GLUFOSINATE-AMMONIUM (175)

EXPLANATION

Glufosinate-ammonium is a herbicide or desiccant. It was first evaluated for residues and toxicology by the 1991 JMPR and subsequently for residues in 1994 and 1998. The 1998 JMPR evaluated trials with glufosinate-ammonium on glufosinate-tolerant crops.

The current definition of the glufosinate residue includes glufosinate and 3-[hydroxy(methyl)phosphinoyl]propionic acid (MPP) and is based on the residues occurring in conventional crops. When glufosinate is used on genetically modified glufosinate-tolerant crops *N*-acetyl-glufosinate (NAG) is produced as a major part of the residue. The 1998 JMPR considered a revised residue definition, but could not recommend its use until the toxicological evaluation of NAG had been completed. This has now been done.

In the use of glufosinate-ammonium on glufosinate-tolerant canola in Canada, the timing of the final application is specified at the early bolting growth stage. The Meeting received new information on the interpretation of 'early bolting.'

Definition of the residue

The 1998 JMPR suggested a revised residue definition to take into account the nature of the residue occurring in conventional and transgenic glufosinate-tolerant crops: "sum of glufosinate-ammonium, 3[hydroxy(methyl)phosphinoyl]propionic acid and *N*-acetyl-glufosinate, expressed as glufosinate (free acid)".

When glufosinate is used on genetically modified glufosinate-tolerant crops NAG is produced (Figure 1). It should be included in the residue definition for enforcement because (1) it is sometimes the major residue component, and (2) the same GLC derivative is produced in the analytical method from both glufosinate itself and NAG (Figure 2), so unless the compounds are separated before derivatization they both appear as their common derivative.

The revised definition is also suitable for commodities from conventional crops because if NAG is absent it will not contribute to the analytical result and if present at low levels it is necessarily already included in the analytical result. NAG is a minor metabolite or degradation product in animals, soils and water/sediment systems.

In the light of the current toxicological evaluation of NAG the Meeting confirmed the suggested residue definition as suitable both for compliance with MRLs and for the estimation of dietary intake.

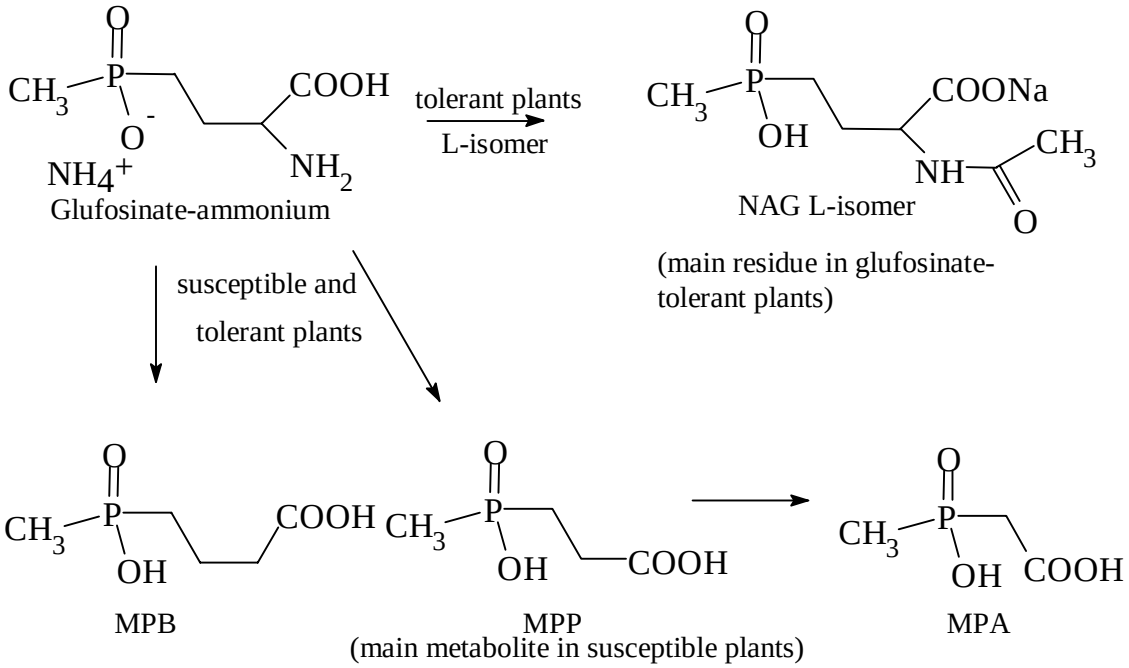

Figure 1. Proposed metabolic pathways of glufosinate-ammonium in plants.

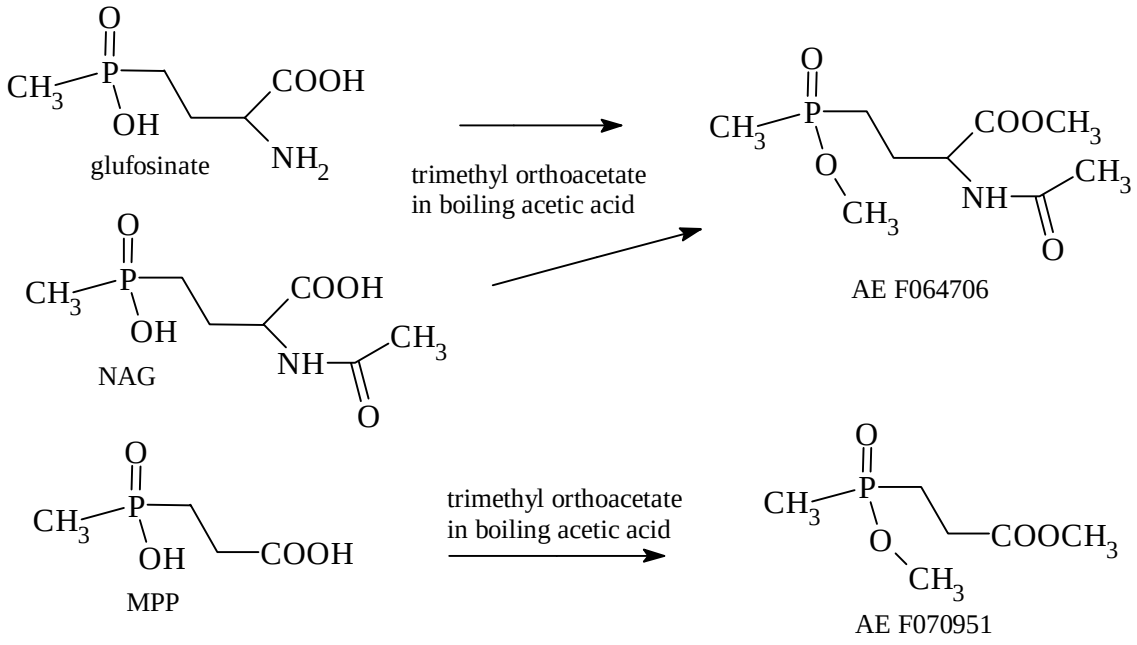

Figure 2. Derivatization of glufosinate and metabolites for determination of residues by GLC.

USE PATTERN

The registered use pattern for glufosinate-ammonium on tolerant canola in Canada shown below (Table 1) is extracted from the Table of registered uses in the 1998 Residue Evaluations.

Table 1. Registered uses of glufosinate-ammonium. Concentrations and rates are expressed in terms of the active ingredient glufosinate-ammonium.

Crop	Country	Form	Application			Number	Growth stage
			Method	Rate, kg ai/ha	Spray conc. kg ai/hl		
Canola (tolerant)	Canada	150 g/l SL	foliar	0.30-0.50	min spray vol 110 l/ha	2	early bolting
Canola (tolerant)	Canada	150 g/l SL	foliar	0.60	min spray vol 110 l/ha	1	early bolting

MacDonald *et al.* (1999) have provided a detailed explanation of 'early bolting'. The Canola Council divides the growth of canola into 6 stages: 0 pre-emergence, 1 seedling, 2 rosette, 3 bud, 4 flower, and 5 ripening. The bud stage is where the flower cluster becomes visible in the centre of the rosette. The formation of the flower buds is accompanied by rapid stem elongation (bolting). Plants at the 5-6 leaf stage under Canadian conditions are likely to be in the bud or early bolting phase of development. It is typical to have several growth stages present simultaneously in a trial, so the growth stage is given as a range. It is possible to have plants in both the rosette and bud stages in a trial where the growth stage is given as 4-6 leaf.

There are two reasons for the discrepancy between the interpretation of the leaf stage for early bolting in oilseed rape in the EU (10 leaf stage) and in Canada. The first is that oilseed rape is sown in the autumn in the EU and the plants require a vernalization period to initiate flowering; the plant grows in the autumn, but the bud stage will not occur until the following spring. The second is that the hot summer temperatures, low soil moisture and long day length in Western Canada are conducive to the rapid initiation of the bud phase.

RESIDUES RESULTING FROM SUPERVISED TRIALS

In the light of the new information on Canadian GAP the Meeting re-evaluated the Canadian trials on glufosinate-resistant canola reviewed by the 1998 JMPR (Table 2).

Table 2. Interpretation table for glufosinate-ammonium residues in canola in trials in Canada recorded in the 1998 JMPR Residue Evaluations. GAP and trial conditions are compared for trials considered valid for the estimation of maximum residue levels and STMRs.

Country	Application				Trial ref	Glufos + NAG +MPP, mg/kg
	kg ai/ha	kg ai/hl	No.	Growth stage		
Canada GAP	0.60		1	early bolting		
Canada trial	0.5	0.45	1	GS 4-5 leaf	XEN93-29-AB-TC-3 A56394	<0.05
Canada trial	0.75	0.68	1	GS 4-6 leaf	XEN93-29-MB-TC-2 A56394	0.12
Canada trial	0.5	0.45	1	GS 4-5 leaf	XEN93-29-MB-TC-3 A56394	<0.05
Canada trial	0.75	0.68	1	GS 4-5 leaf	XEN93-29-MB-TC-3 A56394	<0.05
Canada trial	0.5	0.45	1	GS 4-5 leaf	XEN93-29-MB-TC-4 A56394	<0.05
Canada trial	0.75	0.68	1	GS 4-5 leaf	XEN93-29-MB-TC-4 A56394	<0.05
Canada trial	0.5	0.45	1	GS 10 leaf	XEN93-29-SK-TC-6 A56394	<0.05
Canada trial	0.75	0.68	1	GS 10 leaf	XEN93-29-SK-TC-6 A56394	<0.05
Canada trial	0.8	0.73	1	GS 5-6 leaf	A56392 Minto	<0.05
Canada trial	0.8	0.73	1	GS 5-7 leaf	A56392 Indian Head	0.24
Canada trial	0.8	0.73	1	GS 4-5 leaf	A56392 Portage la Prairie	0.07
Canada trial	0.8	0.73	1	GS 4-6 leaf	Vauxhall	0.17

Residues in animal commodities

The 1998 JMPR evaluated feeding studies in which lactating dairy cows and laying hens were dosed with glufosinate-ammonium + NAG. The present Meeting estimated the dietary burden of residues for the animals using the diets in Appendix IX of the FAO Manual (Table 3). The calculations based on the MRLs and relevant processing factors provide dietary burdens suitable for estimating maximum residue levels for animal commodities, and those based on STMRs for the feed items allow the estimation of STMRs for animal products.

Table 3. Estimated dietary burden of glufosinate residues for beef and dairy cattle and poultry calculated from existing and proposed MRLs (and processing factors for the oilseed meal, and from STMRs where available. DM is dry matter. MRL/DM and STMR/DM are the MRL and STMR expressed on a dry matter basis. STMRs were not available for the components of the poultry diet so the dietary burdens used for estimating maximum residue levels and STMRs in poultry commodities are the same.

Commodity	MRL, mg/kg[1]	Processing factor[2]	DM, %	MRL/DM, mg/kg	% of diet			Residue in diet, ppm		
					Beef	Dairy	Poultry	Beef	Dairy	Poultry
Maize fodder	10		83	12.05						
Maize forage	5		40	12.50	40	50		5.00	6.25	
Almond hulls	0.5		90	0.56	10	10		0.06	0.06	
Maize	0.1		88	0.11	15	15	70	0.02	0.02	0.08
Sugar beet leaves	0.1		23	0.43	20	10		0.09	0.04	
Sunflower seed	5									
Sunflower seed meal	12	2.4	92	13.04			15	0	0	1.80
Rape seed	5									
Rape seed meal	17.0	3.4	88	19.32	15	15	15	2.90	2.90	2.90
Soya bean dry	2									
Soya bean meal	2.6	1.3	89	2.92				0	0	0
							Total dietary burden	11.0	11.1	4.8
	STMR, mg/kg			STMR/DM, mg/kg						
Maize fodder	0.72		83	0.87						
Maize forage	0.54		40	1.35	40	50		0.54	0.68	
Almond hulls	0		90	0	10	10		0	0	
Maize	0.1		88	0.11	15	15	70	0.02	0.02	0.08
Sugar beet leaves	0.1		23	0.43	10	10		0.04	0.04	
Sunflower seed	5									
Sunflower seed meal	12	2.4	92	13.04			15	0	0	1.80
Rape seed	5									
Rape seed meal	17.0	3.4	88	19.32	15	15	15	2.90	2.90	2.90
Soya bean dry	0.87									
Soya bean meal	1.13	1.3	89	1.27				0	0	0
							Total dietary burden	3.7	3.7	4.8

[1]The "MRLs" for the oilseed meals were derived by multiplying the MRLs for the seeds by the corresponding processing factors

[2]The processing factors were derived from processing studies reported by the 1998 and 1994 JMPRs.

APPRAISAL

The 1998 JMPR evaluated glufosinate-ammonium for its uses on glufosinate-tolerant crops. It estimated a number of maximum residue levels, but could not generally recommend them for use as MRLs or propose a revised residue definition until the toxicological evaluation of the metabolite *N*-acetyl-glufosinate (NAG) had been completed. It suggested a provisional revised definition of the residue to take into account the nature of the residue occurring in both conventional and glufosinate-tolerant crops: "sum of glufosinate-ammonium, 3-[hydroxy(methyl)phosphinoyl]propionic acid and *N*-acetyl-glufosinate, expressed as glufosinate (free acid)".

When glufosinate is used on genetically modified glufosinate-tolerant crops *N*-acetyl-glufosinate is produced. It should be included in the residue definition for enforcement because (1) it is sometimes the main residue component, and (2) the same GLC derivative is produced in the analytical method from both glufosinate itself and NAG, so unless the compounds are separated before derivatisation they both appear as their common derivative. The revised definition is also suitable for commodities from conventional crops because if NAG is absent it will not contribute to the analytical result and if present at low levels it is necessarily already included in the analytical result. NAG is a minor metabolite or degradation product in animals, soils and water/sediment systems.

In the light of the current toxicological evaluation of NAG the Meeting confirmed the suggested residue definition as suitable for both compliance with MRLs and for the estimation of dietary intake.

The residue reported in the supervised trials consists of three components: glufosinate, NAG and 3-[hydroxy(methyl)phosphinoyl]propionic acid (MPP). The method of calculating the total residue was described by the 1998 JMPR and is illustrated by example:

Glufosinate	MPP	NAG	Total
<0.05	<0.05	<0.05	<0.05
<0.05	<0.05	0.06	0.06
0.05	<0.05	0.09	0.14

Canadian GAP for canola specifies treatment at 'early bolting'. The 1998 JMPR was informed that the 10-leaf stage is very close to bolting, but subsequent advice from Canada is that under Canadian conditions and practices a 4-6-leaf growth stage corresponds to early bolting.

Twelve Canadian trials on canola were essentially in accord with Canadian GAP (0.60 kg ai/ha, treatment at early bolting) and produced residues of <0.05 (8), 0.07, 0.12, 0.17 and 0.24 mg/kg.

The Meeting estimated a maximum residue level for glufosinate-ammonium in rape seed of 0.3 mg/kg, but noted that the residues arising from this new use were within the existing CXL of 5 mg/kg, which was based on uses on susceptible rape. It is not possible to estimate an STMR on only part of the residue data.

The dietary burden of glufosinate-ammonium for estimating MRLs for animal commodities is 8.1 and 9.3 ppm for beef and dairy cattle respectively and 4.8 ppm for poultry, calculated from MRLs and proposed MRLs for feed commodities.

The levels of 8.1 and 9.3 ppm are comparable to the 9.1 ppm feeding level in the lactating cow feeding study reported in 1998. Residues were not detected in milk (<0.02 mg/kg) or tissues (<0.05 or <0.1 mg/kg) at this feeding level. Occasional residues were detected in milk (0.02, 0.03 mg/kg) at the next feeding level of 27 ppm, but not in the tissues. The Meeting estimated maximum residue levels at the LODs for meat, offal and milk.

The level of 4.8 ppm is equivalent to the nominal 3.6 ppm feeding level in the feeding study on laying hens. No residues were detected in the tissues or eggs at this feeding level. The Meeting estimated maximum residue levels at the LODs for poultry meat, offal and eggs.

The dietary burdens for estimating STMRs for beef and dairy cattle products are 3.5 and 3.6 ppm respectively, derived from the STMRs for maize forage and almond hulls and MRLs for the other feed commodities.

The residues were below the LOD in the muscle, liver and kidneys at feeding levels of 9.1 and 27 ppm. The Meeting noted that the dietary burden of 3.5-3.6 ppm was much less than the feeding level of 27 ppm and as an approximation assumed that tissue residues would be proportional to dietary intake:

STMR for animal commodity = LOD × (STMR dietary burden) ÷ (feeding level)

STMR for meat = 0.05 × 3.6 ÷ 27 = 0.007 mg/kg (no detections at 27 ppm feeding level)

STMR for edible offal = 0.1 × 3.6 ÷ 27 = 0.014 mg/kg (no detections at 27 ppm feeding level)

STMR for milk = 0.02 × 3.6 ÷ 27 = 0.003 mg/kg (no detections at 27 ppm feeding level)

The Meeting agreed that the calculated STMRs were low enough to be treated as effectively zero and estimated STMRs of 0 for meat, edible offal and milks.

STMRs for poultry feed commodities were not produced in this evaluation. Eggs, poultry meat and poultry edible offal were assigned STMRs equivalent to the LODs.

RECOMMENDATIONS

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

Definition of the residue (for compliance with MRLs and for the estimation of dietary intake): sum of glufosinate-ammonium, 3-[hydroxy(methyl)phosphinoyl]propionic acid and *N*-acetyl-glufosinate, expressed as glufosinate (free acid).

Commodity		MRL, mg/kg		STMR, mg/kg
CCN	Name	New	Previous	
MO 0105	Edible offal (Mammalian)	0.1*	-	0
PE 0112	Eggs	0.05*	-	0.05 [1]
AS 0645	Maize fodder	10	-	0.72
AF 0645	Maize forage	5	0.2	0.54

Commodity		MRL, mg/kg		STMR, mg/kg
CCN	Name	New	Previous	
MM 0095	Meat (from mammals other than marine mammals)	0.05*	-	0
ML 0106	Milks	0.02*	-	0
PM 0110	Poultry meat	0.05*	-	0.05 [1]
PO 0111	Poultry, Edible offal of	0.1*	-	0.1 [1]
VD 0541	Soya bean (dry)	2	0.1	0.87

[1]LOD is assigned as STMR level.

DIETARY RISK ASSESSMENT

Chronic intake

A revised maximum residue level for glufosinate-ammonium in soya beans and new maximum residue levels in animal commodities together with corresponding STMRs were estimated and combined with existing CXLs and draft MRLs to estimate the dietary intakes shown in Annex III.

Estimated Dietary Intakes for the 5 GEMS/Food regional diets, based on estimated STMRs and existing MRLs, were in the range of 3-10% of the ADI. The Meeting concluded that the intake of residues of glufosinate-ammonium resulting from its uses that have been considered by the JMPR is unlikely to present a public health concern.

Acute intake

The Meeting concluded that an acute RfD for glufosinate-ammonium is unnecessary. This conclusion was based on a determination that the pesticide is unlikely to present an acute toxicological hazard and residues are therefore unlikely to present an acute risk to consumers

REFERENCES

MacDonald, R., Sonder, K. and Stumpf, K. 1999. Canola residue trials. Further information on canola growth stages. Canola grown under North American (Canadian) conditions. Report PSR99/016. Hoechst Schering AgrEvo GmbH, Germany. Unpublished.