Glyphosate in Urine - Concentrations are far below the range indicating a potential health hazard

BfR Opinion No. 014/2013 of 14 June 2013

According to information provided by Friends of the Earth Germany (BUND), 182 urine samples from people in 18 European countries were tested for the occurrence of the herbicidic active substance glyphosate. The maximum concentration of glyphosate found was 1.82 micrograms per litre of urine. Concentrations of the metabolite (transformation product) AMPA reached a maximum of 2.63 micrograms per litre of urine.

The BUND study results are plausible and indicate a background contamination of glyphosate; however far below a level which poses a potential health risk.

The Federal Institute for Risk Assessment (BfR) evaluated the glyphosate levels measured in the samples with regard to their potential effects on human health. If measured concentrations were attributed to the consumption of contaminated foods, the glyphosate intake via these foods would have been more than 1000 times lower than the concentrations providing a potential health risk. The glyphosate levels found in urine give no indication of a health risk for consumers, nor do the AMPA concentrations due to the low toxicity of the metabolite.

Glyphosate is contained as an active substance in a number of plant protection products authorised in Germany and worldwide. Their uses may result in residues in foods. As long as the established maximum residue levels are not exceeded, the presence of such pesticide residues is safe for consumers and is legal according to the current pesticide legislation. The use of plant protection products is permitted by law by the European Parliament and the German Bundestag as the legislative bodies. Maximum residue levels are established by a European regulation.

Glyphosate residues taken up by consumers along with their food are resorbed from the intestine to a certain extent (roughly 30%). Since glyphosate is excreted rapidly, mainly via urine, the detection of glyphosate in human urine has to be expected.

1 Subject of the assessment

The Federal Institute for Risk Assessment (BfR) was asked to assess the results of a Europe-wide investigation of glyphosate residues in human urine initiated by BUND.

2 Result

The study results are plausible. The study indicates a general background contamination of the European population with glyphosate; however concentrations are far below the level critical to human health.

To the extent that information is available, the analytical method used to determine AMPA and glyphosate appears to be efficient and reliable, although the chromatogram presented for glyphosate is doubtful and could have been mixed up with another.

The glyphosate concentrations detected were between < 0.15 (= LOQ) and 1.82 µg/L, and those of the metabolite AMPA between < 0.15 (= LOQ) and 2.63 µg/L. These levels are

many times below the concentrations calculated under the assumption that all foods contain glyphosate residues at the respective maximum residue level (MRL).

If measured concentrations were attributed to the consumption of contaminated foods, the foods consumed would have contained glyphosate concentrations far below the respective MRL levels, which are still safe for consumers. The levels detected in urine give no indication of a health risk for consumers through glyphosate. The AMPA concentrations pose no health concern either due to the low toxicity of the metabolite.

3 Justification / risk assessment

The BUND study “Determination of Glyphosate residues in human urine samples from 18 European countries“ reports analytical results for urine samples of 182 individuals. However, the study does not constitute a representative examination of the glyphosate contamination of the European population due to the small number of samples from each country. There is no information on the composition and selection of the random sample. The urine samples were tested for glyphosate and its metabolite AMPA, each with an LOQ of 0.15 µg/L. Creatinine levels were also determined in the range from 0.23 to 4.19 g/L. No information on the age, body weight and quantities of excreted urine per person and day was available for the persons involved in the study.

3.1 Assessment of the analytical method used

The analytical method used is very modern, but according to research in the Web of Science not yet published (not by other authors either). The method is based on the conversion of glyphosate and AMPA into two different derivatives with a different molar mass (Glyphosate: N-([Bis-(2,2,2-trifluoroethoxy)-phosphinyl] methyl)-N-(trifluoracetyl)-glycine-2,2,2-trifluoroethyl; molar mass = 511 g/mol and AMPA: Trifluoroacetylamino-methyl-phosphonic acid, bis(2,2,2-trifluoroethyl ester; molar mass 371 g/mol) and has already been applied successfully for soil and air analysis. The quantities of the derivatives were determined by means of GC-MS/MS. This detection method gives maximum selectivity according to current knowledge. Whether or not the method has been sufficiently validated cannot be assessed due to the limited data.

Doubts regarding the correctness of the analytical results for glyphosate are only raised where Figure 1 is concerned (“GC-MS/MS chromatogram of a processed urine sample (Belgium 11). The concentrations were as follows: Glyphosate: 0.6 µg/L; AMPA: 0.4 µg/L”). According to this chart, glyphosate and AMPA were determined with the same mass transition based on a mass of m/z 370. The mass m/z 370 is expected for the [M-H] ion of AMPA. A different mass transfer would be expected for glyphosate due to its much higher molar mass (based on a molar mass of m/z 510). The doubts are fuelled further by the identical retention time of both signals (5.99 min) in the gas chromatography. In earlier studies with these derivatives, a longer retention time was observed for the glyphosate derivative than for the AMPA derivative. Due to the identical appearance of the chromatograms, however, it is possible that the left-hand side of Figure 1 inadvertently also shows a chromatogram measured with AMPA instead of a chromatogram for glyphosate.

3.2 Evaluation of the detected concentrations

The glyphosate concentrations were between < 0.15 (= LOQ) and 1.82 µg/L, those of the metabolite AMPA between < 0.15 (= LOQ) and 2.63 µg/L. For the 10 German participants, the values were between < 0.15 and 0.49 µg/L for glyphosate and < 0.15 and 0.70 µg/L for AMPA.

The AMPA concentrations are sometimes higher, sometimes lower than each corresponding glyphosate concentration. The metabolic degradation of glyphosate into AMPA in the human organism is not distinct and the excretion of AMPA (in low quantities) would be expected more in the faeces than in the urine of humans. For this reason, the measured AMPA residues can only be explained by the intake of AMPA parallel to glyphosate and not by metabolisation of glyphosate in the body.

In non-genetically modified crops AMPA only occurs to a small extent. It is formed by microbial degradation in the soil from where it can translocate into plants. Higher AMPA residues may occur in glyphosate-tolerant plants. The enzymes “glyphosate oxidoreductase (GOX)”, which causes the rapid degradation of glyphosate into AMPA (detoxification), and “5-enolpyruvylshikimi acid-3 phosphate synthetase” (CP4-EPSPS) were implemented in maize and oilseed rape to improve their resistance. Tolerant soybean, sugar beet and fodder beet plants contain exclusively the enzyme CP4-EPSPS. The latter has no influence on the formation rate of AMPA. Therefore particularly high residues of AMPA are to be found in maize and oilseed rape. Residues in sugar beets consist virtually exclusively of unchanged glyphosate. Due to an unknown mechanism, soybeans (tolerant and non-tolerant) are capable of converting glyphosate into AMPA naturally.
It is also possible that additional exposure pathways other than foods exist and may cause the detected AMPA residues in the urine.

It has to be assumed that approximately 20 - 30 % of the ingested glyphosate are resorbed from the intestine and excreted mainly via the urine. Assuming that European consumers exclusively consume foods containing glyphosate concentrations at the level of the respective MRL, the intake would result in 0.132 mg/kg body weight per day (approx. 44 % of the ADI value of 0.3 mg/kg bw/day). Based on a mean body weight of 60 kg (whether or not this applies to the selected participants is not known), this equates to 7.92 mg per day and person. Under the assumption that 20 - 30 % of this quantity find its way into the urine and that 1.5 to 2 litres of urine are produced every day, urine concentrations in the range of 0.79 - 1.58 mg/L are plausible. Comparison with the measured values shows that the concentrations actually found are many times below these values, which means that residues in food (assuming it to be the main exposure pathway for glyphosate) were well below the established MRLs. Since these MRLs are considered as safe, the actual glyphosate levels found in urine do not indicate a health risk for consumers. The AMPA concentrations pose no health concern either due to the low toxicity of the metabolite.

Comparable glyphosate concentrations have also been detected in other studies. A study on glyphosate residues in the urine of American farmers and their families, for example, has already been published in a scientific journal which is available in the internet (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1241861/)[1]. In this study, the average urine

[1] John F. Acquavella, Bruce H. Alexander, Jack S. Mandel et al. “Glyphosate Biomonitoring for Farmers and Their Families: Results from the Farm Family Exposure Study”; Environmental Health Perspectives, Volume 112, Number 3, March 2004

concentration was 3 µg/L with a maximum value of 233 µg/L. The average value corresponds to the concentrations observed in the BUND study.