検索期間：2010～2019年

区分 a に分類された文献とその理由

農作物及び畜産物への残留

1. Information on the study

Data point	CA 6.10.1
Report author	Berg C.J. et al.
Report year	2018
Report title	Glyphosate residue concentrations in honey attributed through geospatial analysis to proximity of large-scale agriculture and transfer off-site by bees
Document No.	PLoS ONE 13(7): e0198876
Guidelines followed in study	None stated
Deviations from current test guideline	Not applicable
GLP/Officially recognised testing facilities	No, not conducted under GLP/Officially recognised testing facilities (literature publication)
Acceptability/Reliability:	Yes/Reliable with restrictions

2. Assessment and conclusion

Assessment and conclusion by applicant:

The publication provides residue levels for glyphosate in honey produced in Hawaii (majority of samples) but also Argentina, Brazil, Canada, Mexico, Uruguay and USA (mainland). It is considered relevant to the setting of a suitable MRL for glyphosate in honey since according to SANTE/11956/2016 rev. 9 it is possible to derive MRLs in honey based on monitoring data. As honey available to European consumers may originate from outside the EU, it is appropriate to consider honey residue data from outside the EU to derive the EU MRL.

The samples were analysed by means of an ELISA method which was validated indirectly by comparison with an LC-MS/MS method. A total of 14 honey samples were analysed with the two methods and the results were shown to be similar. The publication, however, does not provide validation data for the LC-MS/MS method (recovery rates from fortified samples).

The study showed a higher detection rate of glyphosate than in the EU-monitoring for 2016-2017. Besides the different origin of the samples, this may also be due to the use of different analytical methods with different LOQs. In line with the EU-monitoring the publication shows that glyphosate can occur in honey at levels > 0.05 mg/kg and that it is, therefore, appropriate to increase the existing EU-MRL. The highest measured residue level was 0.342 mg/kg, which is less than the maximum value found during the EU-monitoring for 2016-2017.

1. Information on the study

Data point	KCA 6.10.1
Report author	Chiesa L.M. et al.
Report year	2019
Report title	Detection of glyphosate and its metabolites in food of animal origin based on ion-chromatography-high resolution mass spectrometry (IC-HRMS)
Document No.	Food Additives & Contaminants: Part A, 2019, Vol. 36, No. 4, 592-600
Guidelines followed in study	SANTE/11813/2017
Deviations from current test guideline	None
GLP/Officially recognised testing facilities	No, not conducted under GLP/Officially recognised testing facilities (literature publication)
Acceptability/Reliability:	Yes/Reliable

2. Assessment and conclusion

Assessment and conclusion by applicant:

The purpose of the publication is to describe and discuss the performance of a residue analytical method for glyphosate, AMPA and glufosinate in, food of animal origin. As such, the publication is not relevant to risk assessment. However, since it also reports residue levels for the investigated compounds in 10 honey samples and since according to SANTE/11956/2016 rev. 9 it is possible to derive EU MRLs in honey based on monitoring data, the publication may be considered relevant to risk assessment and MRL setting. Based on the provided validation results, the method is considered reliable. The LOQ (defined as the lowest fortification level yielding acceptable recoveries) was 0.010 mg/kg for both glyphosate and AMPA (although different values, presumably estimated from the signal to noise ratio, are stated in Table 2). None of the 10 analysed honey samples showed residues of glyphosate or AMPA above the LOQ. However, it is important to note that all the samples were from organic production and this may need to be taken into account in the evaluation.

1. Information on the study

Data point	CA 6.10.1
Report author	El Agrebi N. et al.
Report year	2020
Report title	Honeybee and consumer's exposure and risk characterisation to glyphosate-based herbicide (GBH) and its degradation product (AMPA): Residues in beebread, wax, and honey
Document No.	Science of the Total Environment 704 (2020) 135312
Guidelines followed in study	None stated
Deviations from current test guideline	Not applicable
GLP/Officially recognised testing facilities	No, not conducted under GLP/Officially recognised testing facilities (literature publication)
Acceptability/Reliability:	Yes/Reliable

2. Assessment and conclusion

Assessment and conclusion by applicant:

The article describes a survey of pesticide residues (glyphosate/AMPA) in various bee-related matrices (beebread, wax, honey) from Belgium. While the representativeness of the sampling procedures may be questioned and although the results of the analytical method validations are not provided in a high level of details, the results are considered reliable. A considerable number of samples of beebread/pollen (n = 82) and beeswax (n = 100) were analysed for parent glyphosate and its metabolite AMPA. However, according to the guideline SANTE/11956/2016 rev. 9 the intake of pollen and wax by consumers is negligible and, therefore, it is not a regulatory requirement to investigate the residue levels in these commodities. The publication also provides analytical results for 10 honey samples. Only one of these samples was found to contain residues of parent glyphosate above the LOQ of 0.010 mg/kg (at 0.011 mg/kg). None of the honey samples showed detectable residues of AMPA (i.e. these residues were < 0.001 mg/kg). Since according to SANTE/11956/2016 rev. 9 it is possible to derive MRLs in honey based on monitoring data, these results are deemed relevant.

The publication concludes that, based on the observed residue levels, the intake of pollen, beeswax and honey by consumers does not cause any health issue. While this conclusion is certainly correct some of the details of the risk assessment are questionable. For instance, the considered ADI of 0.3 mg/kg bw/day for parent glyphosate is obsolete (and was already obsolete at the time when the publication was issued). Furthermore, the long-term residue intakes were calculated based on maximum residue levels and high percentile consumption figures, which does not correspond to the standard approach.

The publication also includes extensive considerations on bee safety, which, however, are not relevant to this section of the dossier and, therefore, are not discussed here.

1. Information on the study

Data point	CA 6.10.1
Report author	Karise R. *et al.*
Report year	2017
Report title	Are pesticide residues in honey related to oilseed rape treatments?
Document No.	Chemosphere 188 (2017) 389-396
Guidelines followed in study	None
Deviations from current test guideline	Not applicable
GLP/Officially recognised testing facilities	No, not conducted under GLP/Officially recognised testing facilities (literature publication)
Acceptability/Reliability:	Yes/Reliable with restrictions

2. Assessment and conclusion

Assessment and conclusion by applicant:

The publication is considered relevant to the setting of a suitable MRL for glyphosate in honey since according to SANTE/11956/2016 rev. 9 it is possible to derive MRLs in honey based on monitoring data. Although only limited information is given about the validation of the method for the determination of glyphosate residues, the analytical results are most likely reliable. The residue levels found for glyphosate are consistent with the EU-monitoring data published by EFSA for 2016-2017 in that: 1. Most of the samples do not show quantifiable residues of glyphosate. 2. Some samples show residues > 0.05 mg/kg, which indicates that it is appropriate to increase the existing MRL. 3. The measured residue levels are far below the levels found in the tunnel residue study.

1. Information on the study

Data point	CA 6.10.1
Report author	Rubio, R. et al.
Report year	2014
Report title	Survey of glyphosate residues in honey, corn and soy products
Document No.	J Environ Anal Toxicol 2014, Vol 5(1): 249
Guidelines followed in study	None stated
Deviations from current test guideline	Not applicable
GLP/Officially recognised testing facilities	No, not conducted under GLP/Officially recognised testing facilities (literature publication)
Acceptability/Reliability:	Yes/Reliable

2. Assessment and conclusion

Assessment and conclusion by applicant:

The article describes a survey of glyphosate residues in honey (n = 69), pancake and corn syrup (n = 26), soy sauce (n = 28), soy milk (n = 11) and tofu (n = 20) purchased in USA, but originating from various countries around the globe. In the context of the dossier for the renewal of the EU approval of glyphosate and with regard to the supported representative uses, the residue data for pancake and corn syrup, soy sauce, soy milk and tofu are not considered relevant. However, the residue data for glyphosate in honey are potentially relevant since according to the guideline SANTE/11956/2016 rev. 9 it is possible to derive MRLs in honey based on monitoring data. Only few of the analysed honey samples originated from Europe but, as honey available to European consumers may originate from outside the EU, it is appropriate to consider honey residue data from outside the EU to derive the EU MRL.

The samples were analysed by means of an ELISA method which was validated by determining the recovery rates from fortified samples. The validation results are not provided in detail, but the average recoveries and relative standard deviations were satisfactory, although the validation was not conducted exactly in accordance with EU or OECD guidelines (i.e. with at least 5 replicates at the LOQ and 5 replicates at a higher level). The limit of quantification was estimated at 0.015 mg/kg. The specificity of the method was investigated by assessing the response of the ELISA test to a series of substances chemically related to glyphosate and it was shown that the response of these substances was at least 1000 times less than that of glyphosate. While this experiment allows to exclude some possible sources of false-positive results, it does not allow to completely rule out that other (not tested compounds) may yield false positive results. Despite these limitations, the obtained analytical results are considered fairly reliable.

59% percent of the 69 honey samples contained glyphosate residues above the method LOQ (0.015 mg/kg) with a concentration range between 0.017 and 0.163 mg/kg and a mean of 0.064 mg/kg. While the individual results are not provided, it seems that about 31% of the samples (22 from 69) showed residues of glyphosate above the EU MRL of 0.05 mg/kg. The samples originating from the EU all showed residues < 0.05 mg/kg. Overall, the findings reported in the publication are in line with the results of the EU-monitoring since the publication shows that glyphosate can occur in honey at levels > 0.05 mg/kg and that it is, therefore, appropriate to increase the existing EU-MRL. The highest measured residue level was 0.163 mg/kg, which is less than the maximum value found during the EU-monitoring for 2016-2017.

1. Information on the study

Data point	CA 6.4.2
Report author	Schnabel K. *et al.*
Report year	2017
Report title	Effects of glyphosate residues and different concentrate feed proportions on performance, energy metabolism and health characteristics in lactating dairy cows
Document No.	Archives of Animal Nutrition, 2017, Vol. 71, No. 6, 413-427
Guidelines followed in study	None stated
Deviations from current test guideline	Not applicable
GLP/Officially recognised testing facilities	No, not conducted under GLP/Officially recognised testing facilities (literature publication)
Acceptability/Reliability:	Yes/Reliable

2. Assessment and conclusion

Assessment and conclusion by applicant:

About 30 cows (distributed in two subgroups) were fed with glyphosate-treated commodities for 17 weeks. During this period the exposure of these cows to parent glyphosate residues via feed was about 0.110-0.120 mg/kg bw/day (Figure 1). None of the analysed milk samples (presumably about 60 pooled samples from the two subgroups fed with glyphosate-treated commodities) showed residues of parent glyphosate or AMPA above the limit of quantification of 0.01 mg/kg. This is fully in line with the results of the GLP cow feeding studies submitted in the dossier, which also show that the transfer (if any) of glyphosate-derived residues in cow milk is extremely low. Although the residue analytical method and residue analyses are not reported with a high level of detail, the results are considered reliable since the general principle of the described analytical procedures is well known and the validity of the residue determination was obviously demonstrated by suitable fortification trials. The publication, therefore, is considered relevant and reliable.

However, the main objective of the publication was to investigate the impact of glyphosate residues in feed on health and performance of dairy cows. No significant effects were identified but this part of the publication is not considered relevant to the residue section.

1. Information on the study

Data point	CA 6.4.1
Report author	Shehata A.A. *et al.*
Report year	2014
Report title	Distribution of Glyphosate in Chicken Organs and its Reduction by Humic Acid Supplementation
Document No.	J. Poult. Sci., 2014, 51: 333-337
Guidelines followed in study	None stated
Deviations from current test guideline	Not applicable
GLP/Officially recognised testing facilities	No, not conducted under GLP/Officially recognised testing facilities (literature publication)
Acceptability/Reliability:	Yes/ reliable with restrictions

2. Assessment and conclusion

Assessment and conclusion by applicant:

The publication provides information about the levels of parent glyphosate residues in feed and tissues of broiler chicken (including edible tissues such as muscle and liver). This may allow to estimate residue transfer factors from poultry feed to poultry meat. Therefore, the publication is considered relevant. The authors further investigated the impact of a feed supplementation with humic acid on the transfer of glyphosate residues in poultry tissues. It was concluded that the supplementation with humic acid allows to significantly decrease the residues of glyphosate in poultry tissues (-63% in muscle and -28% in liver). Thus, the control group (which received feed without humic acid supplementation) represents a worst case in terms of residues and is more relevant from a regulatory perspective. The highest residues found in chicken muscle and liver were extremely low (ca. 0.005 mg/kg and 0.018 mg/kg, respectively). This is consistent with the results of the submitted poultry feeding studies (which were conducted at dose levels far above the dietary exposure of the broiler chickens in the publication). However, both the experimental procedures and the obtained results are not described with a sufficient level of accuracy and it is difficult to figure out exactly what was done and how the presented results were generated. The sample preparation procedure (with consecutive steps at 100°C and -80°C) is quite unusual and no method validation data are presented. Because of that, the publication is reliable with restrictions.

1. Information on the study

Data point	CA 6.4.2
Report author	Shelver W.L. *et al.*
Report year	2018
Report title	Distribution of chemical residues among fat, skim, curd, whey, and protein fractions in fortified, pasteurized milk
Document No.	ACS Omega 2018, 3, 8697 − 8708
Guidelines followed in study	None stated
Deviations from current test guideline	Not applicable
GLP/Officially recognised testing facilities	No, not conducted under GLP/Officially recognised testing facilities (literature publication)
Acceptability/Reliability:	Yes/Reliable

2. Assessment and conclusion

Assessment and conclusion by applicant:

The purpose of the described work was to investigate the partitioning of 12 environmental chemicals of diverse polarities into various milk fractions. One of the tested chemicals was glyphosate. The experiments were conducted with radio-labelled test materials which were fortified to raw (unpasteurized, non-homogenized) cow milk (3 fortification levels were investigated for each compound). Thereafter, the milk was processed into skim milk, milk fat, curd, whey, whey retentate and whey permeate. A linear model predicting the distribution of chemicals between skim milk and milk fat based on their lipophilicity was established. The distribution between curd and whey was also correlated with lipophilicity. Phenolic compounds had less predictable distribution patterns based on their lipophilicities.

During processing of whole milk to skim milk and milk fat, glyphosate partitioned essentially to skim milk (> 99%). Only about 1% of the glyphosate fortified to whole milk was recovered in milk fat. Following curding of the skim milk, most glyphosate remained in the whey fraction (> 80%). The associations of glyphosate with whey protein (calculated by subtracting the amount present in permeate from the amount present in retentate) was very low (< 5%). As expected due to its hydrophilicity, glyphosate primarily distributes into aqueous products, such as skim milk and whey. The distribution pattern between the various milk fractions was similar for the various amounts of glyphosate fortified to whole milk (range of ca. 0.004 mg/L to 0.348 mg/L).

Although the distribution of residues between skim milk and milk fat is not a data requirement for hydrophilic compounds like glyphosate, this information is considered relevant to risk assessment. Overall, the publication is deemed reliable. Normally, the distribution of residues between skim milk and milk fat should be investigated with raw milk containing incurred residues (in the context of metabolism or feeding studies) and not by (artificially) fortifying raw milk. However, due to the very low transfer of glyphosate-derived residues in milk, the approach used in the publication seems to be the best option to determine the distribution of parent glyphosate residues between skim milk and milk fat.

1. Information on the study

Data point	CA 6.10.1
Report author	Thompson T.S. et al.
Report year	2019
Report title	Determination of glyphosate, AMPA, and glufosinate in honey by online solid-phase extraction-liquid chromatography-tandem mass spectrometry
Document No.	Food Additives & Contaminants: Part A, 2019, Vol. 36, No. 3, 434-446
Guidelines followed in study	None stated
Deviations from current test guideline	Not applicable
GLP/Officially recognised testing facilities	No, not conducted under GLP/Officially recognised testing facilities (literature publication)
Acceptability/Reliability:	Yes/Reliable

2. Assessment and conclusion

Assessment and conclusion by applicant:

The article describes the development and validation of a method for the analysis of glyphosate, AMPA, and glufosinate in honey. Aqueous honey solutions were derivatised offline prior to direct analysis of the target analytes using online solid-phase extraction coupled to liquid chromatography-tandem mass spectrometry (LC-MS/MS). Method validation fulfil EU requirements. The method showed good performance for all analytes with a LOQ of 1 µg/kg for each analyte.

The method can be considered valid for monitoring purposes and has been applied for the analysis of two hundred randomly chosen honey samples from Canada. Virtually all the samples were found to contain measurable residues of glyphosate and/or AMPA, which is at least in part due to the extremely LOQ (1 µg/kg). The ratio between parent glyphosate and AMPA was very variable, which is also in contrast to the findings of the EU monitoring (where no measurable residues of AMPA were found) but may also be accounted for by the very low LOQ. In spite of the large number of samples analysed, none showed residues of parent glyphosate exceeding the current EU MRL of 0.05 mg/kg.

According to SANTE/11956/2016 rev. 9 it is possible to derive MRLs in honey based on monitoring data. As honey available to European consumers may originate from outside the EU, it is appropriate to consider honey residue data from outside the EU to derive the EU MRL. Therefore, the publication is considered relevant and reliable. It also includes a useful discussion of the residue levels of glyphosate in honey reported by other authors.

1. Information on the study

Data point	CA 6.4.2
Report author	Von Soosten D. *et al.*
Report year	2016
Report title	Excretion pathways and ruminal disappearance of glyphosate and its degradation product aminomethylphosphonic acid in dairy cows
Document No.	J. Dairy Sci. 99 :5318–5324
Guidelines followed in study	None stated
Deviations from current test guideline	Not applicable
GLP/Officially recognised testing facilities	No, not conducted under GLP/Officially recognised testing facilities (literature publication)
Acceptability/Reliability:	Yes/Reliable

2. Assessment and conclusion

Assessment and conclusion by applicant:

The publication describes a series of 6 experiments in which dairy cows (n = 4-6 per experiment) were fed with glyphosate-treated feed for 26 days and where the excretion of parent glyphosate and AMPA residues via feces, urine and milk was investigated during the last 5 days of the experiments (i.e. at a time when steady state can be assumed). The intake of parent glyphosate residues ranged between < 0.001 mg/kg bw/day (experiments 4, 5 and 6) and 0.011 mg/kg bw/day (experiment 1) while the intake of AMPA residues ranged between < 0.001 mg/kg bw/day (experiments 4, 5 and 6) and about 0.008 mg/kg bw/day (experiment 1). These intake levels are far below the dose levels investigated in the goat metabolism studies and cow feeding studies submitted in the dossier (since the applicable guidelines require that the dose levels be higher) but are likely to reflect "typical" intake levels of dietary cows. In the experiments it was found that 50-73% of ingested glyphosate was excreted in feces and 4-8% in urine. Similarly, 44-50% of ingested AMPA was excreted in feces and 8-12% in urine (these figures assume that no glyphosate is metabolized to AMPA in the cows). These results are consistent with the results of the submitted goat metabolism studies which show that 47-78% of the administered radioactivity is excreted via feces and 4.7-23% via urine. The residues of parent glyphosate and AMPA in milk were below the limit of quantification of 0.01 mg/kg, which is consistent with the results of the GLP cow feeding studies submitted in the dossier. Although the residue analytical method and residue analyses are not reported with a high level of detail, the results are considered reliable since the general principle of the described analytical procedures is well known and the validity of the residue determination was obviously demonstrated by suitable fortification trials. The publication, therefore, is considered relevant and reliable.

1. Information on the study

Data point	CA 6.9
Report author	Zoller O. et al.
Report year	2018
Report title	Glyphosate residues in Swiss market foods: monitoring and risk evaluation
Document No.	Food Additives & Contaminants: Part B, 2018, Vol. 11, No. 2, 83-91
Guidelines followed in study	None stated
Deviations from current test guideline	Not applicable
GLP/Officially recognised testing facilities	No, not conducted under GLP/Officially recognised testing facilities (literature publication)
Acceptability/Reliability:	Yes/Uncertain reliability

2. Assessment and conclusion

Assessment and conclusion by applicant:

The article describes the results of monitoring analyses for residues of glyphosate and AMPA in food conducted by Swiss authorities between 2012 and 2017. A total of 243 samples of diverse food commodities were analysed for glyphosate and AMPA using an LC-MS/MS method that was developed specifically by the Swiss monitoring laboratory. According to the authors the method has a limit of quantification of 0.001 mg/kg for parent glyphosate and 0.0025 mg/kg for AMPA in solid matrices and 0.0005 mg/kg and 0.001 mg/kg, respectively, in liquid matrices (beer, fruit juice, wine). While it seems that these LOQs were established according to recognized procedures, details are missing and it is, therefore, difficult to evaluate the reliability of the provided analytical results. This would be especially important since the reported LOQs are far below the LOQs achieved by most of the other official monitoring laboratories.

As stated by the authors the publication is not intended to provide a representative picture of the residues of glyphosate and AMPA in food commodities placed on the market in Switzerland since the commodities showing high residues were over-represented. In spite of that, the samples relevant to the uses supported in the renewal dossier (e.g. fruits, vegetables, fruit juice, wine, food of animal origin) all showed residues of glyphosate and AMPA far below 0.05 mg/kg (LOQ of most enforcement method so far).

In total, 16 honey samples from Europe and the Americas were analysed. They showed residues of parent glyphosate between < 0.001 mg/kg and 0.0159 mg/kg while the residues of AMPA were always < 0.0025 mg/kg (details are provided as supplementary data). Since according to SANTE/11956/2016 rev. 9 it is possible to derive EU MRLs in honey based on monitoring data and since honey marketed in Switzerland is likely to be also marketed in the EU, these results are deemed relevant to the setting of an EU MRL for glyphosate in honey. The fact that all the samples showed residues of AMPA < 0.0025 mg/kg is in contrast to another publication in which the analyses were also conducted with a very sensitive analytical method and where the residues of AMPA were often found at levels comparable to or even greater than the levels of parent glyphosate residues.