Pre-submission Meeting with AGG

Glyphosate EU Approval Renewal

October 18, 2019

Residues & dietary safety

Agenda

- // Residue analytical methods [New data]
- // Storage stability in crop and animal commodities (including GM) [New data]
- // Plant metabolism (conventional and GM)
- // Livestock metabolism (including N-acetyl glyphosate)
- // Field residue trials [New data]
- // Feeding studies (including N-acetyl glyphosate)
- // Processing studies [New data]
- // Rotational crops
- // Residues in honey [New data]

Representative uses for the evaluation of residues

(Provisional)

Representative uses for the evaluation of residues (provisional)

Pre-sowing and pre-planting use in annual crops [Renovation / change of land use]

Crop and/or situation (a)	MS Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (m)	Remarks
					Type (d-f)	Conc. a.s. (i)	method kind (f-h)	Growth Stages & season (j)	number min-max (k)	Interval between application min-max	L/ha product min-max (l)	Water L/ha min-max	kg a.s./ha min-max (l)		
Root & tuber vegetables Bulb vegetables Fruiting vegetables Brassica Leafy vegetables Stem vegetables Sugar beet	EU	MON 52276	F	*Emerged weeds*	SL	360 g/L	Spray	Pre-sowing, crop pre-emergence / pre-planting, pre-transplanting.	1-3	21	2	100-400	0.72	-	Renovation / change of land use applications. Broadcast tractor mounted application (to 100% of the field). Use 75% drift reducing nozzles. Maximum application rate of 2.16 kg as/ha glyphosate in any 12 months period across all use types.

Representative uses for the evaluation of residues (provisional)

Pre-sowing and pre-planting use in annual crops [Post-harvest use]

Crop and/or situation (a)	MS Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (m)	Remarks
					Type (d-f)	Conc. a.s. (i)	method kind (f-h)	Growth Stages & season (j)	number min-max (k)	Interval between application min-max	L/ha product min-max (l)	Water L/ha min-max	kg a.s./ha min-max (l)		
Root & tuber vegetables Bulb vegetables Fruiting vegetables Brassica Leafy vegetables Stem vegetables Sugar beet	EU	MON 52276	F	*Emerged weeds*	SL	360 g/L	Spray	Post-harvest, pre-sowing / pre-planting.	1-3	21	2-6	100-400	0.72-2.16	-	Application to existing row cropland after harvest for removal of remaining crop / stubble and for control of actively growing annual weed. Broadcast tractor mounted application (to 100% of the field). Use 75% drift reducing nozzles. Maximum application rate of 2.16 kg as/ha glyphosate in any 12 months period across all use types.

Representative uses for the evaluation of residues (provisional)

Use in top fruit plantations and vineyards

Crop and/or situation (a)	MS Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (m)	Remarks
					Type (d-f)	Conc. a.s. (i)	method kind (f-h)	Growth Stages & season (j)	number min-max (k)	Interval between application min-max	L/ha product min-max (l)	Water L/ha min-max	kg a.s./ha min-max (l)		
Top fruit plantations (including citrus, tree nuts, pome fruit, stone fruit, kiwi and banana)	EU	MON 52276	F	*Emerged weeds*	SL	360 g/L	Spray	Post-emergence of weeds	1-3	21 days	2-4	100-400	0.72-1.44	7	Avoid crop contamination during treatment. Maximum application rate of 2.88 kg as/ha glyphosate in any 12 months period Applications are performed in the rows below the trees or as spot treatments. The rate refers to the treated area only which represents not more than 50% of the total orchard area. The application rate with reference to the total orchard or vineyard surface area is not more than 50% of the stated dose rate.
Grape plantations (table and wine grape)	EU	MON 52276	F	*Emerged weeds*	SL	360 g/L	Spray	Post-emergence of weeds	1-3	21 days	2-4	100-400	0.72-1.44	7	

Residue analytical methods

Residue Analytical Methods

New studies were conducted to address the following points :

- **2015 EFSA Conclusion – supplementary data**
  - Confirmatory method for N-acetyl glyphosate in plant matrices (dry, high water, high fat)
  - Confirmatory method for N-acetyl glyphosate in all animal matrices
  - Confirmatory method for glyphosate in animal fat and kidney/liver
  - Confirmatory method for glyphosate and AMPA in soil
- **New Requirements**
  - Method for the monitoring of residues in body fluids (glyphosate and AMPA)
  - Method in honey (glyphosate and AMPA) for data generation and monitoring (initial validation and ILV)

Residue Analytical Methods

Plant matrices

Method (reports)	Principle	Analytes	Matrices		LOQ* (mg/kg)
			1st validation	ILV	
AG-ME-1294-01 (MSL27298 new, S11-03331, S14-05172 new)	Extraction with 0.1% formic acid and CH_2Cl_2, SPE clean-up, LC-MS/MS with two mass transitions, quantification with stable isotope internal standards**	Glyphosate, AMPA	New : corn grain, corn stover, soybean seed, cotton seed, oranges, sugar beet tops	Potato, carrot, onion, cucumber, cabbage, cauliflower, lettuce, leek, tomato, New : cereal grain, sunflower seed, grape	0.05

* Each compound is expressed as such.
** The stable isotope internal standards are commercially available (for instance at Toronto Research chemicals).

Residue Analytical Methods

Plant matrices

Method (reports)	Principle	Analytes	Matrices		LOQ* (mg/kg)
			1st validation	ILV	
ME-2000-01 (MSL27300 new, S15-04467 new)	Extraction with 0.1% formic acid and CH_2Cl_2, LC-MS/MS with two mass transitions, quantification with stable isotope internal standards**	N-acetyl glyphosate	Corn grain, corn forage, soybean seed, canola seed, orange	Tomato, orange, wheat grain, rape seed	0.025

* Each compound is expressed as such.
** The stable isotope internal standards are commercially available (for instance at Toronto Research chemicals).

Residue Analytical Methods

Animal matrices

Method (reports)	Principle	Analytes	Matrices		LOQ* (mg/kg)
			1st validation	ILV	
ME-1951-01 **ME-1999-01** (MSL27299 new, MSL27301 new, S15-04468 new)	Extraction with 0.1% formic acid and CH_2Cl_2, SPE clean-up (only for glyphosate and AMPA in eggs and liver), LC-MS/MS with two mass transitions, quantification with stable isotope internal standards**	Glyphosate, AMPA, N-acetyl glyphosate	Milk, eggs, muscle, liver, fat	Milk, eggs, muscle, liver, fat	0.025

* Each compound is expressed as such.

** The stable isotope internal standards are commercially available (for instance at Toronto Research chemicals).

Residue Analytical Methods

Honey

Method (reports)	Principle	Analytes	Matrices		LOQ* (mg/kg)
			1st validation	ILV	
ME-2220 (SGS-19-01-01 new) ILV on-going	Extraction with 0.1% formic acid, LC-MS/MS with two mass transitions, quantification with stable isotope internal standards**	Glyphosate, AMPA	Honey	On-going	0.025

* Each compound is expressed as such.
** The stable isotope internal standards are commercially available (for instance at Toronto Research chemicals).

Residue Analytical Methods

Extraction efficiency

- **Established as acceptable in RAR, Vol. 3, B.5, 2015 revision**
  - Water or 0.1% aqueous formic acid in methanol (96+4, v/v) – plant matrices
  - Water, diluted HCl or acetic acid, or 0.1% aqueous formic acid in methanol (96+4, v/v) – animal matrices

- **New methods (in plant and animal matrices)**
  - Extraction in 0.1% formic acid (aqueous)
  - Dichloromethane included at same time as extraction for clean-up purposes only – not necessary for extraction

➡ Considering extraction with water is generally considered to be representative of extraction with 0.1% formic acid in water, our interpretation is that extraction efficiency of the new methods is considered to be sufficiently covered by existing data.

Storage stability

Storage stability in crop commodities

- 11 studies conducted between 1989 and 2012 provide information on the storage stability of residues of glyphosate and its metabolites in plant matrices.
- Some results are difficult to interpret due to low procedural recoveries. Based on the results with satisfactory procedural recoveries, the following stability intervals can be derived :

Matrix type	Storage stability (Months)			
	Glyphosate	AMPA	N-acetyl glyphosate	N-acetyl AMPA
High water	24	12	12	1
High acid	24	24	-	-
High starch	48	48	12	1
High protein	18	-	-	-
High oil	24	24	12	1

➡ A new storage stability study for AMPA in matrices with a high protein content has been initiated.

Storage stability in animal commodities

- The storage stability of glyphosate and AMPA was investigated in animal commodities to support the results of cow, hen and pig feeding studies.

Commo-dities	Storage stability (Months)					
	Cattle		Poultry		Pig	
	Glyphosate	AMPA	Glyphosate	AMPA	Glyphosate	AMPA
Fat	24	24***	25	16**	26	15**
Muscle	24	24	25	25	26	26
Liver	24	24	25	25***	26	26***
Kidney	24	24	13	13	26	26
Milk / Eggs	16	13	14*	14*	n.a.	n.a.

* Degradation observed at longer intervals.
** Stable for longer periods if corrected by procedural recoveries.
*** One interval in-between with low recoveries.

Storage stability in honey

GTF 2

- A storage stability study for glyphosate and AMPA in honey is on-going (new study). The study aims at supporting the honey residue study which is also on-going. It is intended to investigate storage periods up to 6 months.

Plant Metabolism

Plant metabolism studies

Weed control in orchards and vineyards

- Metabolism studies with ^{14}C-glyphosate were conducted in citrus, tree nut, apple, grape and avocado.
- The compound was applied to soil at rates in the range of 0.8-8.0 kg ae/ha. Absorption by trees via roots and further translocation within the trees were extremely low. In two grape studies involving soil treatment at a (total) exaggerated rate of 8 kg ae/ha, the residues in grape 7 days, 14 days and one year after application did not exceed 0.007 mg/kg, thus precluding identification of the residues.
- When the compound was applied to leaves (thus simulating accidental contamination of the crop during soil treatment) the vast majority of extractable residues in treated leaves, new leaves and grapes consisted of parent glyphosate (usually 70-99% of TER) with low levels of AMPA (< 10% TER),
- Tests with soil application of ^{14}C-AMPA also showed a minimal uptake by trees.

➡ Based on the metabolism studies the use of glyphosate in orchards and vineyards is expected to result in a zero residue situation (unless crop contamination occurs during treatment).

Plant metabolism studies

Pre-sowing, pre-planting, pre-emergence uses

- Soybean metabolism study with ^{14}C-glyphosate trimesium (8.4 kg ae/ha at planting).

Sample	TRR (mg/kg)	Extracted residues (mg/kg) *[% TRR]*				Unextracted (mg/kg) *[% TRR]*	Total recovered *[% TRR]*
		Total	Glyphosate	AMPA	Natural products		
Forage	1.76	0.792 *[45.0]*	0.058 *[3.3]*	0.100 *[5.7]*	0.634 *[36.0]*	1.051 *[59.7]*	*104.7*
Straw	0.859	0.321 *[37.4]*	0.005 *[0.6]*	0.023 *[2.7]*	0.293 *[34.1]*	0.497 *[57.9]*	*95.3*
Hulls	0.487	0.233 *[47.9]*	0.020 *[4.1]*	0.007 *[1.5]*	0.206 *[42.3]*	0.222 *[45.7]*	*93.6*
Yellow seeds	1.31	0.696 *[53.1]*	0.034 *[2.6]*	0.021 *[1.6]*	0.641 *[48.9]*	0.613 *[46.8]*	*99.9*
Green seeds	0.772	0.410 *[53.1]*	0.020 *[2.6]*	0.012 *[1.6]*	0.378 *[48.9]*	0.361 *[46.8]*	*99.9*
Hay	0.854	0.414 *[48.5]*	0.020 *[2.1]*	0.020 *[2.0]*	0.420 *[44.4]*	0.470 *[50.0]*	*98.4*

Notes :
- Forage was collected 31 days after treatment. The other commodities were collected at harvest, 97 days after treatment.
- The composition of residues in green seeds was not investigated but assumed to be the same as in yellow seeds.
- Unextracted radioactivity was extensively characterised and shown to mainly consist of ^{14}C incorporated in natural compounds (carbohydrates, proteins, lignin, cellulose).

Plant metabolism studies

Soil application for weed control in annual crops

- Primary crops of rotational crop study with ^{14}C-glyphosate (4.5 kg ae/ha, 16-60 days after planting).

Sample	TRR (mg/kg)	Extracted residues (mg/kg) *[% TRR]*					
		Total	Glyphosate	AMPA	Neutrals	Other	Indeterminate
Peas	0.22	0.20 *[92.2]*	0.137 *[62.0]*	0.013 *[5.9]*	0.014 *[6.2]*	0.010 *[4.7]*	0.029 *[13.4]*
String beans	0.13	0.11 *[87.5]*	0.070 *[54.2]*	0.008 *[6.0]*	0.016 *[12.4]*	0.009 *[7.2]*	0.010 *[7.8]*
Carrot roots	0.11	0.085 *[77.2]*	0.038 *[34.5]*	0.006 *[5.0]*	0.020 *[17.8]*	0.006 *[5.0]*	0.016 *[14.8]*
Carrot leaves	0.17	0.097 *[57.0]*	0.051 *[30.2]*	0.005 *[3.2]*	0.021 *[12.5]*	0.006 *[3.6]*	0.013 *[7.6]*
Cabbage leaves	0.08	0.055 *[69.1]*	0.026 *[32.1]*	0.006 *[7.0]*	0.014 *[17.0]*	0.003 *[4.2]*	0.007 *[8.8]*
Cabbage head	n.d.	n.d. *[65.9]*	n.d. *[39.2]*	n.d. *[3.3]*	n.d. *[18.5]*	n.d. *[2.0]*	n.d. *[2.9]*

➡ Limited up-take of parent glyphosate with even lower residues of AMPA. No other identified metabolite. A significant portion of the radioactivity in crop samples may be attributed to incorporation of ^{14}C in natural molecules (extensive characterisation conducted in the soybean study).

Plant metabolism studies

Pre-harvest application

- ^{14}C-glyphosate trimesium was applied to wheat at the rate of ca. 6 kg ae/ha 7 days before harvest.

Sample	TRR (mg/kg)	Extracted residues (mg/kg) *[% TRR]*				
		Total	Glyphosate	AMPA	Unknown	Unassigned
Grain	2.68	2.52 *[94.2]*	2.43 *[90.8]*	0.08 *[2.8]*	0.01 *[0.5]*	0.03 *[1.3]*
Chaff	327.5	310.8 *[94.9]*	278.4 *[85.0]*	12.8 *[3.9]*	6.55 *[2.0]*	5.60 *[1.7]*
Straw	124.2	114.8 *[92.4]*	102.6 *[82.6]*	4.10 *[3.3]*	2.20 *[1.8]*	3.70 *[3.0]*

➡ As expected, parent glyphosate represents the major part (> 80%) of the TRR. AMPA is present at far lower levels. No other metabolite was identified.

Plant metabolism studies

Conclusion for conventional crops

- The metabolism of glyphosate in conventional primary crops is well understood. The only relevant residue components are parent glyphosate and its metabolite AMPA which are present at various levels, depending on the type of use. After soil application, a significant portion of radioactivity was shown to result from incorporation of ^{14}C in natural molecules.

Plant metabolism studies

Conclusion for genetically modified crops

- In metabolism studies with **CP4 EPSPS genetically modified crops** (soybean, cotton, sugar beet) the only relevant residue components were parent glyphosate and its metabolite AMPA. Other metabolites were only identified at low levels (N-methyl AMPA, glyphosate conjugate, glyphosate and AMPA acetylated conjugates). In cottonseed a significant portion of residues remained unextracted even after extensive hydrolysis with acids and bases.
- In metabolism studies with **CP4 EPSPS & GOX genetically modified crops** (canola, maize) the only relevant residue components were parent glyphosate (except in seed and grain) and its metabolite AMPA. Other metabolites were only identified at low levels (N-glyceryl AMPA, N-acetyl AMPA, glyphosate conjugates). In maize grain a significant portion of extractable residues was incorporated in natural molecules (starch).
- In metabolism studies with **GAT modified crops** (canola, soybean, maize) the relevant residue components were parent glyphosate and its metabolite AMPA, N-acetyl glyphosate and N-acetyl AMPA, which were found in various proportions depending on the commodity.
  <u>Note</u> : Discussions are on-going with the data-holder to check if these studies can be included in the renewal dossier that will be submitted by GTF2.

Plant metabolism studies

Rotational crops

- 4.16 kg ae/ha of ^{14}C-glyphosate to rye grass; after one week, tilling and sowing of soybean as primary crop; 30, 120 and 365 days after treatment, soybean plants removed from plots and rotational crops sown.

Sample	Max. TRR (mg/kg)	@ PBI	Extracted residues (mg/kg) *[% TRR]*				
			Range	Max. Gly.	@ PBI	Max. AMPA	@ PBI
Lettuce	0.108	30 days	*[34.3-56.4]*	0.004 *[3.8]*	30 days	0.016 *[14.6]*	30 days
Barley straw	0.175	30 days	*[19.2-25.9]*	0.002 *[1.0]*	30 days	0.007 *[3.7]*	30 days
Barley grain	0.188	30 days	*[15.3-25.2]*	0.019 *[9.8]*	30 days	0.034 *[17.9]*	30 days
Carrot tops	0.051	30 days	*[22.7-24.5]*	-	30 days	< 0.001 *[1.4]*	30 days
Carrot root	0.037	30 days	*[32.1-54.4]*	-	30 days	0.004 *[11.1]*	30 days

Note : The table shows the maximum residue levels in terms of mg/kg (not with regard to % TRR).

Significant portion of extractable residues characterised as glucose/fructose. Part of unextracted residues shown to result from ^{14}C incorporation in natural molecules (starch, lignin, cellulose).

Plant metabolism studies

Rotational crops

- 6.5 kg ae/ha of ^{14}C-glyphosate to bare soil; rotational crops sown 30, 120 and 365 days after treatment.

Sample	Max. TRR (mg/kg)	@ PBI	Extracted residues (mg/kg) *[% TRR]*				
			Range	Max. Gly.	@ PBI	Max. AMPA	@ PBI
Radish leaf	4.8	30 days	*n.a.*	< 0.05	30 days	< 0.05	30 days
Radish root	0.24	30 days	*n.a.*	< 0.05	30 days	< 0.05	30 days
Lettuce	0.34	30 days	*n.a.*	< 0.05	30 days	< 0.05	30 days
Wheat forage	1.4	120 days	*n.a.*	0.4	120 days	0.2	30 days
Wheat chaff	1.6	30 days	*n.a.*	0.3	120 days	0.4	30 days
Wheat grain	2.0	30 days	*n.a.*	< 0.05	30 days	< 0.05	30 days

n.a. : not available
Note : The TRR was determined in both immature and mature crop commodities; when this is the case, only the results for mature commodities are shown in the above table since metabolite identification was not conducted for immature commodities.

Plant metabolism studies

Rotational crops

- 4.48 kg ae/ha of ^{14}C-glyphosate post-sowing of primary crops; rotational crops sown 1-23 days after harvest of primary crops.

Sample	Max. TRR (mg/kg)	@ PBI*	Extracted residues (mg/kg) *[% TRR]*				
			Range	Max. Gly.	@ PBI*	Max. AMPA	@ PBI*
Carrot root	0.094	40 days	*[41.4-73.4]*	0.018 *[19.6]*	40 days	0.004 *[4.1]*	40 days
Carrot leaves	0.086	40 days	*[30.6-51.6]*	0.018 *[21.5]*	40 days	0.002 *[2.3]*	40 days
Cabbage	0.056	40 days	*[17.3-57.5]*	0.026 *[46.4]*	40 days	0.003 *[4.5]*	40 days
Maize forage	0.09	60 days	*[48.0-59.4]*	0.005 *[5.6]*	60 days	0.008 *[8.9]*	60 days
Maize kernel	0.06	60 days	*[39.9]*	n.a.	n.a.	n.a.	n.a.
Maize cob	0.05	60 days	*[51.5]*	0.002 *[3.3]*	60 days	0.005 *[9.0]*	60 days
Bean pods	0.04	60 days	*[90.3]*	0.016 *[40.1]*	60 days	0.003 *[7.9]*	60 days
Pea pods	0.28	90 days	*[88.5]*	0.13 *[45.8]*	90 days	0.044 *[15.6]*	90 days

* Rough estimate assuming that the rotational crop was sown about two weeks after the primary crop was harvested. n.a. : not analysed, not applicable.
Note : The table shows the maximum residue levels in terms of mg/kg (not with regard to % TRR).

Plant metabolism studies

Rotational crops

- 4.48 kg ae/ha of ^{14}C-glyphosate applied to bare soil 3 days before sowing primary crops;
  - for intermediate and annual rotation, primary crop harvested and rotational crop sown 4 months and one year after application.
  - for emergency rotation, 4.48 kg ae/ha of ^{14}C-glyphosate applied to primary crop 30 days after first treatment; thereafter, the rotational crops were sown.

Sample	Max. TRR (mg/kg)	@ PBI*	Extracted residues (mg/kg) *[% TRR]*				
			Range	Max. Gly.	@ PBI*	Max. AMPA	@ PBI*
Cabbage	0.11	30 days	*[48-67]*	0.005 *[7.6]*	120 days	0.008 *[11.7]*	120 days
Wheat forage	1.08	30 days	*[48-64]*	0.128 *[11.9]*	30 days	0.046 *[4.3]*	30 days
Beet leaves	0.21	30 days	*[37-52]*	0.005 *[2.7]*	30 days	0.004 *[1.6]*	30 days
Beet root	0.33	30 days	*[50-58]*	0.039 *[12.2]*	30 days	0.015 *[4.7]*	30 days

Note : The table shows the maximum residue levels in terms of mg/kg (not with regard to % TRR).

Plant metabolism studies

Rotational crops

- 35 day PBI : 3.8 kg ae/ha of ^{14}C-glyphosate (as trimesium salt) pre-emergence of soybean; 35 days after treatment, immature soybean removed and rotational crops sown.
  63 & 308 day PBI : 4.38 kg ae/ha of ^{14}C-glyphosate (as trimesium salt) pre-emergence of soybean; 35 days after treatment, immature soybean removed and 1.4 + 0.74 kg ae/ha of ^{14}C-glyphosate (as trimesium salt) applied at 1 month interval; rotational crop sown 63 and 308 days after last treatment.

Sample	Max. TRR (mg/kg)	@ PBI	Extracted residues (mg/kg) *[% TRR]*				
			Range	Max. Gly.	@ PBI	Max. AMPA	@ PBI
Lettuce	0.127	63 days	*[44.7-54.2]*	0.001 *[0.9]*	63 days	0.024 *[18.5]*	63 days
Radish roots	0.022	63 days	*[46.7-51.4]*	< 0.001 *[1.7]*	63 days	0.002 *[11.0]*	63 days
Radish tops	0.021	63 days	*[40.6-45.1]*	< 0.001 *[1.1]*	63 days	0.002 *[12.3]*	35 days
Wheat forage	0.033	63 days	*[46.2-49.3]*	< 0.001 *[0.5]*	35 days	0.007 *[20.5]*	63 days
Wheat straw	0.063	63 days	*[23.9-40.7]*	< 0.001 *[0.5]*	35 days	0.008 *[12.7]*	63 days
Wheat grain	0.092	63 days	*[48.1-50.8]*	0.002 *[2.3]*	63 days	0.026 *[34.0]*	35 days

Note : The table shows the maximum residue levels in terms of mg/kg (not with regard to % TRR). ^{14}C was shown to be included in natural molecules.

Plant metabolism studies

Conclusion for rotational crops

- Overall, 5 confined rotational crop studies are available for glyphosate. Diverse study designs were used but ^{14}C glyphosate was always applied in excess of the intended maximum annual application rate of 2.16 kg ae/ha for the representative use in annual crops.
- As expected, the nature of residues in rotational crops is similar to the nature of residues in annual conventional crops after pre-seeding, pre-planting or pre-emergence use of glyphosate. The relevant residue components are parent glyphosate and AMPA. A significant portion of the radioactivity is found in natural molecules (extractable or not) due to incorporation of ^{14}C.
- Overall, the residues of parent glyphosate and AMPA in relevant food and feed commodities were below 0.05 mg/kg (LOQ of the residue analytical method) except in pea pods where residues of glyphosate up to 0.13 mg/kg were found (wheat forage and chaff are not relevant feed commodities in the EU).
- Since parent glyphosate does not accumulate in soil, there is no need to consider any plateau level for parent glyphosate. A more thorough evaluation is necessary for AMPA. Some of the studies include soil analyses which allow comparison with the PEC_{soil}.

Livestock Metabolism

Livestock metabolism studies

Conclusion

- The metabolism of glyphosate, AMPA and N-acetyl glyphosate in ruminants and poultry is well understood.
- In the goat and hen metabolism studies conducted with ^{14}C glyphosate and ^{14}C AMPA the only relevant residue components were parent glyphosate and AMPA. To some extent, radioactivity was also incorporated in natural molecules.
- In the goat and hen metabolism studies with ^{14}C N-acetyl glyphosate, the residues consisted of glyphosate, AMPA, N-acetyl glyphosate and N-acetyl AMPA suggesting the occurrence of both de-alkylation and de-acetylation reactions.
- All the studies were conducted at highly exaggerated dose levels and the transfer of residues in milk, eggs and edible tissues was low. The highest residues were found in the detoxification organs (liver and especially kidney) and, as expected, there was no accumulation in fat tissues.

Field residue studies

Field residue trials

Grape plantations

- A total of 8 trials from the southern zone and 9 trials from the northern zone are available to support the use of glyphosate in grape plantations. The trials from the northern zone are new in that they were not yet evaluated at EU level.
- The compound was applied to the ground at the rate of 3.6 kg ae/ha 7 days before harvest.
- At harvest, 7 days after application, separate samples of grape bunches were collected in duplicate from the lower part of the vines and from the upper part of the vines (4 samples in total).
- All samples of grape bunches showed residues of parent glyphosate < 0.05 mg/kg (LOQ) and also residues of AMPA < 0.05 mg/kg (LOQ, expressed as AMPA).
- Since no residue data are available for vine leaves, harvesting of vine leaves for food purposes must not be allowed (mitigation measure).

➡ Suitable residue data are available to support the representative use of glyphosate in grape plantations.

Field residue trials

Top fruit plantations – Overview of available data

Crop	Company	Number of trials		Number of applications	Rate (kg ae/ha)	PHI (days)	Residue levels (mg/kg)	
		EUS	EUN				Glyphosate	AMPA
Mandarin [new]	SYN	2	-	1	2.5-2.7	0	< 0.05	< 0.05
Tree nuts [new]	BAG	2	-	1	3.2	7	< 0.05	< 0.05
Apple [new]	SYN	2	2	1	2.9-3.0	0	< 0.05	< 0.05
Apricot [new]	BAG	4	-	1	3.2	7	< 0.05	< 0.05
Apricot [new]	NUF	1	-	1	2.9	21	< 0.05	< 0.05
Cherry	BAG	-	2	1	4.2	14	< 0.05	< 0.05
Cherry [new]	SYN	2	-	1	2.8	0	< 0.05	< 0.05
Peach	BAG	2	-	1	4.3	7	< 0.05	< 0.05
Peach [new]	NUF	2	-	1	2.9	21	< 0.05	< 0.05
Plum [new]	NUF	1	3	1	2.9	21	< 0.05	< 0.05
Plum [new]	SYN	2	-	1	2.7-3.0	0	< 0.05	< 0.05
Kiwi [new]	BAG	2	-	1	3.2	7	< 0.05	< 0.05
Banana [new]	BAG	4	-	1	3.2	7	< 0.05	< 0.05

Field residue trials

Top fruit plantations

Question to AGG

Does the AGG agree that the available residue trials allow to support the representative use of glyphosate in top fruit plantations (both in the southern and in the northern zone) ?

Field residue trials

Pre-sowing and pre-planting use in annual crops

- Overview of trials evaluated during the previous EU review

Crop	Number of trials		Number of applications	Rate (kg ae/ha)	Days after treatment	Residue levels (mg/kg)	
	EUS	EUN				Glyphosate	AMPA
Carrot	2	2	1	2.3	93-176	< 0.05	< 0.05
Potato	2	2	1	2.3	98-138	< 0.05	< 0.05
Onion	2	2	1	2.3	129-154	< 0.05	< 0.05
Tomato	-	2	1	2.3	93-94	< 0.05	< 0.05
Cucumber	1	-	1	2.3	42	< 0.05	< 0.05
Courgette	1	1	1	2.3	25-52	< 0.05	< 0.05
Cauliflower	2	2	1	2.3	75-125	< 0.05	< 0.05
Head cabbage	2	2	1	2.3	67-97	< 0.05	< 0.05
Lettuce	2	2	1	2.3	38-56	< 0.05	< 0.05
Leek	2	2	1	2.3	65-183	< 0.05	< 0.05
Sugar beet	-	4	1	1.8	120-157	< 0.05	< 0.05
Sugar beet	2	-	1	2.3	144-152	< 0.05	< 0.05

Field residue trials

Pre-sowing and pre-planting use in annual crops

Question to AGG

Does the AGG consider that the residue trials evaluated during the previous EU review allow to support the representative use of glyphosate for pre-sowing or pre-planting weed control in :

- Root & tuber vegetables
- Bulb vegetables
- Fruiting vegetables
- Brassica
- Leafy vegetables
- Stem vegetables
- Sugar beet

(both in the southern and in the northern zone) ?

Livestock feeding studies

Livestock feeding studies

Dietary burden estimation

- It was assumed that the residues in all raw agricultural commodities are < LOQ (0.126 mg/kg for the sum of glyphosate and AMPA). For the processed commodities, the default processing factors were considered (which results in a gross overestimate of reality).

Relevant groups	Dietary burden expressed in				Most critical diet (a)	Most critical commodity (b)		Trigger exceeded (Yes/No) 0.004 mg/kg bw/d
	mg/kg bw/d		mg/kg DM					
	Median	Maximum	Median	Maximum				
Cattle (all diets)	0.057	0.057	1.49	1.49	Dairy cattle	Beet, sugar	ensiled pulp	Yes
Cattle (dairy only)	0.057	0.057	1.49	1.49	Dairy cattle	Beet, sugar	ensiled pulp	Yes
Sheep (all diets)	0.090	0.090	2.71	2.71	Ram/Ewe	Potato	dried pulp	Yes
Sheep (ewe only)	0.090	0.090	2.71	2.71	Ram/Ewe	Potato	dried pulp	Yes
Swine (all diets)	0.051	0.051	1.69	1.69	Swine (finishing)	Potato	dried pulp	Yes
Poultry (all diets)	0.094	0.094	1.33	1.33	Poultry broiler	Potato	dried pulp	Yes
Poultry (layer only)	0.074	0.074	1.09	1.09	Poultry layer	Potato	dried pulp	Yes

Livestock feeding studies

Conclusion

- The results of the cow, hen and swine feeding studies are consistent with the livestock metabolism studies in that the transfer of residues in milk, eggs and edible tissues was low. The highest residues were found in the detoxification organs (liver and especially kidney) and there was no accumulation in fat tissues.
- Based on the dietary burden estimates for the representative uses, the residues in milk, eggs and edible tissues are not expected to exceed the limit of quantification (0.063 mg/kg for the sum of glyphosate and AMPA, expressed as glyphosate).

Processing studies

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Processing studies

Nature of residues

- A hydrolysis study with ^{14}C-glyphosate shows that glyphosate does not degrade in any other compound under conditions representative of pasteurisation, baking/brewing/boiling or sterilisation.
- A new hydrolysis study to investigate the stability of AMPA upon processing has been commissioned. Since no ^{14}C AMPA is currently available, the study will be conducted with ^{12}C AMPA. If the concentration of AMPA in the buffered solutions remains stable during the tests it can be concluded that AMPA is stable and that no degradation product is formed in significant amounts upon processing.

Question to AGG

Is the proposed study design considered appropriate by the AGG ?

Processing studies

Magnitude of residues

- Since the representative uses are not expected to result in residues ≥ LOQ (0.05 mg/kg per residue component) and since for these representative uses no single commodity is expected to account for more than 10% of the ADI or more than 10% of the ARfD, there is no need to investigate the transfer of glyphosate-derived residues in processed commodities.

Question to AGG

Does the AGG agree that studies on the magnitude of residues in processed commodities are not needed to support the intended representative uses ?

Residues in rotational crops

Residues in rotational crops

- EFSA Conclusions, 2015 : *“Significant residues of glyphosate or AMPA are not expected in rotational crops.”*
- Article 12 review, 2018 : *“In conclusion, (…) residues of glyphosate or AMPA are not expected in rotational root and leafy crops following annual application of glyphosate (…). Residues of glyphosate and its metabolite AMPA above the LOQ of 0.05 mg/kg cannot be excluded in cereals grain (only AMPA), forage and chaff grown in rotation with crops treated with glyphosate. (…) MSs are recommended to implement proper mitigation measures (…) Moreover, as the available studies do not cover the plateau concentration calculated for AMPA, proper mitigation measures should also be implemented to avoid accumulation of AMPA in soil and possible uptake of AMPA in rotational crops.”*

Question to AGG

Owing to the conclusions of the previous EU-review, no field rotational crop trials have been initiated so far. Is it possible to address the possible uptake of parent glyphosate and AMPA residues in rotational crops with trials for pre-sowing, pre-planting, or pre-emergence uses of the active substance ?

Residues in honey

Residues in honey

Data requirements and technical guideline

- The investigation of residues in bee products is a new data requirement according to Regulation (EU) 283/2013.
- A technical guideline “for determining the magnitude of pesticide residues in honey and setting Maximum Residue Levels in honey” (SANTE/11956/2016 rev. 9) was released in September 2018 and applies from 01 January 2020 onwards.
  - *The guideline includes a decision scheme to determine under which conditions a specific MRL needs to be set for honey (other than the default MRL of 0.05 mg/kg).*
  - *The main parameter in the decision scheme is the level of residues in the treated crop aerial parts. This does not seem to properly cover the case of herbicides that are not applied directly to the crop.*
  - *However, the document also states that residues in honey may occur from “uses on non-target plants (in-field weeds and adjacent plants) when a substance is applied during the flowering period from April to September”. It may be inferred that in the case of herbicides the relevant parameter relates to the residues in treated (flowering) weeds and that honey residue studies are triggered if the residues in flowering weeds exceed 0.5 mg/kg (between 0.05 mg/kg and 0.5 mg/kg, the honey MRL may be derived directly from the residues in treated weeds).*

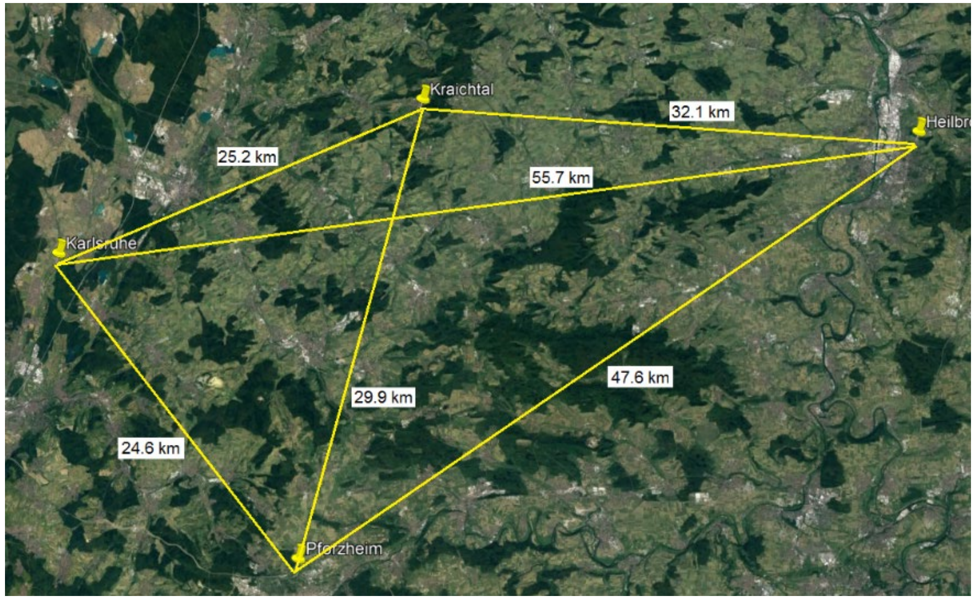
  ➡ *The GTF2, therefore, decided to conduct a (new) tunnel honey residue study.*

Residues in honey

Study design (1)

- The study consists of 4 tunnel trials located at different sites. Due to the short timeline, all the trials were performed in the southern part of Germany. But, in accordance with the guideline, the test sites for the tunnels were located at least 10 km apart. Furthermore, the trials were slightly staggered in time.

Trial	Location	Start (Test item application)
01	Pforzheim	01-04 July
02	Karlsruhe	15 July
03	Kraichtal	18 July
04	Heilbronn	03 September



Residues in honey

Study design (2)

- In order to simulate the case of bees foraging on in-field treated weeds, the flowering phacelia in the tunnel was treated at the maximum supported single rate (i.e. 2.16 kg as/ha). A treatment at the maximum seasonal rate was not considered appropriate since the minimum interval of 21-28 days between applications ensures that the same weed does not receive more than one application.

- The treated phacelia decayed and became unattractive to bees within a few days (end of flowering). In accordance with the guideline, once this happened (i.e. when less than 2 bees/m²/10-15 sec were observed) the colonies were moved to a “monitoring site” with sufficient food sources for the bees to forage on (e.g. wild flowers) but without main flowering crops in the near surroundings. The same monitoring site was used for all trials. Ripe honey was sampled as soon as possible (comb closure).

- The weight of the combs for honey sampling was determined prior to the tunnel phase (when the combs were empty), at the time when the colonies were moved from the tunnel to a monitoring site and again before sampling of mature honey. This allows, if needed, to roughly estimate the relative amount of honey produced during the two parts of the field phase.

Residues in honey

Study results

Trial	Location	Field phase duration (days)		Weight of collected honey (g)		Residue levels (mg/kg)			
						Control		Treated	
		Tunnel	Monitoring	Control	Treated	Glyphosate	AMPA	Glyphosate	AMPA
01	Pforzheim	5	3	127	79	n.d.	n.d.	6.92	0.03
02	Karlsruhe	4	5	84	167	n.d.	n.d.	0.87	n.d.
03	Kraichtal	4	5	89	59	n.d.	n.d.	3.24	< LOQ
04	Heilbronn	5	4	9	6	n.d.	n.d.	n.d.	n.d.

Question to AGG

GTF2 believes that the residues in honey study set-up does not present an appropriate way to conclude on a realistic MRL for Glyphosate in honey. GTF2 proposes to rather use monitoring data (see next slide).

Residues in honey

Monitoring data

- According to the technical guideline an MRL in honey may be set based on monitoring data.
- In total 406 honey samples were analysed for glyphosate residues by Austrian, German and Dutch authorities in 2016-2017 as part of their respective national pesticide residue programme. Some samples were analysed in duplicate. A total of 42 samples showed residues above the LOQ but only 28 samples (6.9%) showed average residues ≥ 0.05 mg/kg. Based on the 99.5th percentile of all data, an MRL of 0.3 mg/kg may be proposed (extraneous MRL approach).
- Based on the available monitoring data, the residue levels found in the honey residue study are highly exaggerated, which may be accounted for by the unrealistic study design (bees foraging almost exclusively on treated weeds).

Question to AGG

In case the honey MRL was set based on monitoring data, would these data have to originate from an official monitoring programme or would they have to be generated by the GTF2 ?

In the latter case, what would be the proper design of a monitoring study for the derivation of an MRL in honey (minimum number of samples, origin of samples, …) ?

Dietary risk assessment

Consumer risk assessment

- Residues in all food commodities of plant origin were assumed to be < LOQ (0.126 mg/kg for the sum of glyphosate and AMPA).
- Residues in all food commodities of animal origin, except honey, were assumed to be < LOQ (0.063 mg/kg for the sum of glyphosate and AMPA).
- The assessment was conducted based on the current toxicity reference values (ADI of 0.5 mg/kg bw/day and ARfD of 0.5 mg/kg bw).
- Based on PRIMo 3.1 the chronic exposure does not exceed 3% of ADI (NL toddler) while the maximum acute exposure is estimated at 4% of ARfD (consumption of potatoes by children).

➡ The representative uses for weed control in established top fruit and grape plantations as well as before sowing or planting annual crops are not expected to harm the health of consumers.

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Thank you!