Peer Community In Ecotoxicology & Environmental Chemistry

The widespread detection of glyphosate, AMPA, and glufosinate in rodents and shrews from French agricultural landscapes underscores significant concerns about their potential toxicological impacts in non-target organisms

Pierre Labadie *based on peer reviews by* ***Sabrina Tartu*** *and 3 anonymous reviewers*

Clémentine Fritsch (2024) Exposure of wild mammals to glyphosate, AMPA, and glufosinate: a case for “emerging organic contaminants”? HAL, ver. 3, peer-reviewed and recommended by Peer Community in Ecotoxicology and Environmental Chemistry. https://hal.science/hal-04485797

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Labadie, P. (2024) The widespread detection of glyphosate, AMPA, and glufosinate in rodents and shrews from French agricultural landscapes underscores significant concerns about their potential toxicological impacts in non-target organisms. *Peer Community in Ecotoxicology and Environmental Chemistry*, 100211. 10.24072/pci.ecotoxenvchem.100211

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Pesticides give rise to considerable concern due to their impact on biodiversity. Amongst the vast range of compounds used as herbicides, glyphosate (GLY) is the most widely applied one at global scale and its transformation product, aminomethylphosphonic acid (AMPA) is also ubiquitous. However, the toxicity of these chemicals on non-target organisms, including mammals, is somewhat overlooked (Kissane et al., 2017). Beside these two chemicals, Fritsch et al. (2024) also considered another organophosphorus herbicide, i.e. glufosinate (GLUF). Their study examined exposure levels in rodents and shrews living in contrasted cropped and semi-natural habitats in France – i.e., conventional farmland, organic fields, and hedgerows – through the analysis of herbicide residues in their hair. The hypothesis that herbicide residues in hair reflect the exposure to multiple pesticides in wildlife is supported by several papers (i.e. Krief et al. 2017; Fritsch et al. 2022).

Results obtained by Fritsch et al. (2024) indicated that the target compounds were widespread in the investigated environments, i.e. GLY, AMPA, and GLUF were detected in 64%, 51%, and 44% of samples, respectively. Diet appeared as a major driver of contamination, as herbivorous and omnivorous voles exhibited higher contamination levels than insectivorous or omnivorous species such as shrews and wild mice. In addition, habitat was also a significant factor: GLY concentrations were particularly high in individuals collected from hedgerows, surpassing those found in crop fields. This unexpected result highlights the contamination of areas considered as ecological refuges for the investigated species. Exposure levels did not show clear differences across sites, based on farming practices or pesticide application intensity.

In addition, the measured concentrations of GLY (median 2.7 pg/mg), AMPA (median 1.4 pg/mg), and GLUF (median 3.5 pg/mg) frequently reached thresholds associated with toxic effects on small mammals. In worst case scenarios, exceedance percentages attained values as high as 94 %.

Altogether, these results definitely raise concerns about the potential impact of GLY, AMPA and GLUF on non-target wildlife species and populations. These findings by Fritsch et al. (2024) therefore emphasize the widespread presence of these chemicals in agricultural landscapes and question the safety of herbicide use, even in habitats meant to protect biodiversity. This study underscores the need for more comprehensive evaluation of the ecological effects of herbicides to guide policy and conservation efforts.

References:

Kissane Z, Shephard JM (2017) The rise of glyphosate and new opportunities for biosentinel early-1068 warning studies. Conservation Biology 31: 1293–1300; https://doi.org/10.1111/cobi.12955

Krief S, Berny P, Gumisiriza F, Gross R, Demeneix B, Fini JB, et al. (2017) Agricultural expansion as risk to endangered wildlife: Pesticide exposure in wild chimpanzees and baboons displaying facial dysplasia. Science of the Total Environment 598:647–656; 1072; https://doi.org/10.1016/j.scitotenv.2017.04.113

Fritsch C, Appenzeller BM, Burkart L, Coeurdassier M, Scheifler R, Raoul F, et al. (2022) Pervasive exposure 1041 of wild small mammals to legacy and currently used pesticide mixtures in arable landscapes. 1042 Sci Rep 12:15904; https://doi.org/10.1038/s41598-022-19959-y

Fritsch C, Appenzeller BM, Bertrand C, Coeurdassier M, Driget V, Hardy EM, Palazzi P, et al. (2024) Exposure of wild mammals to glyphosate, AMPA, and glufosinate: a case for “emerging organic contaminants”?. HAL, ver.3 peer-reviewed and recommended by PCI Ecotoxicology and Environmental Chemistry https://hal.science/hal-04485797

Reviews

Evaluation round #2

DOI or URL of the preprint: https://search-data.ubfc.fr/FR-13002091000019-2024-08-29_Glyphosate-AMPA-Glufosinate-Hair-Small-Mammals.html

Version of the preprint: 2

Authors’ reply, 05 December 2024

Download author’s reply

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Decision by Pierre Labadie, posted 04 November 2024, validated 05 November 2024

Dear author,

Thank you for submitting your revised manuscript to PCI EcotoxEnvChem.

We have now received three reviews. As you will see, all are positive; however, the third review raises some additional questions that need to be addressed. We therefore invite you to submit a revised version of the manuscript, along with a document including a point-by-point reply to each comment and suggestion made by this reviewer.

I look forward to receive your revised manuscript.

Regards,

Pierre Labadie

Recommender for PCI EcotoxEnvChem

Reviewed by anonymous reviewer 3, 28 October 2024

I appreciate the author's diligence in thoroughly revising the manuscript to address all reviewers comments.

The comment aboout feedback on the dose reconstruction was directed at the Editor to notify them this reviewer did not have the expertise to review that section of the manuscript. This was not directed towards the authors.

I have no additional comments as the feedback was addressed and the manuscript revised appropriately or the authors provided excellent rational as to why they opted to not change the sections.

Reviewed by Sabrina Tartu, 06 September 2024

The authors have taken into account all my comments and most comments of the two other reviewers. The manuscript has greatly improved, and I am completely satisfied with this revised version. I therefore recommend this manuscript for the PCI Ecotoxicology and Environmental safety.

Reviewed by anonymous reviewer 2, 03 November 2024

This is a nice, and a very interesting work, however despite the work carried out after the previous revision, it is still too long, and hard to read, and therefore to follow. I agree with other reviewers that it could give rise to two papers. Anyway, if authors prefer to keep it as a single manuscript, I strongly urge to summarise it as much as possible. I have described some crucial aspects that, in my opinion, should be clarified to improve the manuscript before publication.

Sampling

A) I think the authors have made an important effort to capture the micromammals, however, the sampling, and sampling effort is very confused. As I can understand, they used 1 trapline (composed by 25 traps) for each of the 78 plots related to 40 sampling squares of 1km2 (around two plots per square). In this sense traps deployment were: 78 sampling plots x 1 trapline/sampling plot x 25 traps/trapline = 1950 traps deployed, it is correct?. Then in results authors stated that animals were captured in 29 of the 78 traplines deployed, which authors specify that correspond to 25 of the 40 sampling squares selected for this study, this mean that animals were only collected in 25 of the 40 squares?, these 25 squares (Fig B) appear to be in adjacent areas, in relation to Fig. A, then nothing else was captured in the rest of the study area?, because it was tried, right?. Regarding these numbers, in Fig. 1, there are 44 sampling squares, the number of sampling plots is difficult to count, but the number of traplines in Fig 1B are 27 and not 29. I think that an additional effort must be done to clearly describe the sampling carried out to avoid confusion.

B) In addition, regarding sampling, the authors indicate that some animals died during sampling, and that hair was collected from these animals after thawing, but nothing more is indicated afterwards. This issue also

raises doubts about how many animals were found dead in the traps?, if was checked the effect of freezing in the residues analysed? Furthermore, reading that, one might think that the authors would take advantage of it to analyse internal tissues, but was not the case at least in this manuscript. In this context, I think that authors could choose to provide more information on this, or to avoid providing such incomplete information.

C) Figure 1: Despite that this figure can be very useful to know the study area, it should have a better resolution as it is difficult to read. Also, taking advantage of the figure, and being a composite figure, I think it could be called more often in the text.

Chemical analysis and concentration of residues

I am aware of the effort made by the authors to try to follow the recommendations given in the previous review regarding limits of detection/quantification, however, due to the LOQ is defined as the lowest possible concentration of the analyte that can be quantified by the method in a reliable way, it is still strange to see in Table 1 that median concentrations are below to the LOQ for GLY and AMPA, but not for GLUF.

Statical analysis and Results

Due to the length of this manuscript, I think it would be very useful if both the description of the statistical analyses and the results followed the same order and even the same sections.

Results

A) Overall, results must be shortened, for example those described in 3.4.

B) The analysis of hair or other keratinised samples to determine exposure to metals is well established, however the usefulness or information provided by hair analysis is not clear for these compounds. On the one hand authors stated that "measurements in hair represent a temporally integrative exposure assessment during the time of hair growth" (lines 922-923) but on the other hand that "the highest concentrations found here may correspond to animals exposed to GLY soon after its application" (lines 1680-1681), all this when the range of concentrations detected is in the order of pg/mg. I think that this issue must be coherent and consistent throughout the manuscript.

Other comments

Line 43: include the units, please.

Lines 204: why it is negligible?

Lines 407-409: include the units for quantities sold, please.

Line 490: For clarity, please change a.s. by active substance in "expressed as daily doses in mg a.s per kg body weight".

Table 1: Please, check the numbers for not treated or treated animals, NT=41?, and T=20 it is not the contrary??

Table 1: Sales are given in kg? this are sale for township? How many townships?

Lines 878-883: you have tested the correlation between sales of Gly and Gluf and % of animals with residues?

Line 884: indicate what is PING, please.

Lines 917-919: Maybe that can be also due to season effect, due to hunted animals are usually collected from October to January, while here sampling was during spring, may and June, in addition can be interesting include the concentrations detected.

Line 1788. What do authors mean with reference? I suppose that it is referred to the model, but in order to avoid confusion, reference could be replaced with another term.

The reference Pelosi et al. (2022- Agric Ecosyst Environ 305:107167), was eliminated, and I think that due to that was carried out in the same study area of the present study, it represents an interesting work that is worth commenting/discussing because small mammals can be also potentially exposed to many other active substances not included in this manuscript but also with ecotoxicological implications.

Overall, there are many very long sentences, made up of several lines of text, often difficult to follow (87-95,....). In this sense, I think that more effort must be done to make the text fluid and easy to understand.

Evaluation round #1

DOI or URL of the preprint: https://hal.science/hal-04485797
Version of the preprint: 1

Authors' reply, 06 September 2024

Dear Recommender,

We warmly thank you and the editorial board of PCI Ecotox Env Chem for providing us an opportunity to improve and re-submit our manuscript.

We also thank the reviewers for their fruitful remarks and advices.

We have carefully reworked the manuscript, following the comments of the reviewers.

Hereafter we answer in details to comments. In the revised version of the manuscript, changes are highlighted using the "track changes" option. Please note that the numbers of lines cited hereafter refer to the version of the manuscript with track changes.

Another version, the final "clean" one is also provided.

We thank you in advance for considering our new version.

Best,

Clémentine Fritsch

Download author's reply

Download tracked changes file

Decision by Pierre Labadie, posted 30 April 2024, validated 30 April 2024

Major revision needed

Dear author,

Thank you for submitting your manuscript to PCI EcotoxEnvChem.

We have now received three reviews. Based on these reviews, we invite you to submit a revised version of the manuscript, along with a document including a point-by-point reply to each comment and suggestion made by the reviewers. Please note specifically that two reviewers found the manuscript to be too long and dense, and that all reviewers also highlighted concerns regarding QA/QC issues (e.g. definition of LOD/LOQ and treatment of non-detects).

I look forward to receive your revised manuscript.

Regards,

Pierre Labadie

Recommender for PCI EcotoxEnvChem

Reviewed by anonymous reviewer 3, 29 April 2024

The authors have presented a nice study which measures the concentration of glyphosate, AMPA, and glufosinate in small mammals. Overall the article was a pleasure to read and the authors did a lot of work. It might be better to split this into two manuscripts, 1 focused on measuring the herbicides and metabolite and the second focused on dose reconstruction to assess risk.

As you may note in my review below, I began to provide some very specific grammar edits, however there are numerous gramatical issues throughout the manuscript, and it should be throughly edited before submission. My review below does not point out all the gramatical issues. The overall flow of the manuscript was also a little challenging to read. There are a number of sections where information would be better in a different location. I.e. some of the information in the introduction should be moved to results/discussion and some of

the methods should be moved to results/discussion, etc. I have pointed out some of them below, but have not given all specific line numbers for each section that the authors may consider moving.

I also recommend that this manuscript is reviewed by an expert who can better review and provide feedback on the dose reconstruction which was described in sections 2.3 and 3.4.

Introduction.

Line 59-60, since multiple glyphosphate metabolites exist, it would help the reader to understand this is the main degredation product of GLY.

Can you please clarify the statements in line 66 and 67, absence of shikimate pathway, that is GLY target, in animals and hydrophilic, low Kow, poorly metabolised and rapidly eliminated in mammals. For example, it would be helpful to clarify that the pathway is the target pathway in plants and that it doesn't exhist in animals and provide a reference for this statement. In line 67 Kow is used but should be explained for readers who aren't familiar with this.

Line 75, They are associated to risks for chronic low-dose exposure in animals and human,.... Please revise as I think you mean there are risks related to chronic low-dose exposure. An example of a risk would be helpful to the reader.

Line 77-78, "Furthermore, GLY and 77 AMPA may be more bioaccumulative than predicted from their physico-chemical properties". Please try to rephrase "more bioaccumulative" as the sentence does not read smoothly.

Lines 91-93, For those not in the EU, it is unclear what a regulatory exclusion is.

Line 107, seems like (rodents and shrews) should be after mammal species.

Line 116-117 If AMPA is in 93% of cropland soils vs 30% for GLY, how are small mammals exposed to GLY through more pathways than AMPA?

Line 120, mobiles is the wrong tense.

Line 122, the /// doesn't make sense.

Methods

Some of the methods belong in the results section (i.e. outcome of trapping efforts).

It may make more sense to place at the beginning how the farmland was classified before beginning the description of the trapping process.

Please also for each acronym (i.e. NOEL) please make sure to spell it out the first time it is used so the reader can follow.

Line 146, the word alive is not needed.

How were the organic fields confirmed not to be contaminated by run-off or draft as is pointed out in lines 176-177? While these lines refers to hedgerows, etc it still brings up the issue mentioned above.

Would it be better to follow these methods vs setting samples <LOD equal to 0? Critical Review Toward Improved Analysis of Concentration Data: Embracing Nondetects, https://setac.onlinelibrary.wiley.com/doi/full/10.1002/etc.4046?

Lines 219-236, are the methods provided elsewhere for chromotography analysis? Some important details such as the solvents used, flow rates, etc are not throughly described to allow replication. What grade were your reagents as only Methanol and water were provided with this level of detail. Also recommend you cite or provide the formulas for calculating your LOQ, etc.

Results.

This is where you should report the species you captured, numbers, etc.

Lines 330-331, clairfy that you mean all species and not the individual species.

Lines 331-332, quantities, was this grams, kgs, etc?

Lines 367-371, I recommend reviewing the article at the following https://www.intechopen.com/chapters/79317 as it describes the increased risks of pesticide exposure in bats. I also recommend you review

the paper you cited about bats, as the authors did use internal standards (imicloprid-d4 and dicamba-d3) and calculated the recovery rates and matrix effects. A better hypothesis is that their washing method for the hair was inadequate vs what you suggest.

Some of the figures are unable to be read due to low resolution. It is unclear if this is due to an artifact of the submission process or an actual problem with the resolution of the figures.

I would recommend considering which figures are in the manuscript vs which are in the appendix. Should table A.1 be in results as this is a really nice overview. Table A.2 I would also seriously consider putting into the manuscript as it shows the odds ratios which are discussed quite a bit in the manuscript. I bring this up as the majority of your results presented in the results/discussion reference the appendix and not the figures in the manuscript. It is cumbersome to keep going to the appendix and reviewing the results before continuing reading the manuscript.

Could you please clarify if you are viewing a single species as omnivorous/granivorous, etc. It is difficult to tell the ecological traits and what species you are describing throughout the text and should be clarified.

Line 549, However, such an effect of a.s. sales on GLUF detection probabilities, what is a.s.?

Conclusion,

I recommended keeping paragraph 1 and 3, paragraph 2 is out of place here.

Reviewed by anonymous reviewer 1, 08 April 2024

General comments

The authors studied the exposure of small mammals to three substances, the currently used herbicide glyphosate, its primary metabolite AMPA, and glufosinate an herbicide banned for three years when the fieldwork was conducted.

They show overall higher concentrations of GLY in comparison to AMPA and GLUF. With some concentrations exceeding ecotoxicological thresholds leading to health risk. Importantly they show that small mammals are exposed to these compounds despite the environmental measures used to protect the environment and biodiversity (hedgerows and organic farming).

These findings are alarming as they reveal that current surfaces of non-treated habitats within the agricultural landscapes are insufficient to mitigate the exposure of wildlife to GLY, AMPA and GLUF.

The manuscript is of great interest and well-written, the statistical analyses are robustly designed. Yet, I have a few suggestions which I believe could ease the reader's understanding and in some parts I would need additional clarifications on the data provided and its interpretation. For instance, the authors write that glyphosate concentrations are higher than AMPA or glufosinate concentrations, yet no statistical analyses were conducted among species to specifically conclude on this trend. The authors should remain cautious on this point.

At this stage I recommend minor revisions.

Specific comments

l.101: please correct typo for "impediment"

l.151: Please provide the complete name Microtus arvalis and Microtus agrestis in stead of M. arvalis and M. agrestis.

l. 164: It would be very helpful to provide a map showing the localisation of CF, OF and OF/CF, in addition to trapline locations and habitat type (cropland, hedgerows and woodlot). The readers could appreciate the proximity between each type of crop or habitat.

Can you please provide the home range of each species in supporting info, this would help understanding the exposure range of the targeted herbicides.

l.317-318: "The influence of species, habitat, farming practices and proxies for treatment intensity on the detection frequency of GLY, AMPA or GLUF".

This sentence is a bit difficult to understand as is. Maybe you could turn it other ways, for example: we tested whether the detection of GLY, AMPA or GLUF in small mammal's hair was dependent on species, habitat, farming practices and proxies for treatment intensity.

l.350: "gastric content" correct typo

Table 1: Be careful, there has been a shift in your column names for glufosinate. "All species" appears twice and the other species have shifted from one column.

l.361-363: According to the data provided in Table 1 only the common vole shows significantly higher concentrations of Gly than AMPA (probably resulting from the outlier), for the house mouse the differences are small, for the shrew non-significant and for the bank vole AMPA even seems higher. Without comparative statistics between GLU and AMPA concentrations for each species and for common voles with and without the outlier, I would remain cautious writing that GLY concentrations are higher than that of AMPA in hair.

Table A2: correct typo in "the binomial" – In shrews and house mouse, Glufosinate was only detected in one individual, how did you compute confidence intervals for these two species?

l.409-411: How did you calculate slopes when for two species glufosinate was only detected in one individual?

l.428: correct typo "authorized"

l.444: correct typo "Statistical"

l.456: you can run the analyses with a random value between LOQ and LOD instead of setting LOD as 0

l.468: correct typo "comparison"

l.560-561: Did you consider the number of years since the crop was set as organic? The transition period for a field to become organic is three years, but some fields could be organic for a much longer period. It could be interesting to test if the duration in organic farming influences exposure, maybe the persistence of these compounds is much higher than previously thought.

Could you also provide distances between OF and CF crops to have an idea of how close they are?

l.615: correct typo "agroecological"

l.635: correct typo "toxicological impairment"

l.693-694: Check also the studies led by F. Brischoux on the effects of AMPA exposure on spined toad tadpoles mortality and deformity

l. 703: correct typo "soricidae"

Reviewed by anonymous reviewer 2, 17 April 2024

Title and abstract:

- Does the title clearly reflect the content of the article? Yes
- Does the abstract present the main findings of the study? Yes

Introduction:

- Are the research questions/hypotheses/predictions clearly presented? No, please, see comments to author
- Does the introduction build on relevant research in the field? Yes,

Materials and methods

- Are the methods and analyses sufficiently detailed to allow replication by other researchers? No, please, see comments to author
- Are the methods and statistical analyses appropriate and well described? thease are confuse, please, see comments to author

Results

- In the case of negative results, is there a statistical power analysis (or an adequate Bayesian analysis or equivalence testing)? please, see comments to author
- Are the results described and interpreted correctly? please, see comments to author

Discussion

- Have the authors appropriately emphasized the strengths and limitations of their study/theory/methods/argument? please, see comments to author
- Are the conclusions adequately supported by the results (without overstating the implications of the findings)? please, see comments to author

Reviewer Blind Comments to Author

This manuscript addresses de exposure of glyphosate its first metabolite and glufosinate, herbicides widely used, in hair samples of small mammals, namely free-ranging rodents and shrews from treated and nontreated agricultural habitats. In addition, the study investigates the patterns of accumulation according to species, habitats, and treatment intensity at plot, landscape, or township scale. The study detects a generalized exposure of the tree compounds analysed. So far, few studies have addressed the study of these compounds in wildlife, thus, the study may therefore be of particular for researchers, environmental managers and conservationist. Despite this the manuscript is, in my opinion, too long and dense, which makes it difficult to follow and understand the work carried out properly, and thus the results that emerge from it. In this sense, I have described some crucial aspects that, in my opinion, should be clarified to improve the manuscript before publication.

1. Introduction: An example of the problem of density and lack of clarity can be found in the last paragraph related to the aim of the study. It is a one-page paragraph, in which the aim covers the first sentence: "The aim of this study was to investigate wildlife exposure in an arable landscape to GLY, AMPA and GLUF using a lowly invasive sampling method based on residue analyses in hair, and focusing on small mammal species having various ecological traits (rodents and shrews)." The main aim/objective of the study seems clear, but later the work appears to address more than that, e.g. Dose reconstruction to assess risk for deleterious effects in small mammals, which it difficult to extract from the indicated paragraph. I believe that more concrete objectives and/or sub-objectives would be necessary to follow and understand correctly all the work carried out under this manuscript.
2. Material and methods:

a. Sampling was carried out between may and june, were there any recaptures?

b. Was the food analysed to confirm the absence of transfer of any pesticides through this route?

c. Pesticides analysis: hair decontamination, despite it could be a very interesting issue, I am not sure if decontamination with sodium dodecyl sulfate solution and with methanol can be a good procedure for compounds such as glyphosate, which as addressed in the introduction, it has singular physico-chemical properties, characterised by the fact that it is a particularly hydrophilic polar compound. In fact, the hair decontamination procedure used from Duca et al (2014) focuses on different chemical classes, but does not include the glyphosate. Perhaps decontamination by washing with water/formic acid or methanol/formic acid might be more appropriate. In this regard, have you been able to analyse whether you found differences between before and after washing?

d. In general, in the analysis section, more detail on the procedure followed is needed.

i. On which analytical method is it based?

ii. Internal standard concentration

iii. Calibration curve

iv. Mobile phases

e. Limit of detection/quantification: This is maybe one of the most important comment to address, because the number of samples detected as positive depends on it. The authors set the LOD as the lowest detected value, but it is not a formal way of calculating it, indeed it is not a calculation per se. In the case of LOQ, they do not indicate how they calculate it. In view of the extensive literature on this subject (see e.g. Armbruster and Pry 2008, Wenzl et al. 2016), I think that a pre-established methodology should be used. Furthermore, in the Table 1, for glufosinate, LOQ appears to be lower than LOD, which is conceptually impossible. Please check this carefully!

f. Data analysis: This is another confusing subsection. In order to achieve greater clarity, the statistical analyses could be described in the same order used later to explain the results.

g. In general, were the interactions spp/farming and/or spp/habitat included in those models performed?

3. Results: Due to this study is based on a sampling design including conventional/organic farming and two different type of habitat. I think that a table showing the concentrations detected and the number of detection frequencies at least in supplementary information would be appreciated.

4. Discussion: Should focus on the essentials and be shortened, it is too long and difficult to follow.

Other comments

Line 147: please change M. By Microtus due to this is the first time it is appointed.

Lines 164-170: please rewrite these lines, or move the sentence “A total of..” before “Individual samples of “, to avoid misinterpretation.

Lines 340-341: The sentence mixes results of previous work with the present work, please rewrite for clarity.

Lines 343-345: Given that in the previous and subsequent sentences the authors are giving values for detection rates, I think it would make more sense to give these also from the work cited.

Line 364: Please, specify which compound you are referring to.

Lines 376-379: This could be due to differences in the tissue analysed in each study.

Line 477: Please, include the year of the reference cited.

References

Armbruster DA, Pry T. 2008. Limit of blank, limit of detection and limit of quantitation. Clin Biochem Rev 29:S49-52.

Wenzl, T., Johannes, H., Schaechtele, A., Robouch, P. and Stroka, J., Guidance Document on the Estimation of LOD and LOQ for Measurements in the Field of Contaminants in Feed and Food, EUR 28099 EN, Publications Office of the European Union, Luxembourg, 2016, ISBN 978-92-79-61768-3, doi:10.2787/8931, JRC102946.