Taylor & Francis
Taylor & Francis Group

Food Additives & Contaminants: Part B
Surveillance

ISSN: 1939-3210 (Print) 1939-3229 (Online) Journal homepage: http://www.tandfonline.com/loi/tfab20

Glyphosate residues in Swiss market foods: monitoring and risk evaluation

Otmar Zoller, Peter Rhyn, Heinz Rupp, Jürg A. Zarn & Christoph Geiser

To cite this article: Otmar Zoller, Peter Rhyn, Heinz Rupp, Jürg A. Zarn & Christoph Geiser (2018): Glyphosate residues in Swiss market foods: monitoring and risk evaluation, Food Additives & Contaminants: Part B, DOI: 10.1080/19393210.2017.1419509

To link to this article: https://doi.org/10.1080/19393210.2017.1419509

FOOD ADDITIVES & CONTAMINANTS: PART B, 2017
https://doi.org/10.1080/19393210.2017.1419509

Taylor & Francis
Taylor & Francis Group

Glyphosate residues in Swiss market foods: monitoring and risk evaluation

Otmar Zoller, Peter Rhyn, Heinz Rupp, Jürg A. Zarn and Christoph Geiser

Risk Assessment Division, Federal Food Safety and Veterinary Office (FSVO), Bern, Switzerland

ABSTRACT

A total of 243 samples of diverse foodstuffs were analysed for glyphosate and aminomethylphosphonic acid (AMPA) using a liquid chromatography triple quadrupole mass spectrometry (LC/MS/MS) method with a relatively low limit of quantification in the range of 0.0005–0.0025 mg kg^{-1}. Main contributors for dietary glyphosate and AMPA intake were cereals and pulses. The results suggest that pasta is a very important foodstuff for dietary glyphosate residue intake in Switzerland. Interestingly all samples of wine, fruit juice and nearly all samples of honey tested positive for glyphosate although at very low levels. A dietary risk assessment was conducted. Food products for analysis were not selected purely at random, rather products were selected for which high levels of glyphosate residues were suspected. However, even in samples where high residue levels were expected, no exceedances of maximum residue levels were found. Consequently, human exposure did not exceed neither acceptable daily intake nor acute reference dose. Therefore, glyphosate residues found in the sampled foodstuffs from the Swiss market were of no concern for human health.

ARTICLE HISTORY
Received 14 September 2017
Accepted 17 December 2017

KEYWORDS
Glyphosate; aminomethylphosphonic acid; 2-amino-3-phosphonopropionic acid; food monitoring; risk assessment

Introduction

N-(Phosphonomethyl)-glycine (glyphosate, CAS RN® 1071-83-6) is a systemic herbicide that competitively inhibits the enzyme 5-enolpyruvylshikimate-3-phosphate synthase and thereby blocks the plant's biosynthesis of aromatic amino acids (Duke and Powles 2008). The main environmental biodegradation product of glyphosate is aminomethylphosphonic acid (AMPA, CAS RN® 1066-51-9) (Borggaard and Gimsing 2008). In animals and plants, glyphosate is poorly metabolised with AMPA being the main metabolite (EFSA 2015; FAO/WHO 2016). Besides its use as total herbicide and preharvest desiccant, glyphosate has become an important tool in growing genetically modified glyphosate-resistant crops (Benbrook 2016).

In recent years, human health concerns have been raised regarding the exposure of operators, bystanders, and residents to glyphosate-based pesticides during spraying as well as regarding the exposure of consumers to glyphosate residues in food crops (Myers et al. 2016). The major concerns raised were putative carcinogenic and teratogenic potentials of glyphosate. Several bodies have evaluated glyphosate's toxicological profile within their specific remits. The International Agency for Research on Cancer (IARC 2015) has recently evaluated glyphosate for its carcinogenic potential and concluded that "Glyphosate is probably carcinogenic to humans (Group 2A)". This conclusion was based on the evaluation of the publicly available data including data on the active ingredient glyphosate as well as on glyphosate-containing formulated products. The European Chemicals Agency's (ECHA) Committee for Risk Assessment (RAC) concluded that the "available scientific evidence did not meet the criteria in the CLP Regulation to classify glyphosate for specific target organ toxicity, or as a carcinogen, as a mutagen or for reproductive toxicity" based on all available data on the active ingredient glyphosate, including industry data (ECHA 2017). Besides these hazard-related assessments, possible risks to consumers due to glyphosate residues expected in food crops were evaluated. The European Food Safety Authority (EFSA) derived an acceptable daily intake (ADI) and an acute reference dose (ARfD) both amounting to 0.5 mg kg^{-1} body weight (bw)/day (EFSA 2015). The Joint FAO/WHO Meeting on Pesticide Residues derived an ADI of 0–1 mg kg^{-1} bw day^{-1} and considered it not necessary to derive an ARfD in view of glyphosate's low acute toxicity (FAO/WHO 2016). Both bodies concluded that both glyphosate and AMPA are of similar toxic potency and that the maximum residue level (MRL) set for glyphosate and expected exposures of consumers to residues in food crops are safe. The reasons why different evaluating bodies reached

CONTACT Otmar Zoller otmar.zoller@blv.admin.ch
Supplemental data for this article can be accessed here.

contradictory conclusions regarding glyphosate's carcinogenic hazard were recently reviewed (Portier et al. 2016; Tarazona et al. 2017).

Glyphosate containing products for weed control in food crops are authorised in Switzerland for pome and stone fruits, viticulture and blackberries, exclusively. Such applications are considered as not relevant for residues and MRLs are typically set at the limit of quantification (LOQ) of 0.1 mg kg^{-1} (EU 2013). Neither uses on cereals or oilseeds nor applications yielding higher residue levels such as desiccation or applications on genetically modified crops are registered in Switzerland. However, cereals and pulses on which glyphosate has been applied as a preharvest desiccant may be imported to Switzerland and higher MRLs are allocated to cereals, consequently.

In animals, ca. 20% of orally administered glyphosate is absorbed from the gastrointestinal tract whereas the rest is mostly eliminated unchanged via the faeces. Glyphosate does not bioaccumulate and is poorly metabolised (EFSA 2015). Therefore, urine levels of glyphosate and AMPA are good markers for exposure. Exposure of Swiss consumers to glyphosate has been demonstrated. In ca. 40% of a small study of 40 participants, glyphosate was detected in urine at levels of 0.1–1.5 ng mL^{-1} (RTS 2015). More comprehensive data on glyphosate urine levels in Swiss consumers are currently not available. However, analyses in Germany demonstrated low levels of glyphosate and its degradation product AMPA in consumers' urine (Conrad et al. 2017). Roughly, in 30–50% of the urine samples glyphosate and AMPA were found above the LOQ of 0.1 ng mL^{-1}. The median levels for both glyphosate and AMPA were well below 0.5 ng mL^{-1} and maximum values slightly above. From both studies, we estimated consumer exposure to glyphosate in Switzerland to be similar to that in Germany.

Since authorised glyphosate use in Switzerland is not considered to lead to formation of relevant residues in foodstuffs, we assumed that the exposure to glyphosate of the population in Switzerland mainly stems from consumption of imported cereal commodities. This study should help to clarify if this assumption is valid. Moreover, as there are limited data published with a LOQ below 0.05 mg kg^{-1}, it is important to determine if foodstuffs are contaminated on a large scale at very low levels, i.e. clearly below the LOQ as set in EU legislation which is 0.1 mg kg^{-1} for plant products and 0.05 mg kg^{-1} for animal products. There is also lack of information concerning carryover of glyphosate at the low ng g^{-1} level during transportation, storage, and processing of foodstuffs.

The scope of the present work is to identify food commodities significantly contributing to the glyphosate exposure of Swiss consumers. Furthermore, based on the measured residues on assessed food commodities, a dietary risk assessment is performed. Finally, a rough appraisal is conducted regarding a possible correlation between glyphosate levels in urine and in the investigated foods.

Material and methods

Samples

In total, 243 samples were analysed. All samples were bought in retail stores with the aim to represent a wide range of food products. Usually a single consumer package of 500–2000 g was sampled, irrespective of the lot size. When necessary, samples were homogenised using different mills and mixing devices to a particle size of about 0.1 mm before further processing.

Chemicals, reagents, and consumables

All solvents were obtained in LC-MS grade (Chromasolv®) from Sigma-Aldrich (Buchs, Switzerland), as well as formic acid. Ultrapure water, further referred to as water, was obtained from an Elga Purelab ultra-water purification system (Labtec Services, Villmergen, Switzerland). Glyphosate standards and AMPA were obtained from Sigma-Aldrich; glyphosate internal standard (IS) $^{13}C_3$-D_2-Glyphosate from Alsachim (Illkirch-Graffenstaden, France); AMPA IS ^{13}C-^{15}N-AMPA from Dr. Ehrenstorfer (LGC Standards, Teddington, UK). All dilutions of standard solutions were prepared in water except the last dilution for standards ready for injection where dilution solvent was used. These dilutions were made in 20 mL vials, which were rinsed with water and methanol before use.

The extraction solvent was a water/methanol 1:1 (v/v) mixture with 0.5% formic acid; the dilution solvent was a water/acetonitrile 1:1 (v/v) mixture with 0.2% formic acid; the glyphosate IS and the AMPA IS solutions were 5000 ng mL^{-1} in water; the glyphosate and the AMPA stock solutions were 250 ng mL^{-1} in water; the calibration working solutions were 0.004 mL each of glyphosate IS and of AMPA IS solutions, ranging 0–0.060 mL of both stock solutions, respectively and extraction solvent up to 0.500 mL. The calibration injection solutions for solid samples were 0.100 mL of calibration working solutions diluted with 0.400 mL of dilution solvent. Similar for liquid samples, but dilution with 0.200 mL of dilution solvent.

The applied consumables were 2 and 50 mL centrifuge vials, polypropylene (PP) tubes, high density polyethylene (PE) screw caps (Eppendorf, Hamburg, Germany); 20 mL super PE vials for liquid scintillation (PerkinElmer, Waltham, MA, USA); 0.6 mL PE autosampler vials (06-

PESV, Chromacol, Thermo Fisher Scientific Inc., Waltham, MA, USA); PP pipet tips for microman (Gilson Inc., Middleton, WI, USA); solid-phase extraction (SPE) cartridges Oasis HLB, 3 cc, 60 mg sorbent (Waters, Milford, MA, USA).

Sample preparation

Solid samples

Five gram of the homogenous or homogenised sample was weighed (rounded to the next 10 mg) into a 50 mL centrifuge vial and 20 mL of extraction solvent and 0.160 mL each of IS solutions were added. The tube was vigorously shaken by hand, then treated for 10 min in an ultrasound bath and shaken for 30 min on a shaker (Innova 2000, Eppendorf, Hamburg, Germany) at 400 rpm. The mixture was then centrifuged for 10 min at 2500 relative centrifugal force (RCF) and 10°C. Two times 1.5 mL of the supernatant was transferred into a 2 mL centrifuge vial and centrifuged for 10 min at 20,000 RCF. The combined supernatants were the final extract. Clean-up was performed on a SPE cartridge, which was first activated with 2 mL of methanol, conditioned with 2 mL of extraction solvent and pre-rinsed with 0.5 mL of extract. The eluate was discarded up to this step. A further 0.4 mL of extract was loaded onto the cartridge, the eluate collected in a 2 mL centrifuge vial and 0.100 mL of this eluate was diluted with 0.400 mL of dilution solvent in an autosampler vial.

Liquid samples

Five millitre of degassed (20 s in an ultrasound bath) beverage was transferred into a 50 mL centrifuge vial and 5 mL of extraction solvent and 0.080 mL each of IS solutions were added. The tube was shaken by hand. The SPE cartridge clean-up was performed as described above, only differing in the last step where 0.100 mL of the final eluate was diluted with 0.200 mL of dilution solvent in an autosampler vial.

Calibration

A 6-point calibration curve, corresponding to a range of 0–0.120 mg kg^{-1} for solid samples and a range of 0–0.060 mg L^{-1} for liquid samples, was constructed. If a sample contained a higher concentration, an extract using a lower amount of sample was prepared or further calibration points were introduced.

LC/MS/MS conditions

LC-system and conditions

A Symbiosis-System (Spark Holland B.V., Emmen, The Netherlands) was used with the following parameters: injection volume 10 µL; column BioRad Micro-Guard Cation H Refill Cartridge 30 × 4.6 mm (BioRad, Hercules, CA, USA); column oven at 40°C; elution solvent A: water; elution solvent B: acetonitrile with 0.2% formic acid; program: 0:00 flow rate 0.5 mL min^{-1} 60% A; 1:00 flow rate 0.5 mL min^{-1} 60% A; 1:30 flow rate 0.5 mL min^{-1} 99% A; 3:30 flow rate 0.5 mL min^{-1} 99% A; 3:35 flow rate 0.8 mL min^{-1} 99% A; 7:50 flow rate 0.8 mL min^{-1} 99% A; 8:00 flow rate 0.8 mL min^{-1} 60% A; 10:00 flow rate 0.5 mL min^{-1} 60% A; 10:10 flow rate 0.5 mL min^{-1} 60% A. The use of a specific rinsing procedure was important to minimise carryover and contamination. Needle rinsing was performed as follows: 500 µl water/methanol/acetonitrile 8:1:1 (v/v) followed by 700 µl water/methanol 1:1 (v/v) with 0.1% phosphoric acid 85% and finishing with 500 µl water/acetonitrile 6:4(v/v) with 0.1 % formic acid. After each sample, a blank run was carried out.

MS/MS-system and conditions

An API 5000 (AB Sciex Netherlands B.V., Nieuwerkerk aan den Ijssel, The Netherlands) with electrospray ionisation in negative mode was used and scheduled multiple reaction monitoring was applied. The eluent in the first 1.5 min was diverted into waste. The optimised ionisation source parameters were source temperature, 650°C; ionisation voltage –4500 V; curtain gas, 25 units; collision gas, 5 units; gas 1, 60 units; gas 2, 50 units; Dwell time, 50 ms. The transitions measured were the following (quantifier in bold): glyphosate, 168 → 150, 168 → 124, 168 → 79, **168 → 63**; glyphosate IS, 173 → 128, 173 → 81, **173 → 63**; AMPA, 110 → 81, 110 → 79, **110 → 63**; AMPA IS, 112 → 81, 112 → 79, **112 → 63**.

Method validation

The applied anion exchange method was based on the methods published by Guo et al. (2016) and Jensen et al. (2016). Validation of the analytical method was based on repeated experiments verifying limit of detection (LOD), LOQ, repeatability, and recovery in different matrices. Internal reference materials were used in each run. For the LOQ, the signal-to-noise threshold was set at 10 for the quantifier and at 7 for the two qualifiers. In addition, two external reference materials of wheat flour and rapeseed and the respective blank materials were analysed on a regular basis: reference material P1601-RMWh, wheat flour spiked with glyphosate,

AMPA, glufosinate; blank material P1601-BLWh, wheat flour; reference material P1601-RMRape, rapeseed spiked with glyphosate, AMPA, glufosinate; blank material P1601-BLRape, rapeseed; all from PROOF-ACS GmbH (Hamburg, Germany). Further details of these reference materials are given in the explanation to Table 1. A Food Analysis Performance Assessment Scheme (FAPAS 2017) proficiency test on oat test material with chlormequat, mepiquat, and glyphosate was also completed, of which only glyphosate was analysed.

Results and discussion

Method quality assurance

The method showed to be very robust and can be applied for nearly all kind of foodstuffs. It turned out that it is not necessary to use matrix-matched calibration. The absolute recovery was estimated using the absolute peak area of the IS. The absolute recovery was always better than 70% for liquid samples and for solid samples it was always better than 50% and in most cases also better than 70%. Dilution experiments with naturally contaminated samples with concentrations above 0.05 mg kg^{-1} showed identical quantitative results. There was no indication for disturbing matrix effects in the undiluted sample. The LOQ for solid samples was generally 0.001 and 0.0025 mg kg^{-1} for glyphosate and AMPA, respectively. For liquid samples (i.e. beverages like wine and beer), the LOQ was 0.0005 mg kg^{-1} for glyphosate and 0.0005–0.001 mg kg^{-1} for AMPA. Details of the performance data of the method are given in Table 1. The FAPAS proficiency test (2017) was successfully passed with a *z*-score of 0.9 at the assigned value for glyphosate of 0.483 mg kg^{-1}. This level was appropriate for the validation of the higher levels that were measured, for instance in durum wheat and pasta, but not optimal for the lower levels around and below 0.05 mg kg^{-1}. For these levels, the wheat and rapeseed reference materials (PROOF-ACS GmbH)

Table 1. Method performance data.

Analyte	Matrix	LOD [mg kg^{-1}]	LOQ [mg kg^{-1}]	concentration [mg kg^{-1}]	Repetitions (n)	Recovery (%)	RSD (%)	Comments and applied reference materials
Glyphosate	Wheat, white flour	0.0003	0.001	0.001	5	94	9.5	s, st
AMPA	Wheat, white flour	0.001	0.0025	0.005	5	101	6.5	s, st
Glyphosate	Beer	0.0002	0.0005	0.001	5	103	2.2	s, st
AMPA	Beer	0.0005	0.001	0.001	5	97	6.6	s, st
Glyphosate	Beer	0.0002	0.0005	0.010	3	98	7.1	s, st, d
AMPA	Beer	0.0005	0.001	0.010	3	102	0.6	s, st, d
Glyphosate	Wine	0.0002	0.0005	0.010	2	92	9.2	s, st, d
AMPA	Wine	0.0005	0.001	0.010	2	99	5.0	s, st, d
Glyphosate	Milk	0.0002	0.0005	0.004	2	96	1.8	s, st, d
AMPA	Milk	0.0005	0.001	0.004	2	111	1.6	s, st, d
Glyphosate	Honey	0.0003	0.001	0.005	5	92	13.9	s, st, d
AMPA	Honey	0.001	0.0025	0.005	5	115	3.5	s, st, d
Glyphosate	Vegetable oil	0.0004	0.001	0.010	2	102	2.8	s, st, d
AMPA	Vegetable oil	0.001	0.0025	0.010	2	92	6.1	s, st, d
Glyphosate	Smoked salmon	0.0004	0.001	0.010	1	95	N/A	s
AMPA	Smoked salmon	0.001	0.0025	0.010	1	97	N/A	s
Glyphosate	Poultry meat	0.0003	0.001	0.050	3	102	1.3	s, st, d
AMPA	Poultry meat	0.001	0.0025	0.050	3	100	1.3	s, st, d
Glyphosate	Red wine	0.0002	0.0005	0.0132	7	N/A	3.6	nc, lt
AMPA	Red wine	0.0005	0.001	<0.001	7	N/A	N/A	nc, lt
Glyphosate	Whole meal flour	0.0003	0.001	0.051	5	N/A	3.7	nc, st
AMPA	Whole meal flour	0.001	0.0025	0.0036	5	N/A	8.4	nc, st
Glyphosate	Whole meal flour	0.0003	0.001	0.051	22	N/A	5.4	nc, lt
AMPA	Whole meal flour	0.001	0.0025	0.0024	22	N/A	12.5	nc, lt
Glyphosate	Wheat	0.0003	0.001	<0.001	19	N/A	N/A	P1601-BLWh, lt
AMPA	Wheat	0.001	0.0025	<0.0025	19	N/A	N/A	P1601-BLWh, lt
Glyphosate	Wheat	0.0003	0.001	0.0376	21	N/A	8.4	P1601-RMWh, lt
AMPA	Wheat	0.001	0.0025	0.0577	21	N/A	9.1	P1601-RMWh, lt
Glyphosate	Rapeseed	0.0003	0.001	<0.001	3	N/A	N/A	P1601-BLRape, lt
AMPA	Rapeseed	0.001	0.0025	<0.0025	3	N/A	N/A	P1601-BLRape, lt
Glyphosate	Rapeseed	0.0003	0.001	0.0925	3	N/A	2.2	P1601-RMRape, lt
AMPA	Rapeseed	0.001	0.0025	0.0778	3	N/A	3.1	P1601-RMRape, lt

N/A: not applicable; s: spiked; nc: naturally contaminated; st: repetitions within 1 day; lt: repetitions over a time period of 7 months; d: different products; P1601-BLWh; wheat blank material; P1601-RMWh: wheat reference material, spiked level for glyphosate 0.037 mg kg^{-1} and assigned value by proficiency test 0.034 mg kg^{-1}, spiked level for AMPA 0.055 mg kg^{-1} and assigned value by proficiency test 0.050 mg kg^{-1}; P1601-BLRape: rapeseed blank material; P1601-RMRape: rapeseed reference material, spiked level for glyphosate 0.098 mg kg^{-1} and assigned value by proficiency test 0.0859 mg kg^{-1}, spiked level for AMPA 0.088 mg kg^{-1} and assigned value by proficiency test 0.0739 mg kg^{-1}.

with assigned values for glyphosate of 0.034 and 0.086 mg kg^{-1}, respectively, were more appropriate. In Table 1 it is shown that our measurements were in good agreement with the assigned values and also with the spiked values. In the FAPAS 09109b, oats blank material, 0.0057 mg kg^{-1} of glyphosate was measured.

The measurement uncertainty which is indicated in the supporting information is an estimate for the expanded uncertainty with a confidence level of 95%. The values are roughly estimated with the help of the method performance data given in Table 1. Twenty per cent is set as minimum value for the uncertainty. A more conservative approach would be to take the uncertainty from the proficiency tests of the mentioned FAPAS test and PROOF-ACS reference materials. The range of ±2 for *z*-scores is a good estimate for the confidence interval of 95%. In this case, the uncertainty would generally be set at 45% as the uncertainty for all values from the PROOF-ACS materials were between 43.3% and 44.7%. The respective uncertainty for glyphosate in the FAPAS test was 35.6%.

In a few cases where it was suspected that the sample might not be sufficiently homogeneous, another two subsamples were analysed. In all cases, the difference to the first result was well below 10%. In the case of the gram flour with a concentration of 2.756 mg kg^{-1} of glyphosate, which is discussed further down in the text, a package of the same lot could be purchased 6 months later. The measured concentration in the second package differed less than 2% from the first result.

Another peak showing quite similar ion transitions as glyphosate, eluting just after glyphosate, was often observed. This peak was identified as 2-amino-3-phosphonopropionic acid, a substance with identical sum formula and similar functional groups as glyphosate. This compound seems to occur in many products in the range of 0.001–0.5 mg kg^{-1}. For this reason, it can be recommended to check if 2-amino-3-phosphonopropionic acid is properly distinguished from glyphosate in the chromatograms, as to avoid the risk of too high results when analysing glyphosate. 2-Amino-3-phosphonopropionic acid was analysed semi-quantitatively and seems to occur in many products, especially in cereals, in the range of 0.001–0.9 mg kg^{-1}. There was no correlation between the concentration of 2-amino-3-phosphonopropionic acid and glyphosate. From the chemical structure point of view, it seems unlikely that 2-amino-3-phosphonopropionic acid is a metabolite of glyphosate. 2-Amino-3-phosphonopropionic acid may be a natural compound. Its occurrence in the ciliate *Tetrahymena pyriformis* is described by Horsman and Zechel (2017); however, no reference on the occurrence in higher plants is available. This issue will be examined in more detail in the context of another project.

Concentrations in foodstuffs

Food products were sampled with the aim to determine the relevant foodstuffs for glyphosate intake. Samples with higher residue concentrations are probably over-represented to some extent, because categories like pulses and durum wheat were more frequently sampled, since these were suspect to reveal more glyphosate positive results. Additionally, every time when food samples turned out to contain more than 0.01 mg kg^{-1}, a few similar food items were collected. All together survey results are probably not representative for the residue levels in all foodstuffs on the market, as to achieve this goal analysis of a few thousand samples would have been necessary. The results for glyphosate and AMPA are summarised in Table 2 and grouped into different food categories. Detailed data is available as supporting information.

For cereals and pulses, the contamination rate for glyphosate on the level above 0.1 mg kg^{-1} is comparable with data from Germany (Scherbaum et al. 2012) and a bit lower as in the United Kingdom (Stephenson and Harris 2016). The two samples with the highest glyphosate concentration were chickpeas originating from Canada with 2.948 mg kg^{-1} and gram flour (chickpea flour) with 2.756 mg kg^{-1} produced in the United Kingdom with unknown origin of the processed chickpeas. In 24 samples, glyphosate was measured above 0.1 mg kg^{-1}, but all AMPA values were below 0.1 mg kg^{-1} and usually much lower than the respective glyphosate values. Thirteen of 24 samples were durum wheat products like pasta and semolina, 8 samples were pulses and products thereof, 2 further samples were breakfast cereals and the last product was a bread baking mix containing seeds. It could be shown that the main contributor for glyphosate residue in this mix was linseed. There was no hint that 1 of these 24 products contained relevant ingredients of Swiss origin. Pulses are not consumed very often in Switzerland; however, pasta is an important dish of the regional diet. As nearly 100% of durum wheat for the production of pasta is imported, this might be an important commodity regarding glyphosate residues. All samples of wine and fruit juice and all except one sample of honey were positive for glyphosate but all in the low ng g^{-1} range.

Of all analysed samples, 38 were clearly indicated as made of Swiss ingredients. The product with the highest glyphosate concentration of this category was a red

Table 2. Concentrations of glyphosate and AMPA in different food categories.

	Glyphosate								AMPA						
Food category	Number of samples	Number of samples above the LOQ	Proportion of samples above the LOQ	LOQ (mg kg^{-1})	Min (mg kg^{-1})	Median (mg kg^{-1})	Arithmetic mean (mg kg^{-1})	Max (mg kg^{-1})	Number of samples above the LOQ	Proportion of samples above the LOQ	LOQ (mg kg^{-1})	Min (mg kg^{-1})	Median (mg kg^{-1})	Arithmetic mean (mg kg^{-1})	Max (mg kg^{-1})
Beer	15	2	13%	0.0005	<0.0005	<0.0005	0.0006	0.0068	0	0%	0.001	<0.001	<0.001	<0.001	<0.001
Wine	21	21	100%	0.0005	0.0006	0.0031	0.0048	0.0189	4	19%	0.0007	<0.0007	<0.0007	0.0005	0.0034
Mineral water	2	0	0%	0.0005	<0.0005	<0.0005	<0.0005	<0.0005	0	0%	0.0005	<0.0005	<0.0005	<0.0005	<0.0005
Milk	3	0	0%	0.0005	<0.0005	<0.0005	<0.0005	<0.0005	0	0%	0.0025	<0.0025	<0.0025	<0.0025	<0.0025
Fruit juice	11	11	100%	0.0005	0.0005	0.0016	0.0019	0.0035	2	18%	0.0006	<0.0006	<0.0006	0.0002	0.0006
Baby food	11	0	0%	0.001	<0.001	<0.001	<0.001	<0.001	0	0%	0.0025	<0.0025	<0.0025	<0.0025	<0.0025
Potatoes and vegetables	10	3	30%	0.001	<0.001	<0.001	0.0013	0.0077	0	0%	0.0025	<0.0025	<0.0025	<0.0025	<0.0025
Honey	16	15	94%	0.001	<0.001	0.0030	0.0046	0.0159	0	0%	0.0025	<0.0025	<0.0025	<0.0025	<0.0025
Eggs	1	0	0%	0.001	<0.001	<0.001	<0.001	<0.001	0	0%	0.0025	<0.0025	<0.0025	<0.0025	<0.0025
Meat and fish	13	3	23%	0.001	<0.001	<0.001	0.0008	0.0049	0	0%	0.0025	<0.0025	<0.0025	<0.0025	<0.0025
Pulses	41	21	51%	0.001	<0.001	0.0012	0.1733	2.948	10	24%	0.0025	<0.0025	<0.0025	0.0031	0.025
Oilseeds and vegetable oil	6	0	0%	0.001	<0.001	<0.001	<0.001	<0.001	0	0%	0.0025	<0.0025	<0.0025	<0.0025	<0.0025
Pseudo cereals	3	0	0%	0.001	<0.001	<0.001	<0.001	<0.001	0	0%	0.0025	<0.0025	<0.0025	<0.0025	<0.0025
Breakfast cereals	10	8	80%	0.001	<0.001	0.0036	0.0508	0.291	3	30%	0.0025	<0.0025	<0.0025	0.0025	0.010
Durum wheat	18	16	89%	0.001	<0.001	0.139	0.1349	0.421	15	83%	0.0025	<0.0025	0.0107	0.0110	0.0247
Pastry and snacks	11	4	36%	0.001	<0.001	<0.001	0.0037	0.0179	0	0%	0.0025	<0.0025	<0.0025	<0.0025	<0.0025
Bread	10	7	70%	0.001	<0.001	0.0019	0.0069	0.0458	0	0%	0.0025	<0.0025	<0.0025	<0.0025	<0.0025
Flour and baking mixtures	28	8	29%	0.001	<0.001	<0.001	0.0106	0.133	2	7%	0.0025	<0.0025	<0.0025	0.0007	0.0027
Other cereal products	13	2	15%	0.001	<0.001	<0.001	0.0012	0.0124	1	8%	0.0025	<0.0025	<0.0025	0.0007	0.0052

Description of categories: *pulses*: including products thereof like tofu and soy sauce, etc.; *breakfast cereals*: processed breakfast cereals like corn flakes, pops, etc. Rolled oats are placed in the category of other cereal products; *durum wheat*: all products with durum wheat as main ingredient as for instance pasta; *pastry and snacks*: all dry bake goods, sweet or salty, and also tortilla chips and potato chips (crisps); *bread*: also special bread that may contain minor amounts of oilseeds or pulses; *flour and baking mixtures*: flour and baking mixtures for bread making, the main ingredients are bread cereals like wheat, rye, and spelt, but they may also contain minor amounts of other cereals, oilseeds, and pulses; *other cereal products*: category with a wide variety of products like rolled oats, popcorn, semolina of maize (polenta), pasta with wheat instead of durum wheat, etc.; for beverages as beer, wine, milk, fruit juices, and mineral water, the measurement unit is mg L^{-1} instead of mg kg^{-1}. For the calculation of the arithmetic mean, all samples below the LOD were taken as zero; for samples between the LOQ and the LOD, the estimated value was used.

wine containing 0.0132 mg kg^{-1}. All cereal products of this category contained undetectable or low amounts. The highest value found was 0.0025 mg kg^{-1} glyphosate in a wholegrain wheat flour. The number of 38 samples with ingredients of Swiss origin is not large enough as to guarantee that Swiss regulations on the use of glyphosate in agricultural practice are not violated, but at least do not indicate unregistered use of glyphosate, since not one single high contamination was found in food items containing raw products originating from Switzerland.

Also, all products labelled as organic had no or only low residues. In 37 of totally 43 organic samples, the concentration was below the LOQ and only 6 samples showed quantifiable amounts. In three of these six samples the concentration was just above the LOQ and only one sample showed a concentration above 0.01 mg kg^{-1}. This organic sample with the highest glyphosate concentration was a pasta product (spaghetti) containing 0.0123 mg kg^{-1} of glyphosate and 0.0024 mg kg^{-1} of AMPA. On the label, it was indicated that the durum wheat originated from North America, Europe and the eggs from Europe. Carryover during transport and production is conceivable. No detailed data are available to what extent such a contamination is avoidable by using adequate practices. As far as we know there is not yet a binding agreement on how low the residues in organic products should be, but a value of 0.01 mg kg^{-1} is at least under discussion or maybe already partially implemented.

Risk assessment

Based on the measured residues (Table 2), simple exposure estimates were derived (Table 3) and compared to the ARfD and the ADI, both amounting to 0.5 mg kg^{-1} bw day^{-1}, as recently established by EFSA's revaluation (EFSA 2015). Food consumption values applied in the exposure estimation were chosen at a level to overestimate actual daily average consumption. It seems plausible that these amounts of the respective food items are consumed at least occasionally during a single day. Risk assessments, i.e. comparison of estimated residue intake with the ADI and ARfD, were conducted for both the measured median and MRLs found per food item.

None of the median residues found in any food item resulted in an exposure greater than 0.5% of the ADI/ARfD and virtually all are significantly below 0.5% of the ADI/ARfD. If measured MRLs were applied, substantial exposures (ca. 5% of ADI/ARfD in adults and ca. 10% of ADI/ARfD in children) resulted for pulses, exclusively. All other MRLs resulted in exposures that were mostly

Table 3. Exposure to median and maximum glyphosate residue levels and expected urine glyphosate concentrations (nr: not relevant).

	Child of 15 kg body weight				Adult of 60 kg body weight			
		Exposure as % of ADI or ARfD				Exposure of % of ADI or ARfD		
Food category	Consumption (kg or L/day)	At median residue level	At maximum residue level	Expected urine concentration (µg L^{-1})	Consumption (kg or L per day)	At median residue level	At maximum residue level	Expected urine concentration (µg L^{-1})
Beer	nr	nr	nr	nr	0.50	0.0008	0.0113	0.340
Wine	nr	nr	nr	nr	0.25	0.0026	0.0158	0.473
Mineral water	1.00	0.0067	0.0067	0.067	2.00	0.0033	0.0033	0.100
Milk	0.50	0.0033	0.0033	0.033	1.00	0.0017	0.0017	0.050
Fruit juice	0.50	0.0107	0.0233	0.233	1.00	0.0053	0.0117	0.350
Potatoes and vegetables	0.25	0.0033	0.0257	0.257	0.50	0.0017	0.0128	0.385
Honey	0.03	0.0010	0.0053	0.053	0.05	0.0005	0.0027	0.080
Eggs	0.10	0.0013	0.0013	0.013	0.20	0.0007	0.0007	0.020
Meat and fish	0.25	0.0033	0.0163	0.163	0.50	0.0017	0.0082	0.245
Pulses	0.25	0.0033	9.8267	98.27	0.50	0.0017	4.9133	147.4
Oilseeds	0.05	0.0007	0.0007	0.007	0.10	0.0003	0.0003	0.010
Pseudo cereals	0.10	0.0013	0.0013	0.013	0.20	0.0007	0.0007	0.020
Breakfast cereals	0.10	0.0048	0.3880	3.880	0.20	0.0024	0.1940	5.820
Durum wheat	0.25	0.4633	1.4033	14.03	0.50	0.2317	0.7017	21.05
Pastry and snacks	0.05	0.0007	0.0119	0.119	0.10	0.0003	0.0060	0.179
Bread	0.25	0.0063	0.1527	1.527	0.50	0.0032	0.0763	2.290
Flour and baking mixtures	0.25	0.0033	0.4433	4.433	0.50	0.0017	0.2217	6.650
Other cereal products	0.10	0.0013	0.0165	0.165	0.20	0.0007	0.0083	0.248

Exposure per kg body weight is calculated by multiplying the residue concentration in food by the assumed food consumption and dividing the result by body weight (15 kg for children and 60 kg for adults). Risk is expressed by calculating exposure as per cent ADI or ARfD (both amounting to 0.5 mg kg^{-1} bw). Maximally expected urine concentrations are calculated by multiplying maximum residue concentrations in food by the assumed consumption and by the fraction of orally ingested glyphosate excreted by the urine (20%). The obtained result is divided by an assumed daily urine volume of 1.5 L for a child and 2 L for an adult. If residues were below LOQ, the LOQ value was used for risk assessment.

significantly lower than 1% of the ADI/ARfD. It is concluded that none of the residue levels identified in any of the food categories are of any health concern. This is not surprising, as none of the measured residue levels exceeded the legally tolerated MRL.

The exposure estimates for maximum residues derived as described above were also used to predict probable urine concentrations. It was assumed that the amount indicated in Table 3 of the respective food item was ingested and this food item contained the measured MRL of glyphosate (Table 2). Based on toxicokinetic studies, the amount of an orally ingested single dose of glyphosate excreted with the urine was assumed to equal 20% (EFSA 2015). Further, it was assumed that daily urine volumes of 1.5 and 2.0 L are excreted by children and adults, respectively. For glyphosate residues at the maximally measured levels, predicted urine concentrations would be greater than 0.5 µg L^{-1} only for a few commodities. Again, only for the maximum residues found in pulses substantial amounts were predicted in urine of adults (ca. 147 µg L^{-1}). Overall, the predicted urine concentrations correspond very well with actually measured glyphosate urine levels in samples of the human population: Conrad et al. (2017) reported median levels well below 0.5 µg L^{-1} in samples of the German population, while maximum values slightly exceeded 0.5 µg L^{-1}. Also Niemann et al. (2015) concluded that urine concentrations of glyphosate corresponded well with levels in food; however, urine levels of AMPA were somewhat too high and not in good agreement with reported levels in foodstuffs. In a report of glyphosate urine levels in a small, not representative survey of the Swiss population, values in the range of 0.1–1.5 µg L^{-1} (RTS 2015) were measured.

Conclusion

In this market survey, food products for analysis were not selected purely randomly, rather products were selected for which measurable levels of glyphosate residues were suspected. However, even in samples where high residues were expected, no exceedances of MRLs were detected. Consequently, exposures did not exceed neither ADI nor ARfD. Therefore, glyphosate residues found in the sampled foodstuffs from the Swiss market are of no health concern for the consumer. This conclusion may be valid for all food products on the Swiss food market, considering that products for which high residue levels were suspected were over-represented in this survey.

Acknowledgements

The authors thank Emanuel Hänggi from our office and André Känzig from the Cantonal Office of Consumer Protection Aargau for comments on legal issues and for help in sample procurement. We acknowledge Silvia Zeltner and Ursula Ulrich from our office for help with procurement and documentation of samples. We thank as well Vincent Dudler from our office for critically reviewing the manuscript.

Disclosure statement

No potential conflict of interest was reported by the authors.

ORCID

Otmar Zoller http://orcid.org/0000-0003-0956-7604

References

Benbrook CM. 2016. Trends in glyphosate herbicide use in the United States and globally. Environ Sci Eur. 28:3.

Borggaard OK, Gimsing AL. 2008. Fate of glyphosate in soil and the possibility of leaching to ground and surface waters: a review. Pest Manag Sci. 64:441–456.

Conrad A, Schröter-Kermani C, Hoppe HW, Ruther M, Pieper S, Kolossa-Gehring M. 2017. Glyphosate in German adults - time trend (2001 to 2015) of human exposure to a widely used herbicide. Int J Hyg Environ Health. 220:8–16.

Duke SO, Powles SB. 2008. Glyphosate: a once-in-a-century herbicide. Pest Manag Sci. 64:319–325.

ECHA. 2017. Glyphosate not classified as a carcinogen by ECHA. Available from: https://echa.europa.eu/-/glyphosate-not-classified-as-a-carcinogen-by-echa

EFSA. 2015. Conclusion on the peer review of the pesticide risk assessment of the active substance glyphosate. EFSA J. 13(11):4302.

EU. 2013. Commission Regulation (EU) No 293/2013 of 20 March 2013 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for emamectin benzoate, etofenprox, etoxazole, flutriafol, glyphosate, phosmet, pyraclostrobin, spinosad and spirotetramat in or on certain products. Off J Eur Union L. 96:1–30.

FAO/WHO. 2016. Pesticide residues in food 2016. Available from: http://www.fao.org/3/a-i5693e.pdf

FAPAS. 2017. Food Analysis Performance Assessment Scheme. Food Chemistry Proficiency Test Report 09109, Pesticide residues in oats. April-June 2017, Fera Science Ltd (Fera), National Agri-Food Innovation Campus, Sand Hutton, York, YO41 1LZ, UK.

Guo H, Riter LS, Wujcik CE, Armstrong DW. 2016. Direct and sensitive determination of glyphosate and aminomethylphosphonic acid in environmental water samples by high performance liquid chromatography coupled to electrospray tandem mass spectrometry. J Chromatogr. 1443:93–100.

Horsman GP, Zechel DL. 2017. Phosphonate biochemistry. Chem Rev. 117:5704–5783.

IARC. 2015. Some organophosphate insecticides and herbicides: diazinon, glyphosate, malathion, parathion, and tetrachlorvinphos. 112. Available from: http://monographs.iarc.fr/ENG/Monographs/vol112/index.php

Jensen PK, Wujcik CE, McGuire MK, McGuire MA. 2016. Validation of reliable and selective methods for direct determination of glyphosate and aminomethylphosphonic acid in milk and urine using LC-MS/MS. J Environ Sci Health B. 51:254–259.

Myers JP, Antoniou MN, Blumberg B, Carroll L, Colborn T, Everett LG, Hansen M, Landrigan PJ, Lanphear BP, Mesnage R, et al. 2016. Concerns over use of glyphosate-based herbicides and risks associated with exposures: a consensus statement. Environ Health. 15:19.

Niemann L, Sieke C, Pfeil R, Solecki R. 2015. A critical review of glyphosate findings in human urine samples and comparison with the exposure of operators and consumers. J Verbr Lebensm. 10:3–12.

Portier CJ, Armstrong BK, Baguley BC, Baur X, Belyaev I, Bellé R, Belpoggi F, Biggeri A, Bosland MC, Bruzzi P, et al. 2016. Differences in the carcinogenic evaluation of glyphosate between the International Agency for Research on Cancer (IARC) and the European Food Safety Authority (EFSA). J Epidemiol Community Health. 70:741–745.

RTS. 2015. Du glyphosate, herbicide contesté, découvert dans l'urine des Romands. Available from: https://www.rts.ch/info/suisse/7125072-du-glyphosate-herbicide-conteste-decouvert-dans-l-urine-des-romands.html

Scherbaum E, Wolheim A, Kolberg D, Wildgrube C. 2012. Much in Use, Seldom Present – Residues from Glyphosate in Cereals. Report from a day in the lab. Chemisches und Veterinäruntersuchungsamt Stuttgart. Epub 2012/ 09/27. Available from http://www.cvuas.de/pub/beitrag.asp?subid=1&Thema_ID=5&ID=1613&Pdf=No&lang=EN

Stephenson CL, Harris CA. 2016. An assessment of dietary exposure to glyphosate using refined deterministic and probabilistic methods. Food Chem Toxicol. 95:28–41.

Tarazona JV, Court-Marques D, Tiramani M, Reich H, Pfeil R, Istace F, Crivellente F. 2017. Glyphosate toxicity and carcinogenicity: a review of the scientific basis of the European Union assessment and its differences with IARC. Arch Toxicol. 91:2723–27431.