5.21 GLUFOSINATE-AMMONIUM (175)

TOXICOLOGY

Glufosinate-ammonium is the ISO-approved name for ammonium-DL-homoalanin-4-yl(methyl)phosphinate (IUPAC), with CAS number 77182-82-2. Glufosinate-ammonium is used as a non-selective herbicide for total vegetation control and as a desiccant to aid in crop harvesting. Glufosinate-ammonium, a racemic mixture of the D- and L-isomers, is a phosphinic acid analogue of glutamic acid. Its herbicidal action is related to the inhibition of glutamine synthetase, an enzyme that plays an important role in ammonia detoxification, amino acid metabolism, and protein and nucleotide biosynthesis in plants.

Glufosinate-ammonium was previously evaluated by JMPR in 1991 and 1999. In 1999, the Meeting established a group ADI of 0–0.02 mg/kg bw for glufosinate-ammonium, 3-[hydroxy(methyl) phosphinoyl]propionic acid (MPP) and *N*-acetylglufosinate (NAG) (alone or in combination) on the basis of a NOAEL of 2 mg/kg bw per day in a long-term study in rats given technical-grade glufosinate-ammonium.

Glufosinate-ammonium was re-evaluated by the present Meeting as part of the periodic review programme at the request of CCPR. The present Meeting evaluated studies on glufosinate as well as studies on 3-methylphosphinico-propionic acid (= MPP), NAG and 2-methylphosphinico-acetic acid (MPA), three metabolites that are found in plants, soil and livestock. Both the new data and previously submitted studies were considered by the present Meeting.

All critical studies complied with GLP.

Glufosinate-ammonium

Biochemical aspects

After administration of single (2–500 mg/kg bw) or repeated oral doses (2 mg/kg bw), [^{14}C]glufosinate-ammonium was rapidly but incompletely absorbed (approximately 10%). Peak plasma concentrations were reached within 0.5–1 hour. The radiolabel was widely distributed, with highest concentrations in liver and kidneys. Radiolabel concentrations were low in the brain and fetus. The plasma half-life of the initial elimination phase was 4–5 hours. Excretion after single or repeated doses was rapid, with more than 90% excreted within 24 hours after administration of a low dose. Administration of higher doses resulted in slower absorption and excretion. In faeces, mainly glufosinate-ammonium and low concentrations (up to 10% of faecal radioactivity) of NAG were found, indicative of acetylation by microflora in the gut, as this metabolite is not found in urine. In urine, parent compound represented about 50% of the radioactivity, whereas 4-methylphosphinico-butanoic acid (MPB) and MPP each represented 8–22% of the urinary radioactivity. Very low levels of MPA were found in urine. MPP represented 10–20% of residue found in liver. There were no marked sex differences in the kinetics and metabolism of glufosinate-ammonium.

Toxicological data

In 1999, the Meeting considered reports on the relevance of glutamine synthetase activity in the liver, kidney and brain of experimental animals and humans and concluded the following:

- A less than 50% inhibition of glutamine synthetase in rat liver was not associated with increased ammonia concentrations and thus was not considered to be adverse.
- Inhibition of kidney glutamine synthetase in the absence of pathological findings was not considered to be relevant to human risk assessment.
- Any statistically significant inhibition of glutamine synthetase activity in brain by more than 10% was considered a marker of potentially adverse effects on brain biochemistry and behaviour.

The present Meeting confirmed the conclusion of the 1999 JMPR, which is also supported by a recent published study on the essential role of glutamine synthetase in the implantation of mouse embryos.

The acute toxicity of glufosinate-ammonium is low in rats (oral LD_{50} > 1500 mg/kg bw; dermal LD_{50} > 2000 mg/kg bw; inhalation $LC_{50} \geq 1.26$ mg/L). Glufosinate-ammonium is not irritating to the skin or eyes of rabbits and is not a skin sensitizer (Magnusson & Kligman test and Buehler test in guinea-pigs; local lymph node assay in mice).

In acute toxicity studies in mice, clinical signs of neurotoxicity were observed at 231 mg/kg bw (the lowest dose tested) and above. Mortality was observed at doses greater than or equal to 300 mg/kg bw.

In a single-dose toxicity study in dogs, clinical signs of neurotoxicity were observed at 200 mg/kg bw (the lowest dose tested), and mortality was observed at 400 mg/kg bw.

In three 13-week dietary studies in mice, the overall NOAEL was 1280 ppm (equal to 278 mg/kg bw per day), based on clinical signs (ruffled fur, sedation, ventral recumbence or hunched posture, and emaciation) observed at 3500 ppm (equal to 561 mg/kg bw per day).

In a 28-day dietary range-finding and two 13-week dietary studies in rats, the overall NOAEL was 4000 ppm (equal to 263 mg/kg bw per day), based on neurological effects in both sexes and reduced body weight gain and feed consumption, reductions in erythrocyte count and low reticulocyte ratios in males at 7500 ppm (equal to 521 mg/kg bw per day). Glutamine synthetase activity was not measured in these studies.

In a 28-day capsule study in dogs, the NOAEL was 1 mg/kg bw per day, based on reductions in glutamine synthetase activity in the central nervous system (8–53%), a slight increase in spontaneous motor activity that occurred within a few days after the start of treatment and reductions in body weight gain and feed consumption observed during the first week of treatment at 8 mg/kg bw per day.

In a 90-day dietary study in dogs, the NOAEL was 64 ppm (equal to 2.0 mg/kg bw per day), based on a reduction in body weight gain and feed consumption in females at 256 ppm (equal to 7.8 mg/kg bw per day).

In a 1-year dietary study in dogs, mortality on days 10 and 14 and severe clinical signs, starting on day 9 of treatment, were observed after treatment with 375 ppm (equal to 10.6–16.0 mg/kg bw per day). The two deaths out of 16 animals at the high dose were caused by heart and circulatory failure attributed to marked myocardial necrosis in one dog and to severe necrotizing aspiration pneumonia in the other dog. After lowering the dose to 250 ppm (equal to 8.4 mg/kg bw per day), no adverse effects were observed. The NOAEL was 150 ppm (equal to 4.5 mg/kg bw per day). The study indicates that glufosinate-ammonium has a steep dose–response curve in dogs.

In the absence of glutamine synthetase measurements in the 90-day and 1-year studies in dogs, an overall NOAEL of 1 mg/kg bw per day was established for these studies.

In a 2-year feeding study in mice, the NOAEL was 80 ppm (equal to 10.8 mg/kg bw per day), based on increased mortality and reduced body weight gain in males and changes in clinical chemistry parameters in both sexes at 160 ppm (equal to 23 mg/kg bw per day). No effect on tumour incidence was observed.

In a 130-week feeding study in rats, the NOAEL was 140 ppm (equal to 7.6 mg/kg bw per day), based on effects on haematology, glutathione levels in liver and blood, and a reduction of brain glutamine synthetase activity at 500 ppm (equal to 26.7 mg/kg bw per day). In this study and a 2-year carcinogenicity study in rats, no effect on tumour incidence was found.

The Meeting concluded that glufosinate-ammonium is not carcinogenic in mice or rats.

Glufosinate-ammonium was tested for genotoxicity in an adequate range of studies of genotoxicity in vitro and in vivo. No evidence for genotoxicity was observed in any test.

The Meeting concluded that glufosinate-ammonium is unlikely to be genotoxic.

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

A range-finding one-generation study and a two-generation study of reproductive toxicity in rats were available. The overall NOAEL for parental toxicity was 500 ppm (equal to 44 mg/kg bw per day), based on reduced feed consumption in males at 2500 ppm (equal to 206 mg/kg bw per day). At 2500 ppm and above, the dams delivered no pups. The overall NOAEL for offspring toxicity was 500 ppm (equal to 44 mg/kg bw per day), the highest dose at which dams produced a litter. The overall NOAEL for reproductive toxicity was 120 ppm (equal to 8.7 mg/kg bw per day), based on reduced litter sizes in all litters at 360 ppm (equal to 18 mg/kg bw per day). The Meeting considered the possibility that the increased pre-implantation loss observed in the range-finding one-generation study of reproductive toxicity at 2500 ppm (equal to 207 mg/kg bw per day) might be caused by an inhibition of glutamine synthetase prior to implantation; a published mechanistic study in mice indicates that glutamine synthetase activity in pre-implantation embryonic cells is essential for the blastocyst to complete implantation. The Meeting concluded that the pre-implantation loss and early deaths in the reproductive toxicity studies might be caused by a single exposure to glufosinate-ammonium.

In three developmental toxicity studies in rats, the overall NOAEL for maternal toxicity was 10 mg/kg bw per day, based on clinical signs and abortions at 50 mg/kg bw per day. The overall NOAEL for developmental toxicity was 10 mg/kg bw per day, based on intrauterine deaths at 50 mg/kg bw per day.

In a developmental toxicity study in rabbits, the NOAEL for maternal toxicity was 6.3 mg/kg bw per day, based on clinical signs, body weight loss and reduced feed consumption, an increased number of abortions and increased kidney weight at 20 mg/kg bw per day. The NOAEL for developmental toxicity was 6.3 mg/kg bw per day, based on an increased number of dead fetuses at 20 mg/kg bw per day.

The Meeting concluded that glufosinate-ammonium is not teratogenic in rats or rabbits.

In an acute gavage study of neurotoxicity in rats, the NOAEL was 100 mg/kg bw, based on clinical signs at 500 mg/kg bw.

In a dietary 38-day neurotoxicity study in rats and a 90-day dietary study investigating brain and liver glutamine synthetase inhibition in rats, the overall NOAEL was 100 ppm (equivalent to 6.2 mg/kg bw per day), based on a greater than 50% reduction in glutamine synthetase activity in the liver in males at 200 ppm (equal to 15 mg/kg bw per day).

In a dietary developmental neurotoxicity study in rats, the NOAEL for maternal toxicity was 1000 ppm (equal to 69 mg/kg bw per day), based on decreased body weight gain and feed consumption at 4500 ppm (equal to 292 mg/kg bw per day). The NOAEL for offspring toxicity was 200 ppm (equal to 14 mg/kg bw per day), based on reduced body weight gain during the pre-weaning period, effects on motor activity at postnatal days 17, 21 and 62, and hippocampal pathology in males at 1000 ppm (equal to 69 mg/kg bw per day).

Medical surveillance of plant production personnel did not find any effects related to the production of glufosinate-ammonium. Several human poisoning cases, sometimes leading to death, due to (suicidal) ingestion of glufosinate-ammonium have been reported in the literature. A variety of neurological symptoms have been described. It is not clear whether the toxicity was due to the active ingredient, to the surfactant contained in relatively high amounts in the formulation or to the combination of both.

Toxicological studies with the metabolites NAG, MPP and MPA, three metabolites that are found in plants, soil and livestock as well as in laboratory animals, were available. The toxicity of NAG, MPP and MPA is described separately below.

The Meeting concluded that the existing database on glufosinate-ammonium was adequate to characterize the potential hazards to fetuses, infants and children.

N-Acetyl-glufosinate (NAG)

Biochemical aspects

After administration of a single oral dose (3 mg/kg bw) of ^{14}C-labelled NAG to rats, it was rapidly but incompletely absorbed (approximately 5–10%). Peak plasma concentrations were reached within 1 hour. The highest residue levels were found in kidneys, followed by liver. Excretion after a single oral dose (3 mg/kg bw) was rapid, with approximately 95% of the absorbed dose excreted within 24 hours after administration. The absorbed NAG was predominantly excreted in urine. In faeces, mainly unchanged NAG was found, but about 10% was deacetylated to glufosinate by the intestinal microflora. In faeces, urine and tissues, minor amounts of MPP and MPA were found.

Toxicological data

The oral acute toxicity of NAG is low in rats and mice (LD_{50} > 2985 mg/kg bw). NAG is not a skin sensitizer (Magnusson & Kligman test in guinea-pigs).

In 4-week and 13-week dietary studies with NAG in mice, the overall NOAEL was 500 ppm (equal to 83 mg/kg bw per day), based on the inhibition of brain glutamine synthetase activity (11–13%) at 2000 ppm (equal to 233 mg/kg bw per day).

In a 4-week dietary range-finding study, two 13-week dietary studies and a 38-day dietary neurotoxicity study in rats, the overall NOAEL was 2000 ppm (equal to 331 mg/kg bw per day), based on statistically significant inhibition (11–12%) of liver glutamine synthetase activity at 10 000 ppm (equal to 658 mg/kg bw per day). Brain glutamine synthetase activity was reduced at 10 000 ppm (equal to 738 mg/kg bw per day). In the neurotoxicity study, no effects on glutamine synthetase and neurotoxicity parameters were observed at doses up to 2000 ppm (equal to 159 mg/kg bw per day), the highest dose tested.

In a 13-week dietary study in dogs, the NOAEL was 500 ppm (equal to 45 mg/kg bw per day), based on a reduction in brain glutamine synthetase activity (≥ 16%) at 2000 ppm (equal to 171 mg/kg bw per day).

In a 2-year dietary carcinogenicity study in rats, there were no toxicological findings and no increase in tumour incidence at the highest dose tested of 8000 ppm (equal to 1188 mg/kg bw per day). Glutamine synthetase activity was not measured.

In a 2-year dietary toxicity study in rats, the NOAEL was 2000 ppm (equal to 91 mg/kg bw per day), based on decreased body weight gain, increased incidence of soft faeces and increased incidences of polyarteritis nodosa in blood vessels and testes and urolithiasis at 20 000 ppm (equal to 998 mg/kg bw per day).

The Meeting concluded that NAG is not carcinogenic in rats.

NAG was tested for genotoxicity in an adequate range of in vitro and in vivo studies. No evidence for genotoxicity was observed in any test.

The Meeting concluded that NAG is unlikely to be genotoxic.

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

In a range-finding one-generation study and a two-generation study of reproductive toxicity with NAG, the NOAEL for parental, offspring and reproductive toxicity was 10 000 ppm (equal to 622 mg/kg bw per day), the highest dose tested.

In a developmental toxicity study in rats, the NOAEL for maternal and developmental toxicity was 1000 mg/kg bw per day, the only dose tested.

In a developmental toxicity study in rabbits, the NOAEL for maternal toxicity was 64 mg/kg bw per day, based on reduced feed consumption at 160 mg/kg bw per day. The NOAEL for developmental toxicity was 64 mg/kg bw per day, based on an increased incidence of extra thoracic ribs at 160 mg/kg bw per day.

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

In two acute oral (gavage) studies of neurotoxicity in rats, the NOAEL was 1000 mg/kg bw, based on clinical signs (diarrhoea, ruffled fur and sedation) observed at 2000 mg/kg bw. No overt neurotoxicity was observed. Glutamine synthetase activity was not measured.

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

3-Methylphosphinico-propionic acid (MPP)

Biochemical aspects

During the first 24 hours following a single oral dose of ^{14}C-labelled MPP administered to rats, 83% and 4% of the radiolabel were excreted in urine and faeces, respectively.

Toxicological data

The acute oral toxicity of MPP is low in rats (oral LD_{50} = 1900 mg/kg bw). MPP is not a skin sensitizer (Magnusson & Kligman test in guinea-pigs).

In short-term dietary studies in mice (13 weeks, doses up to 8000 ppm, equal to 1288 mg/kg bw per day), rats (4 weeks and 13 weeks, doses up to 6400 ppm, equal to 546 mg/kg bw per day) and dogs (28 days and 90 days, doses up to 1600 ppm, equal to 103 mg/kg bw per day), no toxicity was observed. In the 4-week study in rats, glutamine synthetase activity in liver was not affected at doses up to 5000 ppm (equal to 554 mg/kg bw per day). In the two short-term studies in dogs, glutamine synthetase activity in liver, kidney and brain was not affected at doses up to 1600 ppm (equal to 103 mg/kg bw per day).

No long-term studies with MPP were available.

Glufosinate-ammonium was tested for genotoxicity in a limited range of studies in vitro. No evidence for genotoxicity was observed in any of these tests.

In a developmental toxicity study in rats, the NOAEL for maternal toxicity was 300 mg/kg bw per day, on the basis of one death out of 20 animals, clinical signs of toxicity, and reduced body weight gain and feed consumption observed at 900 mg/kg bw per day. The NOAEL for fetal toxicity was 300 mg/kg bw per day, on the basis of 3 dams out of 20 with total litter loss at 900 mg/kg bw per day.

In a developmental toxicity study in rabbits, the NOAEL for maternal toxicity was 50 mg/kg bw per day, on the basis of one death out of 15 animals, one abortion, clinical signs of toxicity, and reduced body weight gain and feed consumption observed at 100 mg/kg bw per day. The NOAEL for fetal toxicity was 50 mg/kg bw per day, on the basis of one dam with seven conceptuses undergoing resorption at 100 mg/kg bw per day.

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

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

2-Methylphosphinico-acetic acid (MPA)

The acute oral toxicity of MPA in rats was low (LD_{50} > 2000 mg/kg bw). In a 90-day dietary study in rats, the NOAEL was 10 000 ppm (equal to 684 mg/kg bw per day), the highest dose tested. Glutamine synthetase activity was not measured, but in view of the structural similarity between MPA

and MPP, the Meeting considered it unlikely that MPA would inhibit this enzyme. MPA was not genotoxic in three genotoxicity tests in vitro.

Toxicological evaluation

The present Meeting compared the toxicity of NAG, MPP and MPA with that of glufosinate-ammonium and concluded that the toxicity of the metabolites was less than that of the parent compound. The Meeting established an ADI of 0–0.01 mg/kg bw for glufosinate-ammonium, on the basis of an overall NOAEL of 1 mg/kg bw per day, for reductions in glutamine synthetase activity in the brain of dogs. A safety factor of 100 was applied. This ADI also applies to its metabolites NAG, MPP and MPA. In view of the lower toxicity of NAG, MPP and MPA compared with glufosinate-ammonium, the Meeting noted that the application of the ADI to these metabolites is likely to be conservative. This ADI is considered to be adequately protective for any reproductive and developmental effects.

The Meeting established an ARfD for glufosinate-ammonium of 0.01 mg/kg bw, based on the NOAEL of 1 mg/kg bw per day in the 28-day capsule study in dogs for an increase in spontaneous motor activity that occurred within a few days after the start of treatment and reductions in body weight gain and feed consumption observed during the first week of treatment with 8 mg/kg bw per day and application of a safety factor of 100. This ARfD also applies to its metabolites NAG, MPP and MPA. In view of the lower acute toxicity of NAG, MPP and MPA compared with glufosinate-ammonium, the Meeting noted that the application of the ARfD to these metabolites is likely to be conservative. This ARfD is considered to be adequately protective for any reproductive and developmental effects.

A toxicological monograph was prepared.

Levels relevant for risk assessment of glufosinate-ammonium

Species	Study	Effect	NOAEL	LOAEL
Mouse	Two-year study of toxicity and carcinogenicity[a]	Toxicity	80 ppm, equal to 10.8 mg/kg bw per day	160 ppm, equal to 23 mg/kg bw per day
		Carcinogenicity	23 mg/kg bw per day[b]	—
Rat	Short-term studies of toxicity[c,d,e]	Toxicity	100 ppm, equal to 6.21 mg/kg bw per day	200 ppm, equal to 15 mg/kg bw per day
	Two-year study of toxicity and carcinogenicity[a]	Toxicity	140 ppm, equal to 7.6 mg/kg bw per day	500 ppm, equal to 26.7 mg/kg bw per day
		Carcinogenicity	500 ppm, equal to 26.7 mg/kg bw per day[b]	—
	Two-generation study of reproductive toxicity[a]	Parental toxicity	500 ppm, equal to 44 mg/kg bw per day	2500 ppm, equal to 206 mg/kg bw per day
		Offspring toxicity	500 ppm, equal to 44 mg/kg bw per day[b]	—
		Reproductive toxicity	120 ppm, equal to 8.7 mg/kg bw per day	360 ppm, equal to 18 mg/kg bw per day
	Developmental toxicity study[c]	Maternal toxicity	10 mg/kg bw per day	50 mg/kg bw per day
		Embryo and fetal toxicity	10 mg/kg bw per day	50 mg/kg bw per day
	Developmental neurotoxicity study[c]	Maternal toxicity	1000 ppm, equal to 69 mg/kg bw per day	4500 ppm, equal to 292 mg/kg bw per day
		Embryo and fetal toxicity	200 ppm, equal to 14 mg/kg bw per day	1000 ppm, equal to 69 mg/kg bw per day
Rabbit	Developmental toxicity study[c]	Maternal toxicity	6.3 mg/kg bw per day	20 mg/kg bw per day
		Embryo and fetal toxicity	6.3 mg/kg bw per day	20 mg/kg bw per day
Dog	Short-term study of toxicity	Toxicity	1 mg/kg bw per day	8 mg/kg bw per day

[a] Dietary administration.

[b] Highest dose tested.

[c] Gavage administration.

[d] Two or more studies combined.

[e] Based on inhibition of liver glutamine synthetase in a neurotoxicity study.

Levels relevant for risk assessment of NAG

Species	Study	Effect	NOAEL	LOAEL
Mouse	Short-term studies of toxicity[a,b]	Toxicity	500 ppm, equal to 83 mg/kg bw per day	2000 ppm, equal to 233 mg/kg bw per day
	Two-year study of carcinogenicity[a]	Carcinogenicity	8000 ppm, equivalent to 1188 mg/kg bw per day[c]	—
Rat	Short-term studies of toxicity[a,b]	Toxicity	2000 ppm, equal to 331 mg/kg bw per day	10 000 ppm, equal to 658 mg/kg bw per day
	Two-year study of toxicity and carcinogenicity[a]	Toxicity	2000 ppm, equal to 91 mg/kg bw per day	20 000 ppm, equal to 998 mg/kg bw per day
		Carcinogenicity	20 000 ppm, equal to 998 mg/kg bw per day[c]	—
	One-generation study of reproductive toxicity[a]	Parental toxicity	10 000 ppm, equivalent to 622 mg/kg bw per day[c]	—
		Offspring toxicity	10 000 ppm, equivalent to 622 mg/kg bw per day[c]	—
		Reproductive toxicity	10 000 ppm, equivalent to 622 mg/kg bw per day[c]	—
	Developmental toxicity study[d]	Maternal toxicity	1000 mg/kg bw per day[c]	—
		Embryo and fetal toxicity	1000 mg/kg bw per day[c]	—
Rabbit	Developmental toxicity study[d]	Maternal toxicity	64 mg/kg bw per day	160 mg/kg bw per day
		Embryo and fetal toxicity	64 mg/kg bw per day	160 mg/kg bw per day
Dog	Short-term study of toxicity[a]	Toxicity	500 ppm, equal to 45 mg/kg bw per day	2000 ppm, equal to 171 mg/kg bw per day

[a] Dietary administration.

[b] Two or more studies combined.

[c] Highest dose tested.

[d] Gavage administration.

Levels relevant for risk assessment of MPP

Species	Study	Effect	NOAEL	LOAEL
Mouse	Short-term study of toxicity[a]	Toxicity	8000 ppm, equivalent to 1288 mg/kg bw per day[b]	—
Rat	Short-term study of toxicity[a]	Toxicity	6400 ppm, equal to 546 mg/kg bw per day[b]	—
	Developmental toxicity study[c]	Maternal toxicity	300 mg/kg bw per day	900 mg/kg bw per day
		Embryo and fetal toxicity	300 mg/kg bw per day	900 mg/kg bw per day
Rabbit	Developmental toxicity study[c]	Maternal toxicity	50 mg/kg bw per day	100 mg/kg bw per day
		Embryo and fetal toxicity	50 mg/kg bw per day	100 mg/kg bw per day
Dog	Short-term study of toxicity[a]	Toxicity	1600 ppm, equal to 103 mg/kg bw per day[b]	—

[a] Dietary administration.

[b] Highest dose tested.

[c] Gavage administration.

Levels relevant for risk assessment of MPA

Species	Study	Effect	NOAEL	LOAEL
Rat	Short-term study of toxicity[a]	Toxicity	10 000 ppm, equal to 684 mg/kg bw per day[b]	—

[a] Dietary administration.

[b] Highest dose tested.

Estimate of acceptable daily intake for humans

0–0.01 mg/kg bw (ADI for glufosinate-ammonium, also applies to NAG, MPP and MPA)

Estimate of acute reference dose

0.01 mg/kg bw (ARfD for glufosinate-ammonium, also applies to NAG, MPP and MPA)

Information that would be useful for the continued evaluation of the compound

Results from epidemiological, occupational health and other such observational studies of exposures in humans

Critical end-points for setting guidance values for exposure to glufosinate-ammonium and its metabolites NAG and MPP

	Glufosinate-ammonium	NAG	MPP
Absorption, distribution, excretion and metabolism in animals			
Rate and extent of absorption	Rapid, incomplete (~10%)	Rapid, incomplete (5–10%)	Rapid and complete (87%)
Distribution	Extensive; highest concentrations in liver and kidney	Extensive; highest concentrations in liver and kidney	No data
Potential for accumulation	Low	Low	Low
Rate and extent of excretion	> 90% within 24 h, primarily in faeces	> 95% within 24 h, primarily in faeces	87% within 24 h, primarily in urine
Metabolism in animals	Limited	Limited	No data
Toxicologically significant compounds in animals, plants and the environment	Glufosinate-ammonium, NAG, MPP, MPA	NAG, glufosinate-ammonium, MPP, MPA	MPP, MPA
Acute toxicity			
LD_{50}, oral, rat	> 1500 mg/kg bw	> 2985 mg/kg bw	1900 mg/kg bw
LD_{50}, dermal, rat	> 2000 mg/kg bw	No data	No data
LC_{50}, inhalation, rat	≥ 1.26 mg/L air	No data	No data
Rat, dermal irritation	Not an irritant	No data	No data
Rabbit, ocular irritation	Not an irritant	No data	No data
Dermal sensitization	Not a sensitizer (Magnusson & Kligman, Buehler, local lymph node assay)	Not a sensitizer (Magnusson & Kligman)	Not a sensitizer (Magnusson & Kligman)
Short-term studies of toxicity			
Target/critical effect	Brain (inhibition of glutamine synthetase) (dog)	Brain (inhibition of glutamine synthetase) (mouse, rat, dog)	None identified
Lowest relevant oral NOAEL	1 mg/kg bw per day (dog)	500 ppm, equal to 45 mg/kg bw per day (dog)	1600 ppm, equal to 103 mg/kg bw per day, highest dose tested (dog)
Lowest relevant dermal NOAEL	100 mg/kg bw per day (rat)	No data	No data
Long-term studies of toxicity and carcinogenicity			
Target/critical effect	Mortality, body weight gain, clinical chemistry (mouse) Haematology, brain glutamine synthetase (rats)	Body weight gain, clinical signs, polyarteritis nodosa in blood vessels and testes, urolithiasis (rat)	No data

	Glufosinate-ammonium	NAG	MPP
Lowest relevant NOAEL	80 ppm, equal to 10.8 mg/kg bw per day (mouse) 140 ppm, equal to 7.6 mg/kg bw per day (rat)	2000 ppm, equal to 91 mg/kg bw per day (rat)	—
Carcinogenicity	Not carcinogenic (mouse, rat)	Not carcinogenic (rat)	—
Genotoxicity	Not genotoxic	Not genotoxic	Not genotoxic in a limited range of studies
Reproductive toxicity			
Target/critical effect	Reduced litter size (rat)	No reproductive target	No data
Lowest relevant parental NOAEL	500 ppm, equal to 44 mg/kg bw per day (rat)	10 000 ppm, equal to 622 mg/kg bw per day (rat)	—
Lowest relevant reproductive NOAEL	120 ppm, equal to 8.7 mg/kg bw per day (rat)	10 000 ppm, equal to 622 mg/kg bw per day (rat)	—
Lowest relevant offspring NOAEL	500 ppm, equal to 44 mg/kg bw per day (rat)	10 000 ppm, equal to 622 mg/kg bw per day (rat)	—
Developmental toxicity			
Target/critical effect	Intrauterine deaths (rat, rabbit)	Increased incidence of extra thoracic ribs (rabbit)	Intrauterine deaths (rat, rabbit)
Lowest relevant maternal NOAEL	120 ppm, equal to 8.7 mg/kg bw per day (rat)	64 mg/kg bw per day	50 mg/kg bw per day (rabbit)
Lowest relevant developmental NOAEL	10 mg/kg bw per day (rat) 6.3 mg/kg bw per day (rabbit)	64 mg/kg bw per day	50 mg/kg bw per day (rabbit)
Neurotoxicity			
Acute oral neurotoxicity NOAEL	1 mg/kg bw per day (dog); increased motor activity	Not neurotoxic (2000 mg/kg bw)	No data
Short-term neurotoxicity NOAEL	1 mg/kg bw per day (dog); inhibition of brain glutamine synthetase, increased motor activity	500 ppm, equal to 45 mg/kg bw per day (dog); inhibition of brain glutamine synthetase	Not neurotoxic Brain glutamine synthetase was not inhibited in dogs at 1000 ppm, equal to 58 mg/kg bw per day
Developmental neurotoxicity NOAEL	200 ppm, equal to 14 mg/kg bw per day (rat); increased motor activity, hippocampal pathology	No data	No data
Medical data	(Suicidal) poisonings producing several neurological effects and deaths. No adverse effects reported in plant production personnel.	No data	No data

Summary for glufosinate-ammonium

	Value	Study	Safety factor
ADI	0–0.01 mg/kg bw	Short-term studies (dog)	100
ARfD	0.01 mg/kg bw	Short-term studies (dog)	100

RESIDUE AND ANALYTICAL ASPECTS

Glufosinate is a non-selective contact herbicide with uses on many crops, both conventional and glufosinate tolerant. Glufosinate has been evaluated several times by the JMPR with the initial evaluation in 1991 and the latest in 1999. Glufosinate-ammonium was scheduled at the Forty-third Session of the CCPR (2011) for periodic re-evaluation of toxicology and residues by the 2012 JMPR.

Glufosinate is a synthetic version of the natural product, phosphinothricin, and exists as a racemic mixture (i.e., 50:50 D- and L-glufosinate). The D-enantiomer is not herbicidally active. The L-enantiomer of glufosinate acts by inhibition of glutamine synthetase thereby causing accumulation of toxic levels of ammonium ion and indirectly stopping photosynthesis. Two genes for acetyltransferase, *bar* and *pat*, that were isolated from *Streptomyces hygroscopicus* and *Streptomyces viridochromogenes*, respectively, have been used to produce glufosinate-tolerant crops. For the current evaluation data have been submitted covering herbicide use on conventional and crops genetically modified by inclusion of the *pat* and *bar* gene to be glufosinate tolerant. These crops inactivate L-glufosinate by converting it to *N*-acetyl-glufosinate (NAG).

The Meeting received information on the metabolism of glufosinate and NAG (the main metabolite expected to be formed in tolerant plants) in animals, on glufosinate metabolism in conventional crops, and on crops genetically modified to contain the *pat* or *bar* genes and be glufosinate tolerant, methods of residue analysis, freezer storage stability, GAP information, supervised residue trials on conventional and glufosinate tolerant crops, fate of residue during storage and processing, and livestock feeding studies.

Metabolites referred to in the appraisal were addressed by their common names,

NAG	N-acetyl-glufosinate;
MPP	3-methyl-phosphinico-propionic acid;
MPA	2-methyl-phosphinico-acetic acid;
MPB	4-methyl-phosphinico -butanoic acid;
MHB	4-methyl-phosphinico-hydroxy-butanoic acid;
PPO	4-methyl-phosphinico-2-oxo-butanoic acid.

Animal metabolism

Metabolism of glufosinate in cattle and hens involves formation of MPP and the slow transformation to MPA. NAG is metabolized by de-acetylation to form glufosinate with subsequent transformation proceeding as for glufosinate.

In one study a lactating goat was orally treated twice daily for 4 consecutive days with [3,4-^{14}C]- glufosinate at a dose equivalent to 101 ppm in the feed. Approximately 84% of the administered dose was recovered with the majority in the excreta (69% faeces, 3% urine) or gastrointestinal tract (12%). The radioactivity in the tissues ranged from 0.004 in fat to 0.61 mg/kg glufosinate equivalents in kidney. TRR values in milk were 0.003 to 0.022 mg/kg glufosinate equivalents during the dosing period with plateau levels reached after two days of dosing.

Major components of the ^{14}C residues were unchanged glufosinate (kidney 49% TRR, liver 53% TRR, milk 49% TRR) and MPP (kidney 29% TRR, liver 36% TRR and milk 6.3% TRR). The minor metabolites MPA and NAG individually accounted for no more than 5.3% TRR in kidney, liver and milk.

In a separate study a lactating goat was dosed twice a day with NAG at a dose equivalent to 84 ppm in the feed for 3 consecutive days. Most of the administered dose was recovered in the faeces (68%), urine (7.3%) and gastrointestinal tract (19%). Radioactive residues were highest in kidney (0.93 mg/kg NAG equivalents) with lowest levels in fat and muscle (< 0.01 mg eq./kg). ^{14}C levels in milk were 0.023 mg/kg NAG equivalents by the third day of dosing. Major components of the ^{14}C residues were glufosinate (kidney 40% TRR, liver 33% TRR, milk 40% TRR), unchanged NAG

(kidney 32% TRR, liver 19% TRR, milk 9% TRR) and MPP (kidney 20% TRR, liver 21% TRR, milk 14% TRR). MPA was detected as a minor metabolite < 5% TRR.

Laying hens were orally treated twice daily for 14 consecutive days with [3,4-^{14}C]-glufosinate at a dose equivalent to 24.5 ppm in the feed and were sacrificed 15–16 hours after the last dose. The majority (92%) of the dose was eliminated in the excreta with 1.3% of the dose recovered from the GIT. Radioactivity in tissues ranged from 0.11 mg/kg glufosinate equivalents in kidney to 0.003 mg/kg glufosinate equivalents in fat and < 0.004 mg/kg glufosinate equivalents in muscle. The ^{14}C levels in egg whites and yolks reached 0.067 and 0.024 mg/kg glufosinate equivalents respectively by 14 days of dosing.

Unchanged glufosinate was the main residue component (liver 31% TRR, yolk 53% TRR, whites 78% TRR). MPP was a significant component of ^{14}C residues in liver (44% TRR) but a minor component in eggs (< 5%). MPA and NAG were also detected but at levels that represented < 5% TRR in liver and eggs.

The metabolism of NAG was studied in laying hens dosed orally twice daily for 14 consecutive days with [^{14}C]-NAG at a dose equivalent to 27 ppm in the feed and sacrificed 15 hours after the last dose. Most of the administered dose was recovered in the excreta (86%) with an additional portion (1%) found in the gastrointestinal tract at sacrifice. Radioactive residues in egg white reached a plateau by day 9 of dosing with a maximum level of 0.015 mg/kg NAG equivalents while egg yolk reached a plateau by day 12 with a maximum residue of 0.056 mg/kg NAG equivalents. In tissues at sacrifice, ^{14}C residues were highest in liver (0.076 mg/kg NAG equivalents) and much lower in muscle and fat (0.013 and 0.011 mg/kg NAG equivalents respectively).

NAG was a major component of the ^{14}C residues (liver 27% TRR, egg yolk 13% TRR, egg white 5% TRR) together with glufosinate (liver 15% TRR, egg yolk 3% TRR, egg white14% TRR) and MPP (liver 17% TRR, egg yolk 2.2% TRR, egg white 2% TRR). MPA was only detected as a minor metabolite and was present at < 1.1%TRR.

Metabolism in laboratory animals (rat) was summarized and evaluated by the WHO panel of the JMPR in the present meeting.

The metabolism of glufosinate and NAG in ruminants and laying hens is qualitatively the same as observed in rats.

Plant metabolism

Glufosinate-ammonium is used for three different situations:

- Directed sprays for weed control (crop not intentionally treated)
- Use as a crop desiccant to facilitate crop harvest (crop treated)
- Selective use in genetically modified glufosinate-tolerant crops (crop treated)

Plant metabolism studies were conducted with glufosinate-ammonium to investigate these three situations.

Directed sprays to weeds present in conventional crops

For weed control in conventional crops where the crop is not treated, metabolism studies were conducted in apple, grape, lettuce, corn/maize, wheat and potato as well as in artificial systems such as excised roots and leaves and cell cultures of a variety of weed and non-weed species.

The main metabolite observed in excised shots and leaves from conventional plants was MPP with lower amounts of MHB also detected.

When L-glufosinate was applied to conventional tobacco, alfalfa and carrot plants the main metabolites identified were MPP, MPB and MHB.

MPP was the only compound (89% TRR) detected in apples harvested 14 weeks after the soil under the trees was treated at 1.5 kg ai/ha with [2-^{14}C]-glufosinate-ammonium.

There was limited translocation of ^{14}C from soil-applied ^{14}C-glufosinate in a two year trial with grapevines where a single application was made in the first year and two in the second, all at 1.5 kg ai/ha. Levels of ^{14}C in grapes reached a maximum of 0.008 mg eq./kg and were too low to enable identification of components.

In a study where lettuce plants were transplanted in hydroponic solutions to which [3-^{14}C]-glufosinate-ammonium had been added, MPP represented about 90% of the TRR in leaves.

Following pre-crop emergent application of [3,4-^{14}C]-glufosinate-ammonium to potatoes at a rate equivalent to 1.0 kg ai/ha, 90% of the TRR in tubers at harvest was MPP while MPP represented > 80% TRR in leaves, stems and new sprouts.

In studies identifying residues in corn/maize following pre-crop emergent use of [3,4-^{14}C]-glufosinate-ammonium at 1.0 to 1.9 kg ai/ha, only low levels of ^{14}C were found in grain that precluded identification of components. Fodder had higher ^{14}C levels which were mostly MPP (60% TRR) with the remaining attributed to incorporation of ^{14}C into natural components (hemicellulose, lignin, cellulose, proteins and starch).

MPP was also the major component of the solvent extracted residue in wheat when [2-^{14}C]-glufosinate-ammonium is applied to soil at 1.2 kg ai/ha prior to crop emergence (straw 70%; husks 106%; grain 86%).

In summary, following directed application to soil and weeds, glufosinate related residues in conventional plants are almost entirely MPP.

Crop desiccation

The use as a pre-harvest desiccant was investigated in potato, rape and beans following foliar spray application to the crop. When applied to conventional crops for desiccation the residues consist primarily of glufosinate and its metabolite MPP. Since the plants are senescent at the time of application or die quickly after application, metabolism is essentially stopped and translocation from the treated parts of the crops into other plant parts such as seeds and roots is reduced. Following use as a crop desiccant, glufosinate was the major component of the ^{14}C residue in potato leaves and tubers, bean leaves, hulls and seeds and rape leaves, hulls and seeds accounting for more than 80% of TRR in combined surface rinses and solvent extracts. MPP was also detected but generally represented less than 10% of the TRR.

Glufosinate-tolerant crops

The use as a selective herbicide on tolerant plants was investigated following foliar application to glufosinate-tolerant crops such as corn/maize, rape, soya bean, rice, tomato and cotton.

The metabolic fate of [3,4-^{14}C]-glufosinate-ammonium in glufosinate tolerant tomato plants was examined following a single foliar application at 0.8 kg ai/ha at the 7–8 leaf growth stage. Extracts of rinsed leaves (absorbed ^{14}C) contained almost equal amounts of NAG and glufosinate and together accounted for > 90% TRR in the extracts. MPP was present as a minor component (< 10% TRR). Residues in fruit that developed after application were almost completely due to NAG.

The metabolic fate of [3,4-^{14}C]-glufosinate-ammonium in glufosinate-tolerant (*pat* gene) soya bean plants was examined in two studies where plants were sprayed with two applications at about 0.5 kg ai/ha. Soya bean plants were harvested at typical forage stage and at maturity (PHI 84–85 days). In soya forage the major components of the ^{14}C residues were NAG (26–60%) and glufosinate (18–23%) with MPP and MPA present at < 10% TRR. For straw, pods, husks and beans at harvest, NAG (28–63%), glufosinate (11–18%) and MPP (10–22%) were major components of ^{14}C with smaller amounts of MPA also observed (1.3–7.1%).

In a study of [3,4-^{14}C]-glufosinate-ammonium metabolism in glufosinate-tolerant sugar beet plants were sprayed twice, at 5 weeks after sowing and 22 days later, at 0.6 kg ai/ha. At harvest, 146 days after the last application, the major components of ^{14}C identified in leaves and roots were NAG (67–68%) and glufosinate (19–24%) with low levels of MPP (2.7–6%).

The metabolic fate of [^{14}C]-glufosinate-ammonium in tolerant (*pat* gene) corn/maize plants was examined following application at 0.5 kg ai/ha when plants were 40 cm high and 10 days later when 60 cm high. ^{14}C residues in forage at 28 days after treatment were 2.6 mg/kg glufosinate equivalents with major components NAG (52%), glufosinate (13%) and MPP (12%). Maize fodder at harvest contained 0.2 mg eq./kg comprising NAG (54%), MPP (11%) and glufosinate (10%) as the main ^{14}C residue components. In grain at harvest, ^{14}C residues were 0.13 mg/kg glufosinate equivalents comprising MPP (37%), NAG (19%), MPB (9.8%) and MPA (4.4%) with glufosinate present but only at very low levels (< 1.5%). In a comparison of crops made tolerant through incorporation of the *pat* or *bar* genes the same metabolite profile was observed for both modifications.

The metabolic fate of [^{14}C]-glufosinate-ammonium in tolerant rice plants was examined following application at 0.5 kg ai/ha when plants were at the 2–4 leaf stage and then at the 2–4 tiller stage. Plants were managed under two flooding regimes, the first was with flooding 2 days prior to the first treatment and the second regime was flooding one day after the second treatment. There were no significant differences in metabolite profiles between the two management regimes. ^{14}C residues in forage at 18 days after the last treatment were 2.0–2.6 mg/kg glufosinate equivalents with major components NAG (54–64%), glufosinate (8.1%) and MPP (7.8–9%). Straw at harvest (184 days after the last application) contained 9.5–13.1 mg eq./kg comprising NAG (60%), MPP (10–13%) and glufosinate (18%) as the main components. In grain at harvest ^{14}C residues were 1.1–1.4 mg/kg glufosinate equivalents comprising MPP (68–72%), NAG (11%), MPB (9.8%) and glufosinate (5–6%) with MPA also present but only at very low levels (0.6–0.8%).

In an additional study tolerant (*bar* gene) and conventional cotton were treated at the 10 leaf stage with a commercial formulation of glufosinate-ammonium at 0.5 kg ai/ha, and selected individual leaves spotted with a solution of ^{14}C-glufosinate-ammonium. Tolerant cotton showed high levels of metabolism with NAG accounting for 72% TRR at 72 hours after application while in conventional cotton glufosinate accounted for 73% TRR at 72 hours.

The metabolic fate of [^{14}C]-glufosinate-ammonium in tolerant rape plants was examined in several studies. Following application to tolerant rape at the three leaf growth stage at 0.75 kg ai/ha, ^{14}C residues in foliage at 21 days were 4.3 mg/kg glufosinate equivalents with major components NAG (60%), glufosinate (21%) and MPP (6.7%). In seeds at harvest (120 days after application) ^{14}C residues were 0.04–0.11 mg/kg glufosinate equivalents comprising glufosinate (0–14%) and MPP (3-45%) with NAG present but only at very low levels (< 2%). Following two applications at 0.8 kg ai/ha to tolerant (*pat* gene) rape at the 5–6 leaf growth stage and when plants were 50 cm high, residues in forage 154 days after the first application were 0.2 mg eq./kg and with major components NAG (71%) and glufosinate (7.9%). At harvest 102 days after the last application, ^{14}C residues in straw and hulls were 12.7 and 7.1 mg eq./kg respectively with major components NAG (57–77%) and glufosinate (21–31%). Lower levels of ^{14}C were detected in seed (0.5 mg eq./kg) with NAG (32%) the major component and glufosinate (6.2%) and MPP (9.7%) minor components together with trace amounts of MPA and MPB. In a comparison of crops made tolerant through incorporation of the *pat* or *bar* genes, the same metabolite profile was observed in shoots sampled 14 and 28 days after treatment for both modifications.

The pathway of glufosinate-ammonium in tolerant plants genetically modified to contain the *pat* or *bar* genes is rapid deactivation of L-glufosinate through N-acetylation to form NAG. D-glufosinate is not acetylated but rather undergoes slow metabolism to form MPP, MPB and MPA.

The metabolism of glufosinate-ammonium by plants is well understood for the three different situations. The metabolism of glufosinate-ammonium in conventional (glufosinate-susceptible) crops following directed application to weeds or as a pre-harvest desiccation use is in principle identical for the five standard crop groups: fruit crops, cereal/grass crops, leafy crops, root crops and pulses and oilseeds. For these crop groups major residue components consist of parent glufosinate and the metabolite MPP. In case of glufosinate-tolerant crops, NAG, MPP and glufosinate are the major components of the residue.

Environmental fate

The Meeting received information on soil aerobic metabolism, soil photolysis and aqueous hydrolysis properties of [^{14}C]-glufosinate-ammonium. Studies were also received on the behaviour of [^{14}C]-glufosinate-ammonium in a rotational crop situation.

Glufosinate-ammonium residues are not persistent in soils and residues in soils resulting from approved uses should not contribute significantly to the residues in succeeding crops.

In soil incubation studies under aerobic conditions in the dark at 20 °C, glufosinate disappeared with a half-life of 1–25 days. Glufosinate was not significantly metabolized in sterile soil demonstrating the importance of microbial metabolism in its soil degradation. Under aerobic soil incubation, the first metabolite formed was MPP followed by MPA, which mostly disappeared with half-lives in the range of 13–22 days (n=4) and 18 days (n=1) respectively. After 120 days, 17–81% of the applied dose was mineralised with 20–38% remaining unextracted with the solvents used. Further analysis of the unextracted portion of ^{14}C demonstrated incorporation into humin, fulvic acid and humic acid fractions present in the soil.

In a soil photolysis study with application of ^{14}C-glufosinate-ammonium on the surface of a sterilised sandy loam soil, glufosinate was stable to continuous irradiation for 120 hours suggesting photolysis has negligible effect on degradation when compared to metabolism.

Glufosinate-ammonium was also stable to hydrolysis in aqueous solutions at pH 5, 7 and 9 suggesting hydrolysis plays a negligible role in the degradation of glufosinate when compared to metabolism.

In a confined rotational crop study with wheat, lettuce and radish, a plot of sandy loam soil was treated with [^{14}C]-glufosinate-ammonium at the equivalent of 1.0 kg ai/ha and crops sown 28, 119 and 300/364 days. The proportion of ^{14}C residue attributed to glufosinate-related compounds decreased with increasing plant-back interval (PBI). In wheat straw and grain sown at a PBI of 119 days, MPP represented 22% TRR in straw and 12% in grain while MPA represented 6% TRR in straw and 0.3% in grain. Natural products accounted for the remaining TRR.

In summary, glufosinate residues in soil should contribute little to residue levels in rotational crops.

Methods of analysis

The Meeting received description and validation data for analytical methods for residue analysis of glufosinate and its metabolites MPP and NAG in various plant and animal commodities. Most of the analytical methods for the determination of glufosinate-derived residues developed prior to 2006 follow the same general principle. The relevant residues are usually extracted in water. Thereafter, the aqueous extract is concentrated to dryness and reacted with trimethyl orthoacetate in the presence of acetic acid. After silica gel purification the obtained derivatives are measured by GC/FPD or more recently by LC-MS/MS. LOQs are typically 0.01–0.05 mg/kg for glufosinate and MPP.

When reacted with trimethyl orthoacetate in the presence of acetic acid, glufosinate and NAG yield the same derivative. Therefore, glufosinate and NAG are usually determined together as a sum. However, if the two compounds are separated before derivatisation by means of cation exchange clean-up it is possible to determine the residues of glufosinate and NAG separately. In some methods glufosinate, NAG and MPP were measured separately with LOQs typically in the range 0.01 to 0.05 mg/kg.

With the availability of new liquid chromatography-columns specially designed for highly polar character and comparatively low molecular weight compounds such as glufosinate and its metabolites, it is possible to quantify glufosinate, MPP and NAG using LC/MS/MS without prior derivatisation (LOQs 0.01–0.02 mg/kg).

In another method, derivatisation of glufosinate was carried out with a mixture of o-phthalic dialdehyde and mercapto-propionic acid in the presence of sodium borate. The derivative of glufosinate is quantified by LC-MS/MS while the metabolites MPP and NAG are measured by LC-

MS/MS without prior derivatisation as in the previous approach (LOQs 0.01 mg/kg for each analyte for plant and animal matrices).

Multi-residue methods are currently not validated for glufosinate and its metabolites.

Stability of pesticide residues in stored analytical samples

The Meeting received information on the stability of glufosinate-ammonium and its metabolites MPP and NAG in samples of commodities from conventional crops stored frozen. NAG is not expected to be present in commodities from conventional crops.

Glufosinate, NAG and MPP are stable for at least 24 months in peaches when stored frozen. Glufosinate and MPP (NAG not studied) residues are stable for at least 6 months in kiwifruit, 12 months in almond, 20 months in blueberries, 24 months in apple, orange, maize grain and soya bean seeds from conventional crops stored frozen.

Glufosinate, NAG and MPP residues are stable for at least 24 months in tolerant sugar beet roots and tops and for at least 9 months in sugar beet processed fractions, for at least 24 months in soya bean seed and hay and at least 12 months for soya bean processed fractions, at least 23 months for rape seed, at least 24 months in maize forage and grain and at least 12 months in maize processed fractions, at least 26 months for sweet corn forage, at least 30 months for sweet corn ears, and at least 12 months for rice grain.

In animal commodities, glufosinate-ammonium, NAG and MPP were stable for at least 14 months in cow milk, muscle, liver and kidney. Glufosinate, NAG and MPP were stable for at least 15 months in hen eggs, muscle and liver.

The periods of demonstrated stability cover the frozen storage intervals used in the residue studies.

Definition of the residue

Livestock may be exposed to residues present in feeds prepared from conventional and glufosinate-tolerant crops. Residues in conventional crops are principally glufosinate and MPP while in tolerant crops they are glufosinate and NAG. Metabolism of glufosinate in goats and hens involves formation of MPP and the slow transformation to MPA. NAG is metabolized by de-acetylation to form glufosinate with subsequent metabolism proceeding as for glufosinate. The major components of the residue in livestock are glufosinate, MPP and NAG and should be included in the residue definition for compliance with MRLs and estimation of dietary intake in animal commodities.

In the metabolism studies, residues in muscle and fat were too low to identify the proportions of the individual components required to determine relative partitioning between fat and muscle. In the metabolism study for NAG in lactating goats, radioactive residues in whole milk were 0.005–0.023 mg eq./kg, skim milk 0.007–0.023 mg eq./kg and cream 0.022–0.046 mg eq./kg with the profile of components similar in all three products. The data for milk suggest NAG partitions slightly more into the fat than aqueous portions of milk. In eggs, the concentration of glufosinate was greater in whites when compared to yolks while for NAG the opposite occurred. In the lactating cow feeding study with glufosinate and MPP, higher concentrations of glufosinate and MPP were found in fat compared to muscle. The combined residues of glufosinate (glufosinate +MPP+NAG) are borderline fat-soluble. The Meeting decided that residues of glufosinate are not fat-soluble.

Glufosinate ammonium is used on crops for three different situations:

- Directed sprays for weed control (crop not intentionally treated)
- Use as a crop desiccant to facilitate crop harvest (crop treated)
- Selective use in genetically modified glufosinate-tolerant crops (crop treated)

The main metabolite observed in studies with conventional crops (directed sprays for weed control, pre-emergent or pre-sowing applications) is MPP representing greater than 80% of the ^{14}C residue not attributed to natural products in apples, grapes, potatoes, wheat and corn fodder. However,

the residue levels are generally low, less than 0.1 mg/kg, with only occasional higher residues detected.

Following use as a crop desiccant, glufosinate was the major component of the residue in potato leaves and tubers, bean leaves, hulls and seeds and rape leaves, hulls and seeds accounting for more than 80% of TRR. MPP was also detected but generally represented less than 10% of the TRR.

In the case of foliar applications to glufosinate-tolerant crops, glufosinate, NAG and MPP are the major residue components. NAG accounted for 19–77% TRR in soya, maize, rape, rice and sugar beet foliage (forage, fodder, straw), 68% TRR in sugar beet roots, 11–63% TRR in grain and husks (soya, maize, rice, rapeseed). Glufosinate accounted for 8–31% TRR in soya, maize, rape, rice and sugar beet foliage (forage, fodder, straw), 19–24% TRR in sugar beet roots, < 2–18% TRR in grain and husks (soya, maize, rice, rapeseed). MPP generally represented no more than 12% TRR in foliage but was a significant component of the residue in grains at 3–72% TRR.

In plants, the majority of glufosinate-related residues in conventional and tolerant crops are accounted for in the previous residue definition; the sum of glufosinate, MPP and NAG. Although NAG is not a significant residue in conventional crops, some analytical methods do not distinguish between residues of glufosinate and NAG and so NAG should be included in the residue definition for compliance for conventional and tolerant crops.

The toxicological evaluation of glufosinate-ammonium concluded that the ADI and ARfD apply to glufosinate, NAG, MPP and MPA. MPA is a minor component of the residue and does not contribute significantly to dietary intake. The Meeting decided it was not necessary to include MPA in the residue definition for estimation of dietary intake.

Based on the above the Meeting confirmed the previous residue definition for compliance with MRLs and estimation of dietary intake as follows:

Definition of the residue for compliance with MRL and estimation of dietary intake (for animal and plant commodities): *sum of glufosinate, 3-[hydroxy(methyl)phosphinoyl]propionic acid (MPP) and N-acetyl-glufosinate (NAG), calculated as glufosinate (free acid).*

The residue is not fat-soluble.

Results of supervised residue trials on crops

The Meeting received supervised residue trial data for glufosinate-ammonium on citrus fruit, pome fruit, stone fruit, small fruit and berries including grapes, tropical fruit (inedible and edible peel), bulb onions, glufosinate-tolerant sweet corn, leafy vegetables, legume vegetables, pulses including glufosinate tolerant soy beans, carrots, potatoes, glufosinate tolerant sugar beet, asparagus, glufosinate tolerant maize, glufosinate tolerant rice, tree nuts, glufosinate tolerant cotton, conventional rape, glufosinate tolerant rape, sunflower and coffee as well as for some animal feed commodities.

Residues reported in supervised trials consist of glufosinate and NAG, often reported as the sum, and MPP. In metabolism studies, one of the three components comprises the majority of the combined total when all three are present. It is reasonable to assume when all three components are below the LOQ, the combined total is also below or close to the LOQ. Also when one component is above and the others below the LOQ, the combined residue is assumed to be equal to the residue of the main component. This is illustrated below.

Glufosinate	MPP	NAG	Total residues (glufosinate+MPP+NAG)
< 0.05	< 0.05	< 0.05	< 0.05 or where LOQs differ, the highest LOQ
< 0.05	< 0.05	0.06	0.06
0.05	< 0.05	0.09	0.14
< 0.05	0.06	< 0.05	0.06

The OECD calculator was used as a tool in the estimation of the maximum residue level from the selected residue data set obtained from trials conducted according to GAP. As a first step, the Meeting reviewed all relevant factors related to each data set in arriving at a best estimate of the

maximum residue level using expert judgement. Then, the OECD calculator was employed. If the statistical calculation spreadsheet suggested a different value from that recommended by the JMPR, a brief explanation of the deviation was provided.

Some use patterns for field crops include the possibility of pre-planting or pre-emergent applications together with post-emergent applications. Often the supervised trials for these field crops did not include pre-emergent application. However, as metabolism and rotational crop studies suggest the contribution from pre-emergent applications are negligible in comparison to the contribution from post-emergent applications, the lack of a pre-emergent application should not affect the decision as to whether the trials approximate critical GAP.

As no data were available for almond hulls, broad bean (dry) and peas (dry) the previous recommendations for these commodities are withdrawn.

Citrus (application to weeds)

Field trials involving citrus orchards where glufosinate-ammonium was applied to weeds were conducted in Brazil, Europe and the USA and were available to the Meeting.

The GAP for citrus in Brazil is application directed to weeds at 0.4 kg ai/ha with a PHI of 40 days. In the trials matching this GAP total glufosinate residues (glufosinate + NAG + MPP) in ranked order were (n=2): < 0.04 (2) mg/kg.

In Portugal, glufosinate ammonium is applied to weeds in citrus orchards at up to 1.5 kg ai/ha with a 0 day PHI. None of the trials from Europe matched the GAP of Portugal and an approved use on citrus in the USA was not available.

As the use pattern is application to weeds and not the crop, trials from different regions of the world can be used to support maximum residue level recommendations based on GAP from another region. The Meeting noted that total residues were < 0.05 (21) mg/kg in the trials on citrus (oranges, mandarin, grapefruit and lemons) conducted in the USA that utilized rates higher than permitted in Portugal (3×1.7 kg ai/ha USA versus 1–2 × 0.4–1.5 kg ai/ha in Portugal). Additionally, no residues were detected in trials in Europe that were conducted at rates lower than the maximum Portugal rate (2 sprays the last at 0.75 to 1.0 kg ai/ha). One trial from Brazil conducted at a much lower rate (0.4 kg ai/ha) reported very high residues at 10, 20 and 30 days after application with glufosinate the major component of the residue in fruit suggesting application to the fruit. This trial was not used in maximum residue estimation. The Meeting concluded that residues above LOQ are not expected in citrus fruit following application of glufosinate-ammonium to weeds growing in orchards.

The Meeting estimated a maximum residue level of 0.05 mg/kg for citrus fruit to replace its previous recommendation of 0.1 mg/kg. The Meeting estimated an STMR of 0.05 mg/kg and an HR of 0.05 mg/kg for citrus fruit.

Pome fruits (application to weeds)

Field trials involving apples and pears conducted in Brazil, Europe and the USA were made available to the Meeting.

Apples

The GAP for apples in Brazil is application directed to weeds at 0.4 kg ai/ha with a PHI of 7 days. In the trials matching this GAP the total glufosinate residues were (n=4): < 0.04 (4) mg/kg.

In Germany, glufosinate-ammonium is applied to weeds in apple orchards as two applications at up to 1.5 (spring) + 1 (spring/summer) kg ai/ha with a 14 day PHI. No residues (total glufosinate) were observed in 10 trials from Europe that approximated maximum GAP for Germany (n=10): < 0.05 (8) and < 0.06 (2) mg/kg.

GAP in the USA is application to weeds at a maximum rate of 1.7 kg ai/ha with a maximum annual rate of 5 kg ai/ha/year. The PHI is 14 days. No residues (total glufosinate) were detected (< 0.05 mg/kg) in 10 trials where application rates ranged from 1 × 1.1 kg ai/ha to 3 × 4.5 kg ai/ha.

The Meeting decided that residues of glufosinate are not expected in apples following directed application to orchard weeds.

Pears

Trials on pears with application to weeds were conducted in the USA but use of glufosinate-ammonium in pear orchards is not listed on USA labels. The use pattern in Germany allows glufosinate-ammonium to be applied to weeds in pear orchards as two applications at up to 1.5 (spring) + 1 (spring/summer) kg ai/ha with a 14 day PHI. Trials in the USA were assessed against the GAP of Germany. Total residues in six trials that approximated maximum GAP for Germany (n=6) were: < 0.05 (5) and 0.08 mg/kg.

In 25 of 26 trials on apples and pears that approximated the GAP of Germany or the USA, total residues were < LOQ. The residue value of 0.08 mg/kg in pear was due to MPP, likely taken up from soil. In the apple metabolism study where the soil beneath a tree was treated at 1.5 kg ai/ha, total residues in fruit were 0.1 mg/kg at harvest, fourteen weeks after the soil treatment. Occasional residues due to uptake of the soil degradation product MPP are expected, as are occasional residues of glufosinate due to spray directed to weeds inadvertently contacting fruit. As location of the trials should not be an important factor in the residues, the Meeting decided to combine the results for apples and pears and estimated a maximum residue level of 0.1 mg/kg for glufosinate residues in pome fruit replacing its previous recommendation of 0.05* mg/kg.

The STMR and HR for pome fruit are 0.05 and 0.08 mg/kg respectively.

Stone fruit (application to weeds)

Field trials involving application to weeds under apricot, cherry, peach, plum and nectarine trees were made available from Brazil, Europe and the USA.

In Brazil, weeds under peach and nectarine trees may be treated at 0.4 kg ai/ha with a PHI of 7 days. In the Netherlands weeds in fruit tree orchards may be sprayed at up to 1 kg ai/ha, no PHI required. In Canada weeds in peach and plum orchards may be sprayed at up to 0.75 kg ai/ha, maximum 1 kg ai/ha/year with a PHI of 40 days. In Portugal and Germany (except peach), weeds under stone fruit trees may be sprayed at up to 1.5 kg ai/ha with PHIs of not required for Portugal and 14 days for Germany. Use on stone fruit in the UK as at rates up to 0.75 kg ai/ha with no PHI required.

The location of the trial sites should not be a significant influence on residues in fruit when glufosinate-ammonium is applied to weeds. In a large number of trials from various locations total residues above the LOQ were infrequent. Occasional residues due to uptake of the soil degradation product MPP might be expected as are occasional residues of glufosinate due to spray directed to weeds inadvertently contacting fruit. Total residues in fruit from trials carried out with application rates ranging from 1 × 0.4 to 2 × 1.7 kg ai/ha were (n=42): apricot < 0.02, 0.05; cherry 0.02, < 0.05 (7); peach and nectarine < 0.02 (2), < 0.05 (19), 0.08; plum < 0.01 (5), 0.01 (3), < 0.05 (4), 0.06 and 0.07 mg/kg.

The Meeting estimated a maximum residue level of 0.15 mg/kg for stone fruit to replace its previous recommendation of 0.05* mg/kg. The Meeting estimated an STMR of 0.05 mg/kg and an HR 0.08 mg/kg.

Berries and other small fruit (application to weeds)

Currants

Glufosinate-ammonium is approved for application using spray shields to weeds between currant bushes in the Netherlands (1 kg ai/ha, no PHI required), the UK (soft fruit 0.75 kg ai/ha, no PHI required) and the USA (1.7 kg ai/ha, maximum 3.4 kg ai/ha/year, PHI 14 days). In twelve trials conducted in France, Germany and the UK where glufosinate-ammonium was applied as two sprays at 1 kg ai/ha, as two sprays with one at 1.6 kg ai/ha and the other at 1 kg ai/ha or as three sprays at

0.75 kg ai/ha, total residues in currants at PHIs of 0 to 28 days were (n=11): < 0.01_s (3), 0.01_s, < 0.02, $\underline{0.02}_s$, 0.05, 0.08_s, 0.12, 0.43_s and 0.48 mg/kg. Trials indicated with an "s" utilized a spray shield to reduce crop contamination. The major component of the samples with total residues 0.43 and 0.48 mg/kg were glufosinate and MPP respectively. Residues in currants appear to be from both uptake of MPP from soil and inadvertent contamination when spraying weeds. A trial with a total residue of 2.4 mg/kg was not used as the level was much higher than observed in the other trials with the residue due almost entirely to glufosinate. The magnitude of the residue was considered too high to represent good practice in application of glufosinate.

The Meeting estimated a maximum residue level of 1 mg/kg for currants to replace its previous recommendation of 0.5 mg/kg.

The Meeting estimated an STMR of 0.02 mg/kg and an HR of 0.48 mg/kg for currants.

Grapes

Trials were available from Brazil, Europe and the USA. The use pattern in Argentina is application to weeds at up to 1.6 kg ai/ha, no PHI required while Brazil allows application to weeds at 0.4 kg ai/ha with a PHI of 7 days. In Australia application to weeds is at up to 1 kg ai/ha no PHI required. Germany allows an application to weeds at 1.5 kg ai/ha in spring and one in summer at 1 kg ai/ha with a 14 day PHI. In the USA application to weeds is at up to 1.4 kg ai/ha with a maximum of 5 kg ai/ha/year and a PHI of 14 days. Residue data were available from 30 different trial locations with data presented for berries in accordance with the Codex Classification or for bunches. Where both berries and bunches were analysed only values for berries were considered.

In trials from Brazil matching GAP of that country total residues were: < 0.04 (3) mg/kg.

In trials from Europe approximating the GAP of Germany total residues were (n=14): < 0.01 (3), < 0.02 (3) $\underline{0.02}$ (2), < 0.05 (4), 0.06 and 0.12 mg/kg.

Total residues in grapes from US trials that approximated the GAP of the USA were (n=5): < 0.05 (5) mg/kg.

The Meeting considered the number of trials available from Brazil and the USA too few and utilized the trials from Europe approximating German GAP to estimate a maximum residue level of 0.15 mg/kg for grapes. The Meeting estimated an STMR of 0.02 mg/kg and an HR of 0.12 mg/kg for grapes.

Strawberries

Trials were available from Finland, France and Germany. GAP in strawberry in Australia is application to weeds at 1 kg ai/ha with no PHI required, Germany as a single shielded application to weeds at 0.8 kg ai/ha (pre-flowering of strawberry plants) with a 42 day PHI and UK one to two applications to weeds at up to 0.75 kg ai/ha with no PHI required.

Total residues in three trials approximating German GAP (but not using spray shields) were: < 0.05 (3) mg/kg.

Total residues in 8 trials approximating UK GAP, conducted as one to four sprays at 0.75 kg ai/ha with harvest 4 days after last application, were (n=8): < 0.01_s, < 0.01_s, 0.02_s, $\underline{0.02, 0.02}$, 0.03, 0.06 and 0.15 mg/kg. Trials indicated with an "s" utilized a spray shield to reduce crop contamination. Although the number of applications was greater than recommended, earlier applications should not contribute significantly to residues as the interval between sprays was 21–101 days compared to a typical interval between flowering and harvest of about 28 days.

The Meeting utilized trials approximating UK GAP to estimate a maximum residue level of 0.3 mg/kg for strawberries. The Meeting estimated an STMR of 0.02 mg/kg and an HR of 0.15 mg/kg for strawberries.

Blueberries

In trials conducted in the USA according to US GAP (application to weeds at 1.7 kg ai/ha, maximum 3.4 kg ai/ha/year, PHI 14 days) total residues in blueberries were (n=5): < 0.05 (4) and 0.06 mg/kg. The individual component responsible for the highest residue was glufosinate, possibly reflecting inadvertent exposure to spray during application. An additional trial with residues < 0.05 mg/kg had residues in control samples of 0.07 mg/kg and was therefore not considered. Inadvertent contamination of blueberries with glufosinate may occur when spraying weeds between bushes. The Meeting estimated a maximum residue level of 0.1 mg/kg, an STMR of 0.05 mg/kg and an HR of 0.06 mg/kg for blueberries.

Gooseberries

GAP in Germany is application using spray shields to weeds between bushes at 1×1 kg ai/ha, PHI 14 days, in the UK (soft fruit) application to weeds at 0.75 kg ai/ha with no PHI required and in the USA application to weeds at1.7 kg ai/ha with a maximum of 3.4 kg ai/ha/year and a PHI of 14 days). In three trials from Germany where weeds were sprayed at 2 × 1.5 kg ai/ha and approximating the GAP of the USA total residues were (n=3): < 0.02 (3) mg/kg.

Inadvertent contamination of gooseberries with glufosinate may occur when spraying weeds between bushes. The Meeting estimated an STMR of 0.02 mg/kg, an HR of 0.02 mg/kg and a maximum residue level of 0.1 mg/kg for gooseberries.

Raspberries

Trials were conducted on raspberry bushes in France, Germany and Italy. GAP in Australia is application to weeds at up to 1 kg ai/ha with no PHI required; Canada application to weeds at 1 kg ai/ha with no PHI required; Germany application using spray shields to weeds at 1 kg ai/ha with a PHI of 14 days; in the Netherlands application using spray shields to weeds at 1 kg ai/ha with no PHI required; and in the UK (soft fruit) application to weeds at 0.75 kg ai/ha with no PHI required. Total residues, after application at 3 × 0.75 kg ai/ha approximating the GAP of the UK were: < 0.01, 0.03 and 0.03 mg/kg. A spray shield was used in these trials to minimise crop contamination.

Inadvertent contamination of raspberries with glufosinate may occur when spraying weeds between raspberry plants. The Meeting estimated an STMR of 0.03 mg/kg, an HR of 0.03 mg/kg and a maximum residue level of 0.1 mg/kg for raspberries.

The Meeting agreed to withdraw its previous recommendation for berries and other small fruits (except currants) of 0.1 mg/kg.

Assorted tropical and sub-tropical fruit, edible peel (application to weeds)

Carambola

In Malaysia, weeds under carambola trees may be sprayed at 0.5 kg ai/ha, PHI 14 days. In two trials approximating GAP of Malaysia total residues were: < 0.05 (2) mg/kg.

Olives

Trials on olives were available from Europe and the USA. GAP in Portugal and Spain is application to weeds at up to 1.5 kg ai/ha, no PHI required in Portugal and 21 days in Spain while in Australia application to weeds of up to 1 kg ai/ha is permitted with no PHI required. In four trials from Europe where weeds in orchards were sprayed with two applications, the first at 1.1 and the second at 0.75 kg ai/ha, total residues at a PHI of 0 days were < 0.01 (2), 0.01 and 0.03 mg/kg. In three trials from the USA where weeds were treated at 3 × 1.5 kg ai/ha, total residues were all < 0.05 mg/kg 14 days after the last application.

Following the use of glufosinate-ammonium as a directed spray to control weeds in orchards residues of glufosinate are generally not expected as glufosinate is not readily taken up by roots. Occasional residues of MPP, the main degradation product in soil, are expected as MPP is

translocated through the crop. Inadvertent contamination of fruit by small amounts of glufosinate spray may also occur. The Meeting agreed that recommendations for maximum residue levels for assorted tropical and sub-tropical fruit, edible peel should accommodate the occasional residues that occur by the routes discussed above and that a level of 0.1 mg/kg would be adequate to accommodate such residues.

The Meeting estimated an STMR of 0.05 mg/kg, an HR of 0.05 mg/kg and a maximum residue level of 0.1 mg/kg for assorted tropical and subtropical fruit, edible peel.

Assorted tropical and sub-tropical fruit, inedible peel (application to weeds)

Banana

Glufosinate-ammonium is permitted to be used for weed control in banana plantations in Australia (1 kg ai/ha, PHI 0 days), Brazil (0.4 kg ai/ha, PHI 10 days), Columbia (0.3 kg ai/ha, PHI 0 days), Malaysia (0.5 kg ai/ha, PHI 14 days), Mexico (0.56 kg ai/ha, PHI 0 days), Philippines (2 kg ai/ha, PHI 0 days), Portugal (1.5 kg ai/ha, PHI 0 days) and Taiwan (1 kg ai/ha PHI 0 days).

Residues do not show a decline typical for application to fruit or foliage of bananas but rather following application to weeds and soil residues often only develop in fruit following a significant interval between spraying weeds and harvest of bananas, presumably due to uptake of MPP or D-glufosinate from soil. The Meeting decided to use the highest residue observed at any interval after application to weeds. In addition in many of the trials multiple applications were made at relatively long intervals between sprays (23 to 137 days) with harvest between sprays. The conditions preceding each harvest are sufficiently different to be considered as independent trials. Total residues in trials from Central and South America and the Philippines where weeds were treated at 1 × 0.3 kg ai/ha to 5 × 2 kg ai/ha + 8 × 1.2 kg ai/ha were (highest of pulp or peel if whole fruit not measured) (n=86): 0.02, < 0.04 (2), 0.04, < 0.05 (56), 0.05 (3), < 0.06 (3), 0.06 (8), 0.07 (3), 0.08 (4), 0.09, 0.10, 0.11 (2) and 0.13 mg/kg.

In two trials from Brazil conducted at a much lower rate (0.4 kg ai/ha), residues at 0 days after a single application at 0.4 kg ai/ha were 0.49 and 0.53 mg/kg with residues also observed at 3 and 7 days after application. As the high residue levels and the observation that glufosinate was the major component of the residue in fruit suggest direct application to the banana plants the Meeting could not be sure the residues represent inadvertent contamination. These two trials were not used for maximum residue estimation.

Using the available data, the Meeting estimated an STMR of 0.05 mg/kg, an HR of 0.13 mg/kg and a maximum residue level of 0.2 mg/kg to for bananas to confirm its previous recommendation of 0.2 mg/kg. The Meeting noted that for banana the IESTI accounts for 110% of the ARfD. The residues arise from uptake of glufosinate related residues from the soil. No suitable alternative GAP was identified that would resolve the intake concern.

Kiwifruit

Trials were available from Italy and the USA. GAP in Australia is application to weeds at 1 kg ai/ha with no PHI required and in Japan 1.4 kg ai/ha with a PHI of 21 days. Weeds under “woody crops” in Spain may be treated at 0.45–1.5 kg ai/ha, no PHI required. Total residues in nine trials conducted approximating the GAP of Spain with applications ranging from two sprays at 1.4 and 1.0 kg ai/ha to three sprays at 2.0 kg ai/ha were: < 0.01 (2), < 0.05 (4), 0.07, 0.10 and 0.37 mg/kg.

Using GAP of Spain, the Meeting estimated an STMR of 0.05 mg/kg, an HR of 0.37 mg/kg and a maximum residue level of 0.6 mg/kg to for kiwifruit. The Meeting noted that for kiwifruit the IESTI accounts for 110% of the ARfD. No residue data were identified that complied with an alternative GAP that would resolve the intake concern.

Avocado

In two trials approximating GAP in Australia for application to weeds in avocado orchards (1 kg ai/ha, no PHI required) total residues were: < 0.06 (2) mg/kg.

Guava

In two trials approximating GAP in Malaysia for weed control in guava orchards (0.5 kg ai/ha, PHI 14 days) total residues were: < 0.05 (2) mg/kg.

Mango

In two trials approximating GAP in Australia for weed control in mango orchards (1 kg ai/ha, no PHI required) total residues were: < 0.05 (2) mg/kg.

Papaya

In one trial approximating GAP in Australia for weed control in papaya orchards (1 kg ai/ha, no PHI required) total residues were: < 0.06 mg/kg.

As noted earlier, following the use of glufosinate-ammonium as a directed spray to control weeds in orchards residues of glufosinate are generally not expected as glufosinate is not readily taken up by roots. Occasional residues of MPP, the main degradation product in soil, are expected as MPP is translocated through the crop. Inadvertent contamination of fruit by small amounts of glufosinate spray may also occur. The Meeting agreed that recommendations for maximum residue levels for assorted tropical and sub-tropical fruit, inedible peel should accommodate the occasional residues that occur by the routes discussed above and that a level of 0.1 mg/kg would be adequate to accommodate such residues for fruit other than banana and kiwifruit.

The Meeting estimated an STMR of 0.05 mg/kg, an HR of 0.05 mg/kg and a maximum residue level of 0.1 mg/kg for assorted tropical and subtropical fruit, inedible peel (except banana and kiwifruit).

The Meeting agreed to withdraw its previous recommendation for assorted tropical and sub-tropical fruits-inedible peel (except banana) of 0.05* mg/kg.

Onion, bulb (pre-crop emergence or pre-sowing)

Use on glufosinate-ammonium on onions for control of weeds when applied pre-emergent or pre-sowing of onions is permitted in Canada (GAP 0.75 kg ai/ha, no PHI required). In twenty trials approximating Canada GAP total residues were: < 0.01 (6) and < 0.05 (14) mg/kg. The Meeting estimated an STMR of 0.05 mg/kg, an HR of 0.05 mg/kg and a maximum residue level of 0.05 mg/kg for bulb onions to confirm its previous recommendation of 0.05 mg/kg.

Sweet corn (tolerant)

Residue trials from the USA were received for use on glufosinate tolerant sweet corn however there is no associated GAP in the USA.

Corn salad (pre-crop emergence)

In Germany glufosinate-ammonium is approved for control of weeds in corn salad (lambs lettuce) when applied prior to emergence of the crop. The application rate is 0.6 kg ai/ha with no PHI required. Four trials were available from Germany on corn salad that matched GAP with total residues < 0.05 (4) mg/kg. The Meeting estimated an STMR of 0.05 mg/kg, an HR of 0.05 mg/kg and a maximum residue level of 0.05 mg/kg for corn salad to replace its previous recommendation of 0.05* mg/kg.

Lettuce (application to weeds)

Residue trials were available from Brazil and various countries from Europe following one directed spray to weeds or one spray pre-planting or a combination of the two. GAP was available for Brazil (directed application to weeds at 0.4 kg ai/ha, PHI 7 days, protect plants with plastic cups), Canada (pre-crop emergence, pre-crop sowing application to weeds at 0.75 kg ai/ha, no PHI required), Japan (directed application to weeds at 0.7 kg ai/ha, PHI 60 days) and Portugal (application to weeds pre-sowing/pre-emergence/pre-planting at 0.75 kg ai/ha, no PHI required). The Meeting decided to combine the dataset to recommend a maximum residue level for lettuce (leaf and head).

Total residues in trials approximating GAP of Brazil (0.4 kg ai/ha, PHI 7 days) were: < 0.04 (4) mg/kg.

Total residues from Europe approximating GAP of Portugal and following a single application to weeds at 0.75 kg ai/ha prior to planting the crop were: < 0.05 (7), 0.10 and 0.29 mg/kg.

The Meeting used the data from Europe to estimate an STMR of 0.05 mg/kg, an HR of 0.29 mg/kg and a maximum residue level of 0.4 mg/kg for both leaf lettuce and head lettuce. The Meeting noted that for lettuce the IESTI accounts for 180% of the ARfD. No suitable alternative GAP was identified that would resolve the intake concern.

Legume vegetables

Common bean (pre-crop emergence or application to weeds)

Glufosinate-ammonium is permitted to be used as a spray directed to weeds (Portugal 0.75 kg ai/ha, no PHI required; Germany 1 kg ai/ha, using a screen to protect the crop PHI 14 days; France 0.75 kg ai/ha no PHI required) and also as a spray to control weeds prior to crop emergence (the Netherlands 0.6 kg ai/ha, no PHI required).

Total residues in beans harvested immature (pods and/or immature seeds) from trials that did not use a screen to protect the crop from accidental contamination but otherwise complied with German GAP (1.0 kg ai/ha) were (n=7): < 0.05 (7) mg/kg. If a protective screen were used during application of glufosinate-ammonium, lower total residues would be expected.

The Meeting estimated an STMR of 0.05 mg/kg, an HR of 0.05 mg/kg and a maximum residue level of 0.05* mg/kg for common bean (pods and/or immature seeds) confirming its previous recommendation of 0.05 * mg/kg.

Pulses

Common beans (dry) (pre-harvest desiccation)

Residue data from trials in beans were made available from Brazil for pre-harvest desiccation use. The use pattern in Brazil is 0.4 kg ai/ha with a PHI of 5 days. The UK use is for pre-harvest desiccation at 0.45 kg ai/ha with a 7 day PHI.

In seven trials conducted in Brazil approximating Brazil GAP total residues were < 0.04 (4) and < 0.05 (3) mg/kg.

Common beans (dry) (directed application to weeds)

Directed sprays in the Portugal are permitted at up to 0.75 kg ai/ha with no PHI required and in Germany at up to 1 kg ai/ha using spray shields with a 14 day PHI. In eight trials conducted in Germany, total residues following a directed application at 1 kg ai/ha and after a 14 day PHI were: < 0.05 (8). In eight trials in Europe, total residues following two directed sprays at 0.75 kg ai/ha residues were: < 0.01 (8) at 62 to 122 days after the last application.

Rotational crop metabolism studies gave detectable residues suggesting the STMR should not be zero.

Residues were less than the limit of quantification following both pre-harvest desiccation and directed sprays to weeds. Utilising the dataset from Brazil, the Meeting estimated an STMR of 0.04 mg/kg and a maximum residue level of 0.05 mg/kg for common beans, dry to replace its previous recommendation of 2 mg/kg.

Soya beans, tolerant

The Meeting received field trials performed in the USA involving glufosinate tolerant soya beans. GAP for USA is for (1) one application pre-planting or pre-emergence at 0.59–0.74 kg ai/ha with additional applications from post-emergence to the early bloom growth stage at 0.45–0.59 kg ai/ha with a maximum seasonal rate of 1.3 kg ai/ha/year or (2) post-emergence only with applications from post-emergence to the early bloom growth stage at 0.41–0.50 kg ai/ha with a maximum seasonal rate of 0.91 kg ai/ha/year. The PHI is 70 days. Post-emergent application leads to higher residues. In trials approximating critical GAP in the USA total residues in soya bean seeds were (n=24): 0.22, 0.32, 0.39, 0.43, 0.51, 0.51, 0.56, 0.68, 0.70, 0.71, 0.78, 0.81, 0.84, 0.89, 0.96, 1.0, 1.1, 1.2, 1.2, 1.3, 1.3, 1.6, 1.7 and 1.9 mg/kg.

The Meeting estimated an STMR of 0.825 mg/kg and a maximum residue level of 3 mg/kg for soya bean, dry to replace its previous recommendation of 2 mg/kg.

Carrots (pre-crop emergence)

In Canada glufosinate-ammonium is approved for pre-emergent weed control in carrot crops (GAP: 0.41–0.75 kg ai/ha, PHI not required). The Netherlands permits the pre-crop emergence use of glufosinate-ammonium for weed control at a rate of 0.6 kg ai/ha and France allows bare soil cultivation at 0.75 kg ai/ha. In seventeen trials conducted in Europe with pre-crop emergence application at 0.6–0.75 kg ai/ha residues were: < 0.05 (17) mg/kg. Confined rotation crop studies suggest the residue is not zero.

The Meeting estimated an STMR of 0.05 mg/kg, an HR of 0.05 mg/kg and a maximum residue level of 0.05* mg/kg for carrots to confirm its previous recommendation of 0.05* mg/kg.

Potato (pre-harvest desiccation)

Glufosinate-ammonium is approved for pre-crop emergence or pre-harvest desiccation of potato crops in various countries. Use of glufosinate-ammonium prior to crop emergence does not lead to significant residues compared to use for pre-harvest desiccation. The Meeting agreed to use trials involving pre-harvest desiccation, with or without an application prior to crop emergence, to estimate a maximum residue level. Pre-harvest desiccation use-patterns approved in various countries include Brazil (GAP 0.4 kg ai/ha, PHI 10 days), France (GAP 2 × 0.38 kg ai/ha, PHI 14 days), Germany (GAP: 0.5 kg ai/ha at BBCH 90, PHI 14 days), Mexico (GAP 0.6 kg ai/ha), the Netherlands (GAP: 0.45 kg ai/ha or 0.38 kg ai/ha if crop is flailed), Portugal (GAP: 0.45 kg ai/ha, PHI 14 days), the UK (GAP:0.45 kg ai/ha, PHI 7 days) and the USA (GAP:0.42 kg ai/ha, PHI 9 days).

In trials conducted according to the GAP of Brazil total residues were: < 0.04 (4), < 0.05 (3) mg/kg.

In residue trials involving pre-harvest desiccation and approximating GAP of France total residues were: < 0.01, < 0.05 (6), 0.07, 0.08, 0.09, 0.11, 0.15, 0.16 (2) and 0.22 mg/kg.

In residue trials involving pre-harvest desiccation and approximating GAP of Germany total residues were: < 0.01 (3), 0.01, < 0.05, 0.06, 0.12, 0.21, 0.27 and 0.34 mg/kg.

In residue trials involving pre-harvest desiccation and approximating GAP of USA total residues were: < 0.05 (4), 0.06 (2), 0.1 (2), 0.11, 0.12 (2), 0.14, 0.16, 0.18, 0.24, 0.26, 0.28, 0.32, 0.38 and 0.62 mg/kg.

Using the residue data from the USA, the Meeting estimated an STMR of 0.12 mg/kg, an HR of 0.62 mg/kg and a maximum residue level of 0.8 mg/kg. The Meeting noted that for potatoes the IESTI accounts for 320% of the ARfD.

An alternative GAP was available from Brazil for pre-harvest desiccation at an application rate of 0.4 kg ai/ha with a PHI of 10 days. Total residues were < 0.04 (4), < 0.05 (3) mg/kg. The Meeting estimated a maximum residue level of 0.1 mg/kg for potatoes and noted in estimating STMR and HR values of 0.05 and 0.05 mg/kg respectively that occasional finite residues are expected.

Sugar beet, tolerant

In the USA glufosinate-ammonium is approved for use on glufosinate tolerant sugar beet. GAP for USA is for either (i) a pre-planting or pre-emergence application at 0.59–0.74 kg ai/ha or (ii) post-emergence application from post-emergence from the cotyledon stage up to the 10-leaf stage (BBCH 19) at 0.29–0.61 kg ai/ha with a maximum seasonal rate of 1.2 kg ai/ha/year and a PHI of 60 days. Post-emergent application leads to higher residues. In trials approximating critical GAP in the USA total residues in sugar beet roots were (n=13): 0.06, 0.11, 0.14, 0.20, 0.27, 0.27, 0.28, 0.31, 0.39, 0.42, 0.54, 0.62 and 0.67 mg/kg.

The Meeting estimated an STMR of 0.28 mg/kg and a maximum residue level of 1.5 mg/kg for sugar beet to replace its previous recommendation of 0.05 (*) mg/kg.

Asparagus (pre-crop emergence)

Trials were available following application pre-crop emergence for weed control in asparagus. In Canada pre-crop emergence application is permitted with an application rate of 0.4–0.75 kg ai/ha with a PHI not required while the Netherlands permits pre-emergence application to crops at 0.6 kg ai/ha with application no later than 3 days before crop emergence (PHI 3 days). GAP in Germany is application at prior to crop emergence at 0.6 kg ai/ha with no PHI required.

The trials were assessed against the GAP of Canada providing total residues of 0.01, < 0.05 (6), 0.16 and 0.27 mg/kg.

The Meeting estimated an STMR of 0.05 mg/kg, an HR of 0.27 mg/kg and a maximum residue level of 0.4 mg/kg for asparagus to replace its previous recommendation of 0.05* mg/kg.

Maize, tolerant

The Meeting received field trials performed in the USA involving glufosinate tolerant maize. GAP for USA is for (i) pre-planting or pre-emergence application at 0.59–0.74 kg ai/ha with a maximum seasonal rate of 0.74 kg ai/ha or (ii) post-emergence application from post-emergence until corn is 61 cm tall or in the V-7 growth stage (i.e., 7 developed collars) at 0.41–0.5 kg ai/ha with a maximum seasonal rate of 0.91 kg ai/ha/year and a PHI of 70 days. Post-emergent application leads to higher residues. In trials approximating critical GAP in the USA total residues in maize grain were (n=32): < 0.05 (27), 0.05, 0.06 and 0.07 (3) mg/kg.

The Meeting estimated an STMR of 0.05 mg/kg and a maximum residue level of 0.1 mg/kg for maize confirming its previous recommendation of 0.1 mg/kg.

Rice, tolerant

The Meeting received field trials performed in the USA involving glufosinate tolerant rice. GAP for USA is for (i) pre-planting or pre-emergence application at 0.59–0.74 kg ai/ha with a maximum seasonal rate of 0.74 kg ai/ha or (ii) applications post-emergence from the 1-leaf stage through the mid-tillering stage of crop development at 0.41–0.5 kg ai/ha with a maximum seasonal rate of 0.91 kg ai/ha/year and a PHI of 70 days. Post-emergent application leads to higher residues. The Meeting considered the growth stage at last application to be an important factor in considering whether or not trials were conducted according to critical GAP. In trials approximating critical GAP in the USA total residues in rice grain (with husk) were (n=20): < 0.05 (5), 0.05, 0.07, 0.07, 0.08, 0.08, 0.10, 0.10, 0.14, 0.15, 0.17, 0.20, 0.35, 0.47, 0.51 and 0.73 mg/kg.

The Meeting estimated an STMR of 0.09 mg/kg and a maximum residue level of 0.9 mg/kg for rice.

Tree nuts (application to weeds)

Application to tree nuts is for weed control in the orchard including under the tree canopy. The use pattern in the USA is application to weeds at 0.84–1.68 kg ai/ha with a maximum seasonal rate of 5.0 kg ai/ha and a PHI of 14 days. Application to tree nuts in Australia is at 0.2–1.0 kg ai/ha and in the UK at 0.45–0.75 kg ai/ha, both with a PHI not required. In trials approximating GAP, total residues in tree nuts were:

Almonds: < 0.05, < 0.05, < 0.05, 0.07 mg/kg (GAP of USA)

Hazelnut: < 0.05, < 0.05, < 0.05 mg/kg (two times GAP of UK)

Macadamia: < 0.06, < 0.12 mg/kg (GAP of Australia)

Pecan: < 0.05, < 0.05, < 0.05 mg/kg (GAP of USA)

Walnut: < 0.05, < 0.05, < 0.05, < 0.05, < 0.05 mg/kg (GAP of USA).

Residues for the sum of glufosinate and NAG were: Almonds: < 0.05 (4) mg/kg (GAP of USA), Hazelnut: < 0.05 (3) mg/kg (two times GAP of the UK), Macadamia: < 0.05, < 0.09 mg/kg (GAP of Australia), Pecan: < 0.05 (3) mg/kg (GAP of USA) and Walnut: < 0.05 (5) mg/kg (GAP of the USA).

The Meeting considered the four almond, three pecan, five walnut, two macadamia and three hazelnut trials as a group. The Meeting estimated an STMR of 0.05 mg/kg and a maximum residue level of 0.1 mg/kg for tree nuts confirming its previous recommendation.

Cotton seed, tolerant

The Meeting received field trials performed in the USA involving glufosinate tolerant cotton. GAP for USA is for (i) pre-planting or pre-emergence application at 0.59 kg ai/ha and post-emergence use from emergence up to the early bloom stage at 0.45–0.59 kg ai/ha with a maximum seasonal rate of 1.8 kg ai/ha/year or (ii) pre-planting or pre-emergence application at 0.561–0.88 kg ai/ha and post-emergence use from emergence up to the early bloom stage at 0.45–0.59 kg ai/ha with a maximum seasonal rate of 1.5 kg ai/ha/year or (iii) post-emergence use from emergence up to the early bloom stage at 0.29–0.58 kg ai/ha with a maximum seasonal rate of 1.2 kg ai/ha/year. The PHI is 70 days. Post-emergent application leads to higher residues. In trials approximating critical GAP in the USA total residues in cotton seed were (n=14): 0.15, 0.24, 0.30, 0.30, 0.34, 0.57, 0.63, 0.78, 1.1, 1.1, 1.3, 1.7, 2.3 and 3.2 mg/kg.

The Meeting estimated an STMR of 0.705 mg/kg and a maximum residue level of 5 mg/kg for cotton seed.

Rape seed, conventional (pre-harvest desiccation) and tolerant

Glufosinate-ammonium is approved for pre-harvest desiccation of conventional rape in Germany (GAP: 0.5 kg ai/ha, PHI 14 days) and the UK (GAP: 0.45 kg ai/ha, PHI 7 days). Total residues in rape seeds from trials conducted in Germany approximating German GAP were (n=12): < 0.05, 0.15, 0.19, < 0.2, < 0.2, < 0.2, 0.25, 0.25, 0.26, 0.63 and 0.76 mg/kg.

The Meeting received field trials performed in the USA involving glufosinate tolerant rape. GAP for USA is for (i) pre-planting or pre-emergence application at 0.59–0.74 kg ai/ha with a maximum seasonal rate of 0.74 kg ai/ha or (ii) application post-emergence from the cotyledon stage up to the early bolting stage of crop development at 0.47–0.5 kg ai/ha with a maximum seasonal rate of 0.99 kg ai/ha/year and a PHI of 65 days. Post-emergent application leads to higher residues. In trials approximating GAP in the USA total residues in rape seeds were (n=5): < 0.05, 0.06, 0.19, 0.22 and 7.9 mg/kg.

The Meeting considered five trials inadequate to estimate a maximum residue level for rape when glufosinate-ammonium is used on tolerant crops and decided to use the trials for pre-harvest desiccation of conventional crops to estimate an STMR of 0.225 mg/kg and a maximum residue level of 1.5 mg/kg for rape seed replacing its previous recommendation of 5 mg/kg.

Sunflower seed (pre-harvest desiccation)

Glufosinate–ammonium is approved for pre-harvest desiccation of sunflowers in Germany (GAP: 0.5 kg ai/ha, PHI 14 days). Total residues in trials from Germany approximating German GAP were: 0.43, 0.79, 1.2 and 2.3 mg/kg (all at 0.6 kg ai/ha). Additional trials from Hungary had total residues: 0.05, 0.25, 0.38, 0.27 and 0.46 mg/kg (all at rates 0.34–0.36 kg ai/ha)

The Meeting noted that the number of trials available from Germany is inadequate for the purpose of estimating a maximum residue level and the trials from Hungary do not match a relevant GAP. However, as the application of glufosinate-ammonium is for desiccation, the Meeting considered it valid to scale the residues in both sets of trials to the German GAP application rate. Total residues (scaled to an application rate of 0.5 kg ai/ha) in sunflower were (n=9): 0.07, 0.36, 0.36, 0.40, 0.53, 0.66, 0.68, 1.0 and 1.9 mg/kg.

The Meeting estimated an STMR of 0.53 mg/kg and a maximum residue level of 3 mg/kg for sunflower seed replacing its previous recommendation of 5 mg/kg.

Coffee beans (application to weeds)

In two trials from Brazil residues in coffee beans were < 0.04 (2). The Meeting considered two trials inadequate to estimate a maximum residue level. However, the Meeting considered there is sufficient other evidence, including from other fruiting trees and shrubs, to conclude the use pattern should not lead to residues above the LOQ although occasional residues of MPP through uptake from soil may occur and decided to estimate an STMR of 0.04 mg/kg and a maximum residue level of 0.1 mg/kg for coffee beans.

Animal feeds

Sweet corn forage, tolerant

The current Meeting received trials on glufosinate tolerant sweet corn forage and stover performed in USA. No GAP for the USA was available.

Bean forage and fodder (Common bean) (pre-crop emergence or application to weeds in crop)

Residue levels occurring in shoots and green material of conventional beans were evaluated. Glufosinate-ammonium is permitted to be used as a spray directed to weeds growing in bean crops (Portugal 0.75 kg ai/ha, no grazing restriction; Germany 1 kg ai/ha, using a screen to protect the crop, no grazing restriction; France 0.75 kg ai/ha no grazing restriction) and also as a spray to control weeds prior to crop emergence (the Netherlands 0.6 kg ai/ha, no grazing restriction).

In considering the available trials it was agreed that shoots at 14 or more days after application at beginning of flowering would be representative of forage. Total residues approximating GAP of France and Portugal (0.75 kg ai/ha) were (n=8): < 0.05, < 0.05, < 0.05, < 0.05, < 0.05, 0.06, 0.08 and 0.19 mg/kg. The Meeting estimated a median and a highest residue level of 0.05 mg/kg and 0.19 mg/kg respectively for bean forage (both on an as received basis).

Residue levels occurring in straw of conventional beans following directed application use were also available to the Meeting. In eight trials conducted in Germany, total residues following a directed application at 1 kg ai/ha with harvest 39 to 65 days after application were: < 0.05 (4), < 0.1, 0.15, 0.22 and 0.63 mg/kg (on an as received basis). The Meeting estimated a median residue of 0.075 mg/kg, a highest residue of 0.63 mg/kg (both on an as received basis) and a maximum residue level of 1 mg/kg for bean fodder (on a dry weight basis).

Miscellaneous fodder and forage crops

Sugar beet tops, tolerant

The Meeting received trials on glufosinate tolerant sugar beet) performed in the USA.

GAP for USA is for either (i) a pre-planting or pre-emergence application at 0.59–0.74 kg ai/ha or (ii) post-emergence application from post-emergence from the cotyledon stage up to the 10-leaf stage (BBCH 19) at 0.29–0.61 kg ai/ha with a maximum seasonal rate of 1.2 kg ai/ha/year and a PHI of 60 days. There is a restriction on the use of treated glufosinate tolerant sugar beet tops for livestock feed: Do not graze the treated crop or cut for hay. The Meeting did not receive GAP relevant to the use of sugar beet tops for livestock feed.

Straw, forage and fodder of cereal grains and grasses

Maize forage and stover, tolerant

For the current evaluation the Meeting received field trials involving glufosinate tolerant maize performed in USA. GAP for USA is for (i) pre-planting or pre-emergence application at 0.59–0.74 kg ai/ha with a maximum seasonal rate of 0.74 kg ai/ha or (ii) post-emergence application from post-emergence until corn is 61 cm tall or in the V-7 growth stage, (i.e., 7 developed collars) at 0.41–0.5 kg ai/ha with a maximum seasonal rate of 0.91 kg ai/ha/year and a PHI of 60 days for forage and 70 days for fodder. Post-emergent application leads to higher residues.

Total residues in maize forage from trials approximating USA critical GAP were (n=13): < 0.05, 0.06, 0.33, 0.50, 0.53, 0.54, 0.78, 0.82, 0.89, 1.1, 1.2, 1.5 and 1.6 mg/kg (fresh weight basis). The Meeting estimated median and highest residues of 0.78 and 1.6 mg/kg respectively.

Total residues in maize silage from trials approximating critical GAP in the USA were: < 0.05, 0.11, 0.12, 0.15, 0.32, 0.34, 0.36, 0.40, 0.43, 0.90, 1.2, 1.2, 1.6, 1.7 and 2.1 mg/kg (fresh weight basis). The Meeting estimated median and highest residues of 0.40 and 2.1 mg/kg respectively, both on a fresh weight basis.

Total residues in maize fodder/stover (fresh weight basis) from trials approximating USA GAP were (n=31): < 0.05, 0.09, 0.12, 0.13, 0.16, 0.17, 0.18, 0.24, 0.33, 0.41, 0.50, 0.53, 0.64, 0.68, 0.69, 0.72, 0.78, 1.3, 1.4, 1.4, 1.4, 1.4, 1.5, 1.7, 1.8, 1.9, 1.9, 2.8, 2.9 and 5.3 mg/kg. The Meeting estimated median and highest residues of 0.72 and 5.3 mg/kg respectively, both on a fresh weight basis and a maximum residue level of 8 mg/kg for maize fodder.

Rice, tolerant

The Meeting received field trials performed in the USA involving glufosinate tolerant rice. GAP for USA is for (i) pre-planting or pre-emergence application at 0.59–0.74 kg ai/ha with a maximum seasonal rate of 0.74 kg ai/ha or (ii) application post-emergence from the 1-leaf stage through the mid-tillering stage of crop development at 0.41–0.5 kg ai/ha with a maximum seasonal rate of 0.91 kg ai/ha/year and a PHI of 70 days. Post-emergent application leads to higher residues.

In the trials matching the critical GAP, glufosinate total residues in rice straw on an as received basis were (n=21): 0.05 (2), 0.06, 0.11, 0.12 (2), 0.14, 0.16, 0.24, 0.25, 0.26, 0.29, 0.30, 0.34, 0.35, 0.37, 0.54, 0.62, 0.63, 0.93 and 1.3 mg/kg.

The Meeting estimated median and highest residues of 0.26 and 1.3 mg/kg respectively together with a maximum residue level of 2 mg/kg for rice straw.

Cotton (tolerant) gin trash, tolerant

The Meeting received field trials performed in the USA involving glufosinate tolerant cotton. GAP in the USA is (i) pre-planting or pre-emergence application at 0.59 kg ai/ha and post-emergence use from emergence up to the early bloom stage at 0.45–0.59 kg ai/ha with a maximum seasonal rate of 1.8 kg ai/ha/year or (ii) pre-planting or pre-emergence application at 0.561–0.88 kg ai/ha and post-emergence use from emergence up to the early bloom stage at 0.45–0.59 kg ai/ha with a maximum seasonal rate of 1.5 kg ai/ha/year or (iii) post-emergence use from emergence up to the early bloom stage at 0.29–0.58 kg ai/ha with a maximum seasonal rate of 1.2 kg ai/ha/year. Post-emergent application leads to higher residues. In trials approximating critical GAP in the USA total residues in cotton gin trash were (n=7): 0.62, 0.65, 1.1, 1.5, 3.4, 4.0 and 7.4 mg/kg (on an as received basis).

The Meeting estimated a median residue of 1.5 mg/kg for cotton gin trash.

Rotational crop residues

Soil residues of glufosinate, MPP and NAG are not persistent and the maximum single spray application rate for weeds in non-permanent crops of 1 kg ai/ha can be used (after adjusting for likely interception of spray by crops and weeds) as a basis for estimating likely residues in soil that might transfer to rotational (follow) crops. If it is assumed weeds and crop present at the time of application intercept 50% of the spray, the amount reaching the soil would be equivalent to an application rate to bare soil of 0.5 kg ai/ha. Trials on residues in follow crops were made available to the Meeting. At plant-back intervals of 69 to 174 days after application at 0.6 to 0.9 kg ai/ha to cotton, residues in follow crops (mustard greens, turnips) were < LOQ except for some wheat forage, straw and hay samples for which total residues ranged from < 0.05 to 0.14 mg/kg. Residues were also < 0.05 mg/kg in wheat commodities grown following a potato crop treated at 0.45 kg ai/ha and at plant back intervals of 30 days.

In the confined rotation crop study where crops were rotated into soil previously treated with ^{14}C-glufosinate-ammonium at the equivalent of 1 kg ai/ha, total residues (sum of glufosinate, MPP and NAG) were < 0.05 mg/kg in radish tops and lettuce at a plant back interval of 28 days and 0.15, 0.38 and 0.12 mg/kg in wheat forage, straw and grain respectively. At longer plant back intervals residues were all < 0.05 mg/kg.

The Meeting considered residues in rotational crops above the LOQ would be unlikely.

Fate of residues during processing

The Meeting received information on the nature of residues under simulated processing condition on the fate of incurred residues of glufosinate during the processing of oranges, plums, grapes, olives, potatoes, sugar beet, soy bean, oilseed rape/canola, cotton seed, sunflower seed, maize and rice. A study of the nature of the residue of glufosinate, NAG and MPP under simulated processing conditions (pasteurization, baking/brewing/boiling, sterilization) showed glufosinate, MPP and NAG are stable.

Summary of selected processing factors for glufosinate

Raw commodity	Processed commodity	Individual PF	Best estimate PF	$STMR_{RAC}$ (mg/kg)	$STMR_{RAC}$ × PF (mg/kg)
Orange	Juice	0.71	0.71	0.05	0.036
	Dried peel / pulp	2.21	2.21		0.11
	Molasses	2.65	2.65		0.13
	Oil	< 0.13	< 0.13		< 0.0065
Plum	Dried fruit	1.79	1.79	0.05	0.090
Olive	Oil	< 0.65	< 0.65	0.05	< 0.0325
Potato	Chips	2.2	2.2	0.05	0.11
	Flakes	1.78 2.77 2.91 3.43 3.06	2.91		0.146
	Crisps	1.61 1.61 1.70 2.12	1.655		0.083
	French fries	0.89 1.18 1.30 1.48	1.24		0.062
	Boiled potatoes	0.47 0.60 0.79 0.99	0.695		0.035
	Fried potatoes	0.95 1.48 1.78 2.01	1.63		0.082
	Baked potatoes	1.05 1.26 1.29 1.54	1.275		0.064
Sugar beet	Dried pulp	0.59	0.59	0.28	0.168
	Molasses	3.70 4.94 6.32 6.82	5.63		1.568
	Raw or refined sugar	< 0.08 < 0.10 < 0.29 < 0.91	< 0.195		0.056
Soya bean	Aspirated grain fraction	2.73 8.89	5.81	0.825	4.78
	Hulls	3.15, 11.4	7.275		6.02
	Meal	1.22	1.22		0.99
	Oil	< 0.04 < 0.74	< 0.74		< 0.61
Rape/canola	Meal	1.74, 1.94, 2.44, 2.55	2.19	0.225	0.495
	Oil	< 0.13 < 0.22 < 0.48 < 0.94 < 0.94	< 0.48		< 0.108
Cottonseed	Hulls	1.16	1.16	0.705	0.818

Raw commodity	Processed commodity	Individual PF	Best estimate PF	$STMR_{RAC}$ (mg/kg)	$STMR_{RAC}$ × PF (mg/kg)
	Meal	1.25	1.25		0.881
	Oil	< 0.02	< 0.02		< 0.014
Sunflower seed	Oil	< 0.03 < 0.07 < 0.08	< 0.07	0.53	< 0.037
Maize	Aspirated grain fraction	8.85 12.06	10.455	0.05	0.52275
Rice	Hull	1.85 2.29	2.07	0.09	0.1863
	Bran	0.74 0.87	0.805		0.0724
	Polished grain	0.60 0.94	0.77		0.0693

Residues are not expected in oils obtained from treated crops and did not concentrate in bran.

Residues in sugar beet molasses were much higher than in sugar beets. The Meeting estimated a maximum residue level of 8 mg/kg based on the recommended maximum residue level for sugar beet (1.5 mg/kg) and a processing factor of 5.63.

Residues in prunes were also higher than in fresh plums and the Meeting estimated a maximum residue level of 0.3 mg/kg for dried prunes based on the recommended maximum residue level for stone fruit (0.15 mg/kg) and a processing factor of 1.79.

Residues in animal commodities

Farm animal feeding studies

The Meeting received information on the residue levels arising in tissues and milk when dairy cows were fed a diet containing glufosinate and MPP at total dietary levels of 4, 12 and 40 ppm for the sum of glufosinate and MPP expressed as glufosinate free acid for 28 consecutive days. The ratio of glufosinate to MPP in the feed was 3:1. Apart from milk of a single dosed cow on days 0, 1 (0.03 mg/kg) and 9 (0.02 mg/kg) and a control milk sample (0.03 mg/kg), no residues were detected in milk (LOQ of 0.02 mg/kg) samples analysed at all dose levels and time intervals. The highest total residues (mean in brackets) in liver, kidney, fat and muscle from the highest dose animals were 10.7 (9.0), 7.5 (5.4), 0.16 (0.10) and < 0.05 (< 0.05) mg/kg respectively.

In an additional study dairy cows were fed glufosinate and NAG at total dietary levels of 9.1, 27.3 and 91 ppm for the sum of glufosinate and NAG expressed as glufosinate free acid for 28 consecutive days. The ratio of glufosinate to NAG in the dose was 1:5.5. Milk residues for the highest dose group were 0.07 mg/kg. Milk from one animal had much higher residues on two consecutive days that coincided with a dramatic reduction in feed consumption. These results were excluded from the analysis. The highest total residues (mean in brackets) in liver, kidney, fat and muscle from the highest dose animals were 0.13 (0.11), 0.29 (0.27), < 0.05 (< 0.05) and < 0.05 (< 0.05) mg/kg respectively.

The Meeting also received information on the residue levels arising in tissues and eggs, when laying hens were fed a diet containing glufosinate and MPP at total dietary levels of 4.5, 13.5 and 45 ppm glufosinate and MPP (both as glufosinate free acid) for 28 consecutive days. The ratio of glufosinate to MPP in the feed was 3.5:1. Residues in eggs for the highest feed group reached a maximum of 0.07 mg/kg at between day 7 and 13 of exposure. The mean total residues in liver, fat and muscle from the highest dose animals were < 0.10, 8.0, < 0.05 and < 0.05 mg/kg respectively.

In an additional study laying hens were dosed with glufosinate and NAG at levels equivalent to 0.44, 1.3 and 4.4 ppm in the feed for the sum of glufosinate and NAG expressed as glufosinate free acid for 28 consecutive days. The ratio of glufosinate to NAG in the dose was 1:5.3. Egg residues were < 0.05 mg/kg for all dose groups. Similarly, residues in liver, kidney, fat and muscle were all < LOQ (< 0.05 mg/kg for muscle, kidney, skin and fat and < 0.1 mg/kg for liver).

Animal commodity maximum residue levels

Dietary burden calculations for beef cattle and dairy cattle and poultry are provided below. The dietary burdens were estimated using the OECD diets listed in Appendix IX of the 2009 edition of the FAO Manual.

Potential cattle feed items include: soya bean hulls, cotton gin by-products, sugar beet molasses, cottonseed meal, maize forage/silage, soya bean meal, soya bean seed, potato culls, maize aspirated grain fractions, rice straw.

Potential poultry feed items include: soya bean hulls, cotton seed meal, maize forage/silage, soya bean meal, soya bean seed, potato culls, rice grain, rice bran/pollard, bean seed, maize grain.

Summary of livestock dietary burden (ppm of dry matter diet)

	US-Canada		EU		Australia		Japan	
	max	mean	Max	mean	max	Mean	max	Mean
Beef cattle	2.4	1.8	4.7[a]	2.4[c]	4.3	1.8	1.3	0.9
Dairy cattle	2.7	1.4	4.0	2.3[d]	4.4[b]	1.8	2.5	1.5
Poultry Broiler	0.5	0.5	1.2	1.2[f]	0.7	0.7	0.4	0.4
Poultry Layer	0.5	0.5	1.4[e]	0.9[g]	0.7	0.7	0.4	0.4

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

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

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

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

[e] Highest maximum poultry dietary burden suitable for MRL estimates for poultry meat and eggs.

[f] Highest mean poultry dietary burden suitable for STMR estimates for poultry meat.

[g] Highest mean poultry dietary burden suitable for STMR estimates for poultry eggs.

Animal commodity maximum residue levels

Two lactating dairy cow feeding studies were available to the Meeting. The first addressed feed consisting of ingredients selected from conventional crops and therefore with residues dominated by glufosinate (crop desiccation uses) and MPP (weed control uses). Estimates of highest and median residues made using the first feeding study are relevant if glufosinate is the major component of the total glufosinate residue in the feed. A review of metabolism and residue studies available for feed items that contribute most to the dietary burden for dairy and beef cattle showed that glufosinate is the major component of the total residues in livestock feed. Therefore the first feeding study is used to estimate residues in meat, edible offal and milk.

The calculations used to estimate highest total residues for use in estimating maximum residue levels, STMR and HR values are shown below.

Glufosinate + MPP feeding study	Feed level	Residues	Feed level	Residues (mg/kg) in			
	(ppm) for milk residues	(mg/kg) in milk	(ppm) for tissue residues	Muscle	Liver	Kidney	Fat
Maximum residue level beef or dairy cattle							
Feeding study [a]	4.0 12	< 0.02 0.02	4.0 12	< 0.05 < 0.05	1.63 4.2	0.41 2.0	0.06 0.08
Dietary burden and high residue	4.4	< 0.02	4.7	< 0.05	1.85	0.55	0.062
STMR beef or dairy cattle							
Feeding study [b]	4.0	< 0.02	4.0	< 0.05	1.18	0.38	0.05
Dietary burden and residue estimate	2.3	< 0.012	2.4	< 0.03	0.708	0.228	0.03

[a] highest residues for tissues and mean residues for milk

[b] mean residues for tissues and mean residues for milk

The Meeting estimated the following STMR values: milk 0.012 mg/kg; muscle 0.03 mg/kg; edible offal 0.708 mg/kg for liver and 0.228 mg/kg for kidney and fat 0.03 mg/kg. The following HR values are also estimated: milk 0.02 mg/kg; muscle 0.05 mg/kg; edible offal 1.85 mg/kg for liver and 0.55 mg/kg for kidney and fat 0.062 mg/kg.

The Meeting estimated the following maximum residue levels: milk 0.02 mg/kg; meat (mammalian except marine mammals) 0.1 mg/kg and edible offal 3 mg/kg to replace its previous recommendations of: milk 0.02* mg/kg; meat (mammalian except marine mammals) 0.05* mg/kg and edible offal 0.1* mg/kg. The Meeting noted that for cattle liver the IESTI accounts for 140–170% of the ARfD.

The corresponding calculations for poultry are provided below.

	Feed level	Residues	Feed level	Residues (mg/kg) in			
	(ppm) for egg residues	(mg/kg) in egg	(ppm) for tissue residues	Muscle	Liver	Skin	Fat
Maximum residue level broiler or laying hen							
Feeding study [a]	4.5	< 0.05	4.5	< 0.05	< 0.1	< 0.05	< 0.05
Dietary burden and residue estimate	1.4	< 0.016	1.4	< 0.016	< 0.031	< 0.016	< 0.016
STMR broiler or laying hen							
Feeding study [b]	4.5	< 0.05	4.5	< 0.05	< 0.1	< 0.05	< 0.05
Dietary burden and residue estimate	0.9	< 0.01	1.2	< 0.013	< 0.027	< 0.013	< 0.013

[a] highest residues for tissues and mean residues for egg

[b] mean residues for tissues and mean residues for egg

For poultry no residues are expected. The Meeting estimated the following maximum residue levels for poultry commodities: poultry meat 0.05* mg/kg; poultry edible offal 0.1* mg/kg and eggs 0.05* mg/kg.

The mean dietary burden of poultry is 0.9 ppm for layers and 1.4 ppm for broilers. The Meeting estimated the following STMR values: poultry meat 0 mg/kg; poultry fat 0 mg/kg; poultry edible offal (based on liver) 0 mg/kg and eggs 0 mg/kg.

DIETARY RISK ASSESSMENT

Long-term intake

The WHO Panel of the 2012 JMPR established an Acceptable Daily Intake (ADI) of 0–0.01 mg/kg bw for glufosinate.

The evaluation of glufosinate resulted in recommendations for maximum residue levels and STMR values for raw and processed commodities. Where data on consumption were available for the listed food commodities, dietary intakes were calculated for the 13 GEMS/Food Consumption Cluster Diets. The results are shown in Annex 3.

The IEDIs in the thirteen Cluster Diets, based on the estimated STMRs were 6–10% of the maximum ADI (0.01 mg/kg bw). The Meeting concluded that the long-term intake of residues of glufosinate from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The WHO Panel of the 2012 JMPR established an Acute Reference Dose (ARfD) of 0.01 mg/kg bw for glufosinate.

For bananas, kiwifruit, lettuce, soya bean (dry) and cattle liver, the IESTI represented 110, 110, 180, 120 and 170% respectively of the ARfD of 0.01 mg/kg bw. Since MPP represents the

majority of the residue in bananas, kiwifruit, lettuce and cattle liver, and because MPP is of lower toxicity than glufosinate, these exceedances are unlikely to present a public health concern. Although the IESTI for soya beans represented 120% of the ARfD, MPP represents about 15% of the residues. The Meeting concluded that the short-term intake of residues of glufosinate resulting from uses that have been considered by the JMPR is unlikely to present a public health concern.