094	0.018	0.094	<sup>c</sup>

<sup>a</sup> Highest mean and maximum beef or dairy cattle dietary burden suitable for maximum residue level and STMR estimates for mammalian meat.

<sup>b</sup> Highest mean and maximum dairy cattle dietary burden suitable for maximum residue level and STMR estimates for milk.

<sup>c</sup> Highest mean and maximum poultry dietary burden suitable for maximum residue level and STMR estimates for poultry meat and eggs.

### *Animal commodities maximum residue level estimation*

Clothianidin residues in animal commodities from both thiamethoxam (metabolite CGA322704) and clothianidin use are considered below.

#### *Cattle-clothianidin residues from thiamethoxam use*

The residues of clothianidin were evaluated in the same way as described for thiamethoxam (see appraisal 2010) for maximum residue level estimation, the highest residue in the tissues and milk were calculated by interpolating the maximum dietary burden (6.1 ppm) between the relevant feeding levels (6-20 ppm) from the dairy cow feeding study and using the highest tissue concentrations based on the residue definition for enforcement from individual animals within those feeding groups and using the mean milk concentration from those feeding groups (see table below).

The STMR values for the tissues and milk were calculated by interpolating the mean dietary burden (2.4 ppm) between the relevant feeding levels (2-6 ppm) from the dairy cow feeding study and using the mean tissue and milk concentrations based on the residue definition for dietary risk assessment from those feeding groups (see table below).

	Feed level (ppm) for milk residues	Total residues in milk (mg/kg)	Feed level (ppm) for tissue residues	Total residue (mg/kg) in			
				muscle	Liver	kidney	fat
Maximum residue level – beef or dairy cattle							
Feeding study	6, 20	0.013, 0.043	6, 20	< 0.01, < 0.01	0.14, 0.38	< 0.01, 0.04	< 0.01, < 0.01
Dietary burden and residue estimate	6.1	0.013	6.1	< 0.01	0.14	< 0.01	< 0.01
STMR – beef or dairy cattle							
Feeding study	2, 6	0.005, 0.013 <sup>a</sup>	2, 6	< 0.01, < 0.01	0.049, 0.14	< 0.01, < 0.01	< 0.01, < 0.01
Dietary burden and residue estimate	2.4	0.0060	2.4	< 0.01	0.058	< 0.01	< 0.01

<sup>a</sup> Calculated mean (day 3-26), data retrieved from JMPR 2010 evaluation

#### *Cattle-clothianidin residues from clothianidin use*

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 0.75 and 1.1 ppm based on the new clothianidin dietary burden calculation.

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 (0.87 ppm) between the relevant feeding levels (0.8 and 2.6 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 (0.61 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.

	Feed level (ppm) for milk residues	Total residues in milk (mg/kg)
Maximum residue level – dairy cattle		
Feeding study	0.80, 2.6	0.0020, 0.012
Dietary burden and residue estimate	0.87	0.002
STMR – dairy cattle		
Feeding study	0.27, 0.80	< 0.0020, < 0.0020
Dietary burden and residue estimate	0.61	< 0.0020

#### *Cattle- data combined from clothianidin and thiamethoxam use*

Based on the combined data, the clothianidin data from the thiamethoxam cattle feeding studies were used to support the estimation of maximum residue levels, STMR and HR values for mammalian meat and milk.

The Meeting confirmed the previous maximum residue level recommendations for clothianidin in milk, liver, muscle, fat and edible off al (except liver). The Meeting also confirmed the previous recommended STMR and HR values for meat, muscle, fat, and edible off al (except liver).

The Meeting estimated a new STMR for clothianidin in milk of 0.006 mg/kg and recommended to withdraw the previous recommendation of 0.002 mg/kg. The Meeting estimated a new STMR and HR value for clothianidin in liver of 0.058 and 0.14 mg/kg, respectively and recommended to withdraw the previous recommendations of 0.034 and 0.10 mg/kg, respectively.

#### *Poultry-clothianidin*

The new maximum and mean dietary burdens of clothianidin through clothianidin and thiamethoxam use for poultry are marginally lower or unchanged. No new estimations are required. The Meeting agreed that the previous recommendations were confirmed.

### RECOMMENDATIONS

The 2011 Meeting recommended the following residue definition for clothianidin (through thiamethoxam and clothianidin use):

Definition of the residue for compliance with the MRL and for estimation of dietary intake for plant and animal commodities: *clothianidin*.

*The residue is not fat soluble.*

CCN	Commodity Name	CLOTHIANIDIN Maximum residue level recommendations (mg/kg)		STMR or STMR-P (mg/kg)		HR or HR-P (mg/kg)	
		New	previous	New	previous	new	previous
FI 0326	Avocado	0.03 T		0.01 T		0.02 T	
VP 0061	Beans, except broad bean and soya bean	0.2 T		0.07 T		0.10 T	
DH 1100	Hops, dry	0.07 T		0.026 T		0.028 T	
FI 0345	Mango	0.04 T		0.02 T		0.02 T	
HH 0738 <sup>a</sup>	Mints	0.3 T		0.11 T		0.12 T	
-	Mango pulp			0.02 T		0.02 T	
-	Mango dried			0.13 T		0.13 T	
MM 0095	Meat (from mammals other than marine mammals)		0.02* C,t		0.02		0.02
MF 0100	Mammalian fats (except milk fats)		0.02* C,t		0.02		0.02
MO 0105	Edible offal (mammalian) (except liver)		0.02* C,t		0.02		0.02
MO 0099	Liver of cattle, goats, pigs and sheep		0.2* T,c	0.058 T,c	0.034 <sup>a</sup>	0.14 T,c	0.10 <sup>a</sup>
ML 0106	Milk		0.02*	0.006 T,c	0.002		

T = based on thiamethoxam use; T,c or C,t = combined clothianidin and thiamethoxam use

<sup>a</sup> Not reported in Annex 1 of clothianidin report 2010, retrieved from 2010 appraisal and based on Thiamethoxam use.

CCN	Commodity Name	CLOTHIANIDIN Maximum residue level recommendations mg/kg	Median residue mg/kg	Highest residue mg/kg
AL	Bean forage	n.a.	0.075	0.11

## 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 clothianidin in the 17 food cluster diets, based on the estimated STMRs was in the range 1–3% of the maximum ADI of 0.1 mg/kg bw. The Meeting concluded that the long-term intake of residues of clothianidin arising from uses of thiamethoxam and clothianidin considered by the 2010, 2011, 2012 and the present 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.

The IESTI for the general population represented 0% of the ARfD (0.6 mg/kg bw) and the IESTI for children represented 0–0% of the ARfD. The Meeting concluded that the short-term intake of residues of clothianidin, from uses of thiamethoxam considered by the present Meeting, is unlikely to present a public health concern.

