

5.21 GLYPHOSATE (158)

RESIDUE AND ANALYTICAL ASPECTS

Glyphosate is an herbicide with uses on many crops, conventional and glyphosate tolerant. Glyphosate has been evaluated several times with the initial evaluation in 1986 and the latest in 2011 where the use of glyphosate on glyphosate tolerant crops was reviewed.

The 2011 JMPR established a residue definition for compliance with MRLs for plant commodities as the sum of glyphosate and N-acetyl-glyphosate, expressed as glyphosate in the case of soya bean and maize and glyphosate for other crops. The definition of the residue for compliance with MRL for animal commodities is the sum of glyphosate and N-acetyl-glyphosate, expressed as glyphosate. For estimation of dietary intake it is the sum of glyphosate, AMPA, N-acetyl-glyphosate and N-acetyl AMPA, expressed as glyphosate. The toxicology of glyphosate was re-evaluated by the 2011 JMPR which estimated group ADI of 0–1 mg/kg bw for the sum of glyphosate, N-acetyl-glyphosate, AMPA and N-acetyl-AMPA. The same Meeting confirmed that an ARfD was unnecessary.

For the current evaluation data have been submitted covering the use on genetically modified rape crops containing the *gat* trait (glyphosate-N-acetyl transferase or GAT gene). These crops inactivate glyphosate by converting it to N-acetyl-glyphosate. The Meeting received information on glyphosate metabolism in genetically modified rape containing the *gat* trait, methods of residue analysis, GAP information, supervised residue trials on *gat* rape crops and the fate of residue during storage and processing.

To assist uniform interpretation of GAP application rates have been expressed in terms of glyphosate acid equivalents (ae), unless indicated otherwise.

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

N-acetyl-glyphosate	N-acetyl-N-(phosphonomethyl)glycine
AMPA	aminomethyl phosphonic acid
N-acetyl-AMPA	[(acetylamino)methyl]phosphonic acid.

Plant metabolism

The metabolic fate of [¹⁴C] glyphosate in *gat* rape plants was examined following a single pre-emergence soil application of 4.5 kg ae/ha, followed by three foliar applications at 1.0 kg ae/ha at three different growth stages (2 and 5 leaf stage and 1 week before harvest). Rape plants were harvested as immature foliage, immediately prior to the final application and at maturity (PHI 7 days).

N-acetyl-glyphosate was the major metabolite in immature foliage (90% TRR; 5.4 mg/kg glyphosate equivalents). Glyphosate, AMPA and N-acetyl-AMPA were also detected accounting for 3.0, 1.4 and 3.4% of TRR respectively. At the intermediate harvest prior to the final application the only glyphosate related compound detected in foliage and immature pods (with seeds) was N-acetyl-glyphosate representing 93% TRR in foliage and 80% TRR in immature pods (with seeds). The residue in seeds at harvest, seven days after the final application, comprised glyphosate (21% TRR; 0.45 mg/kg), N-acetyl-glyphosate (51% TRR; 1.1 mg/kg), AMPA (1.9% TRR; 0.04 mg/kg) and N-acetyl-AMPA (15% TRR; 0.32 mg/kg).

The proposed pathway of glyphosate in rape plants with the *gat* trait is deactivation to N-acetyl-glyphosate which can be further metabolized to N-acetyl-AMPA and AMPA. The metabolism is similar to that observed for maize and soya bean crops with the *gat* trait previously reviewed by the 2011 JMPR.

Methods of Analysis

The Meeting received description and validation data for analytical methods for residue analysis of glyphosate and its metabolites in various plant commodities using LC-MS/MS. The LOQs are 0.05 mg/kg.

Stability of pesticide residues in stored analytical samples

No new information was received on the stability of glyphosate and its residues in samples stored frozen. The periods of demonstrated stability reported by the 2011 JMPR for other high oil and high protein crops cover the frozen storage intervals used in the residue studies.

Definition of the residue

The 2011 JMPR reviewed glyphosate metabolism studies in tolerant maize and soya bean containing the *gat* trait. Glyphosate, AMPA, *N*-acetyl-glyphosate and *N*-acetyl-AMPA were the major components of the residue in both maize and soya bean. In seeds from *gat* rape, *N*-acetyl-glyphosate was the major component of the residue (51% TRR) followed by glyphosate (21% TRR) and *N*-acetyl AMPA (15% TRR). In *gat* rape forage, *N*-acetyl glyphosate was the major metabolite (90–93% TRR).

To accommodate the use of glyphosate on rape plants containing the *gat* trait the Meeting concluded that the previously established residue definition for enforcement in plants of “glyphosate” should be replaced by “*the sum of glyphosate and N-acetyl-glyphosate expressed as glyphosate*” for soya bean, maize and rape crops and remain “*glyphosate*” for all other crops.

Based on the above the Meeting agreed to amend the previous definition for glyphosate for compliance with MRL for plant commodities as follows:

Definition of the residue for compliance with MRL (for plant commodities): for soya bean, maize and rape - *sum of glyphosate and N-acetyl-glyphosate, expressed as glyphosate*, and for other crops - *glyphosate*.

The Meeting confirmed the residue definition for estimation of dietary intake as (for plant and animal commodities: *glyphosate, N-acetyl-glyphosate, AMPA and N-acetyl AMPA, expressed as glyphosate*).

Results of supervised residue trials on crops

The Meeting received supervised residue trial data for glyphosate on glyphosate-tolerant rape (*gat* trait).

For estimation of maximum residue levels for rape crops glyphosate and *N*-acetyl glyphosate levels are summed and expressed as glyphosate equivalents.

For estimation of the residue levels for dietary risk assessment of glyphosate in *gat* crops, in general all four analytes may be present in significant amounts. In the *gat* modified rape, *N*-acetyl glyphosate is the major residue found in rape seed, followed by glyphosate and *N*-acetyl AMPA. AMPA is a minor component of the residue and is included in the sum of residues when AMPA is reported as < LOQ.

The current Meeting received field trials performed in the USA and Canada involving glyphosate tolerant rape containing the *gat* trait. GAP for Canada is for application pre-emergence at 0.68 kg ae/ha, post-emergence at the 0–6 leaf stage at 0.3–0.68 kg ae/ha followed by a pre-harvest application at 0.9 kg ae/ha (PHI 7 days).

Residues of glyphosate and *N*-acetyl-glyphosate in rape seed trials matching Canada GAP were: 0.775, 1.8, 1.9, 2.4, 2.85, 3.05, 3.05, 7.8, 9.2 and 15 mg/kg (n=10). The Meeting estimated a

maximum residue level of 30 mg/kg for glyphosate in rape seed to replace its previous recommendation of 20 mg/kg.

Corresponding total residues, for dietary intake estimation, were: 0.795, 1.8, 1.95, 2.4, 2.9, 3.1, 3.1, 7.8, 9.2 and 15 mg/kg. The Meeting estimated an STMR for glyphosate in rape seed of 3.0 mg/kg.

It was assumed that rape forage is plant material available from 25 days after planting. Residues in rape forage matching Canada GAP were: 0.4, 0.48, 1.0, 1.1, 1.5, 1.6, 2.1, 2.4, 2.5, 2.5, 3.3, 3.6, 4.7, 5.1, 8.0 and 16 mg/kg (dry matter basis). The Meeting estimated median and highest residues for glyphosate in rape forage of 2.25 and 16 mg/kg respectively, both on a dry-matter basis.

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 glyphosate during the processing of rape seeds. Calculated processing factors for total glyphosate acid equivalents (combined results of the four metabolites) are summarized below.

Summary of calculated processing factors and estimated STMR-P values

Commodity	PF _{total}	Best estimate PF _{total}	STMR _{RAC} (mg/kg)	STMR _{RAC} ×PF (mg/kg)
Refined oil-cold press	< 0.0009 < 0.003 < 0.003	< 0.003	3.0	< 0.009
Refined oil-solvent extracted	< 0.0009 < 0.003 < 0.003	< 0.003		< 0.009
Meal-cold pressed	0.311 1.47 1.57	1.47		4.41
Meal-solvent extracted	0.107 1.13 1.43	1.13		3.39

The estimated STMR-P values in oil are lower than the previous values reported by the 2011 JMPR (previous 0.093 mg/kg) while the STMR-P estimated for rape seed meal is higher (previous 2.3 mg/kg).

Residues in animal commodities

Animal commodity maximum residue levels

The current evaluation has not led to recommendations that would alter the dietary burdens calculated using the livestock intake figures employed by the 2011 JMPR. The glyphosate dietary burdens for cattle (dairy and beef) were based on grass, cotton seed and barley grain while those for poultry were based on barley, soya bean grain and soya bean hulls and as such do not require a re-evaluation of animal commodity maximum residues levels.

RECOMMENDATIONS

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

Definition of the residue for compliance with MRL (for plant commodities) for soya bean, maize and rape: *sum of glyphosate and N-acetyl-glyphosate, expressed as glyphosate*, and for other crops - *glyphosate*.

The Meeting confirmed the residue definition for estimation of dietary intake as (for plant and animal commodities): *glyphosate, N-acetyl-glyphosate, AMPA and N-acetyl AMPA, expressed as glyphosate*.

Definition of the residue for compliance with MRL (for animal commodities): *sum of glyphosate and N-acetylglyphosate, expressed as glyphosate.*

Definition of the residue for estimation of dietary intake (for plant and animal commodities): *glyphosate, N-acetylglyphosate, AMPA and N-acetyl AMPA, expressed as glyphosate.*

The residue is not fat soluble.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes (IEDI) of glyphosate for the 13 GEMS/Food regional diets, based on estimated STMRS were in the range 0–1% of the maximum ADI of 1 mg/kg bw for the sum of glyphosate, *N*-acetyl glyphosate, AMPA and *N*-acetyl AMPA, expressed as glyphosate. The Meeting concluded that the long-term intake of residues of glyphosate, *N*-acetyl glyphosate, AMPA and *N*-acetyl AMPA from uses that have been considered by the JMPR is unlikely to present a public health concern. The results are shown in Annex 4 of the JMPR 2013 Report.

Short-term intake

The International Estimated Short Term Intake (IESTI) of glyphosate was not calculated. The 2004 and 2005 JMPR concluded that it was unnecessary to establish an ARfD for glyphosate. The Meeting therefore concluded that short-term dietary of glyphosate residues is unlikely to present a risk to consumers.