Letter to the editor

The authors of this study assert that it was conducted in a GLP environment and according to OECD guidelines. They did not follow OECD GLP guidelines nor OECD testing guideline (TG) 453 for conduct of a combined chronic toxicity/carcinogenicity study. OECD GLPs require “Detailed information on the experimental design, including a description of the chronological procedure [e.g., start date, end date] of the study, all methods, materials and conditions, type and frequency of analysis, measurements, observations and examinations to be performed, and statistical methods to be used (if any)” and “The study should be conducted in accordance with the study plan”. Apparently, the authors’ original intent was not to conduct a carcinogenicity study “…we had no reason to settle at first for a carcinogenicity protocol using 50 rats per group.” (Seralini et al., 2012), but at some point during the in-life phase, they changed the purpose of the study by extending it for 2 years to assess potential carcinogenicity. Assuming they had a protocol at the start of the study, they did not follow it as they substantially altered the purpose and the design of the study while it was in progress. This should be considered a violation of GLP guidelines as the study was not conducted in accordance with the original study plan. If they wanted to carry out a carcinogenicity study, they should have terminated the existing study and prepared a new study plan adapted from OECD TG 453. They did recognize, as stated above, that they needed a larger number of animals (a minimum of 50 rats/sex/group) for a carcinogenicity study, instead of the 10 rats/sex/group that they had in their existing study. For reasons which will be discussed later, their study did not have enough animals to draw any meaningful conclusions.

1. Experimental design

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1 Roundup agricultural herbicides are registered trademarks of Monsanto Technology, LLC.

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2. Statistical analysis and presentation of data

The authors have a history of inappropriate application of statistical methods to analyze toxicology data (Séralini et al., 2007; Spiroux de Vendômois et al., 2009) which has been criticized by regulatory agencies and other experts (EFSAS, 2007, 2010; FSANZ, 2009a,b; HCB, 2009; Doull et al., 2007). There are numerous problems in the way the data were statistically analyzed in this study.

For example, in Table 3, mean values are not presented for each group and sex to allow comparison of measured parameters. Control data are not presented. Instead, the authors used a statistical method that is not traditionally used to present toxicology data, a multivariate technique called Partial Least Squares Discriminant Analysis (PLS-DA). Mean differences (%) of variables (discriminant at 99% confidence intervals) were presented to investigate the relationship among 48 blood and urine measurements relative to the different treatment groups. PLS-DA can be used to identify patterns in the data and to develop a function which can be used to discriminate between the groups. However, any differences between groups must be further evaluated for toxicological relevance. Presentation of the data in this manner does not lend itself to straightforward interpretation of the study findings.

In Fig. 5, the same PLS-DA procedures were followed with jackknifed confidence intervals at 99% confidence level. This procedure may be familiar to statisticians, but it is not commonly used to...
present toxicity data and is difficult to interpret, particularly when the data used to construct these graphs are not presented. Examination of Fig. 5a would suggest that the majority of measured parameters fall within 99% confidence intervals with the exception of serum and urine electrolytes. Unfortunately, no data were provided from other intervals when these data were collected to determine if the same patterns were evident. No laboratory historical data were provided to put these data in perspective. As stated earlier, just because one can discriminate between the groups, it does not make the result toxicologically relevant. There was no presentation of actual statistical analysis to compare the means for each measured parameter.

To determine if there are patterns of differences in toxicologically related findings, the toxicologist expects to see the actual mean data for each parameter/group and the standard deviation and the control data should also be provided for comparison. The test and control values for measured parameters should also be compared to the historical control data from the testing laboratory and/or the literature to determine if differences were within or outside of the normal range. As presented, the reader has no way of determining whether the conclusions drawn by the authors are supported by the actual data, or are merely statistical anomalies resulting from non traditional analysis. The manuscript contained figures with graphs that were difficult to read because lines overlapped, and percent variations were presented rather than the mean test and control data which is the more standard practice in presenting toxicity data. For instance, incidences of 1 vs. 2 or 5 vs. 10 both represent a change of 100%, however, these absolute values would likely result in different conclusions.

The same criticism can be made for Fig. 2 and Table 2 where the data are not broken out in the tables so the reader can actually see what changes were observed for each group. The incomplete presentation of study data, which was acknowledged by the authors – “all data cannot be shown in one report, and the most relevant are described here” precludes meaningful review and evaluation of study results (Serainli et al., 2012). For example, histopathology incidence/severity data are not presented (e.g., Table 2); nor is any laboratory historical control data provided to help interpret the biological relevance of clinical pathology and histopathology findings. Did the testing laboratory have historical pathology data for chronic studies? The generalized statements of increased liver disorders cannot be verified without presenting the actual data in a table to review.

3. Misinterpretation of study findings

3.1. Mortality data

The authors stated that male and female rats in all treatment groups had more and earlier deaths than the controls. However, they acknowledge that mortality was not dose related. For example, according to Fig. 1, low dose males fed NK603 grain (unsprayed with Roundup) had more early deaths and overall mortality (5/10), while the mid and high dose group mortality near the end of the study was similar to controls (3/10). In the male group fed NK603 (sprayed with Roundup), the mid dose males had more early deaths (4/10), followed by the low dose, and the high dose had the lowest mortality of the NK603 fed groups. For rats administered Roundup in drinking water, high dose males had the lowest mortality compared to the other Roundup treated groups. Similar examples of lack of dose relationships in mortality were observed in the treated female groups. In consideration of the fact that there were 9 treatment groups compared to one control group, some variability in mortality between groups would be expected by chance and could well have explained the distribution of mortality in the study. Given the small group size of 10 rats/sex/group, differences in mortality between groups generally involved only a few animals, and it would be difficult to interpret the biological relevance of such small differences. If dose is not important in this design, it is a 90% probability that one of the test groups would numerically have the highest incidence of mortality.

The authors should have used the adjusted analysis of survival to determine if there were more dead animals in the treated groups compared to the control group, and if there were earlier deaths in the treated groups than in the control group. The most useful statistical approach used to compare survival between groups (not followed by the authors) is the following procedure: Adjusted survival rates are estimated using Kaplan Meier estimation procedures (Kaplan and Meier, 1958). Kaplan Meier estimates are calculated separately for each sex and treatment group. Mortalities which are the result of animals dying following accidents (accidental trauma, died during anesthesia, killed at study director request) or at scheduled sacrifice have to be considered as censored observations. In a second step, statistical significance of differences in survival rates between treated and control groups and dose related trend in survival could be assessed using Cox’s and Tarone’s tests on life table data.

The authors did not indicate whether the tumor classification was done according to the PETO codes (incidental, fatal, observed in life). At least a PETO analysis or a mortality-adjusted analysis for tumor incidences should have been performed.

The authors reported higher survival than is typically reported for female Harlan SD rats in 2-year studies. According to Fig. 1, only 2 of 10 animals died before the end of the study resulting in survival rate of 80%. The SD rat is known to exhibit low and variable survival after 18 months of age (Nohynek et al., 1993; Keenan, 1996). Therefore, as discussed earlier, many more animals than 10/sex/group would be needed to ensure that there would be a sufficient number surviving to the end of the study. This would be needed to conduct a meaningful statistical analysis and to draw solid conclusions regarding biological significance. Average survival in 7 NTP 2-year studies with female Harlan SD rats was reported to be 41.5% (Brix et al., 2005). In a later published review, a survival rate of 42.5% was reported for 2-year studies conducted by the NTP with female Harlan SD rats (Dinise et al., 2010). Charles River SD female rats were reported to have a 2-year survival ranging for 20–60% with an average of 37% (Giknis and Clifford, 2004). Given the high survival rate of female rats in this study, it would be very interesting to learn what the historical 2-year survival rate was for female Harlan SD rats in the testing facility that performed the authors’ study. No historical control data from the testing laboratory were provided for any of the parameters measured.

3.2. Tumor findings

The manuscript misleads readers by attributing the tumors observed in the study to treatment with NK603 grain administered in the diet or Roundup via drinking water. For example, the authors failed to acknowledge that mammary and pituitary tumors observed in this study are very common in untreated female SD rats fed ad libitum for 2 years. They included color pictures of treated rats bearing large mammary tumors, but did not did not include photos of control rats or acknowledge that similar tumors were also observed in controls. Mammary gland tumors are observed not only in older control female SD rats, but can also appear early in a chronic study (Dunbin et al., 1966). Older control female Harlan SD rats have a high background tumor incidence, e.g., for the mammary gland, adenoma 3%; adenocarcinoma 11%; fibroadenoma 71%; adenomas of the pituitary gland are reported at an incidence of approximately 41% (Brix et al., 2005). Pituitary adenomas (prolactinomas) contribute to the development of mammary tumors in SD rats. These historical observations can ac-
count for the finding of one mid dose female in the mid dose
NK603 group (unsprayed) exhibiting a mammary tumor earlier
in the study, and the other mammary and pituitary tumors ob-
served in both control and treated female groups later in the study.
In Table 2, the authors report that treated females had more mam-
mary tumors/rat than controls. However, they do not follow the
standard convention of listing the tumor types confirmed patho-
logically for each group and incidence of animals in each group
bearing those tumors. The authors have instead combined all of
the tumors together/animals in a group so the reviewer cannot
compare the actual tumor data by type between groups. The ab-
sence of a dose relationship in some of tumor findings was evi-
denced by the high dose Roundup group females having lower
incidence of total tumors than the low dose group. The authors
also noted that the size and number of tumors were not propor-
tional to the treatment dose. Since the low dose of the high dose,
yet the lowest dose had a higher tumor incidence, the Roundup
administered in drinking water was orders of magnitude lower
than data are clearly not dose related and most likely reflect nor-
mal variability in the incidence of common tumors that have a
high background rate.

3.3. Other pathologic findings

Other pathological changes reported by the authors as
treatment-related are similarly prevalent in the aged SD rat,
including multiple diet-related disorders, degenerative renal and
degenerative diseases, etc. (Keenan, 1996).

The authors reported treatment-related liver and kidney
pathologies in males. As evidence of kidney effects, they refer to
Table 2 where the incidence of chronic progressive nephropathy
(CPN) was 3/10 control animals compared to 7/10 animals in the
high dose NK603 group (non-sprayed). However, they neglect to
mention that the incidence of CPN in the NK603 sprayed groups
and the Roundup groups are similar and that the high dose groups
had the lowest incidence. They did not report the severity grades
of CPN to learn whether it was increased in a dose related manner. A
similar pattern was observed for liver findings, although Table 2
does not state what the liver pathologies were. This is an unac-
ceptable way to present pathology data. As the study progressed, there
were insufficient numbers of male animals left to make meaningful
comparisons for liver and kidney pathology changes. The authors
reported that only 3/10 control male animals were found to have
CPN. This pathologic change has been reported to occur commonly
in male rats (Hard and Khan, 2004) and in one chronic rat study
with Harlan SD male rats, the incidence was 100% in control male
rats (Petersen et al., 1996). One might have expected a higher
incidence of CPN in control males. In Petersen et al. (1996), CPN
accounted for 48% of the early deaths in control males. Given the
very high background incidence of this disease, and the fact that
9 treatment groups are being compared to one control, some var-
ation in the number of CPN afflicted animals would be expected
between groups. Unfortunately, no historical control lab data for
pathologic lesions were made available for comparisons. The
author’s misquoted the aforementioned Hard and Khan (2004)
publication stating that only elderly rats are sensitive to CPN
whereas the publication states “Although usually regarded as a
disease of the aging rat, incipient lesions of CPN are detectable in
hematoxylin and eosin (H&E)-stained sections of male rat kidney
at least as early as 2 months of age.”

The authors have asserted in previous publications (Séralini
et al., 2007; Spiroûx de Vendômois et al., 2008) that GM crops
cause liver and kidney pathologies based on their statistical re-
analysis of published 90 day feeding studies mentioned earlier.
However regulatory agency scientists and other experts have not
supported these claims and find no evidence of treatment related
liver or kidney pathology changes in any of these studies (EFSA,
2007, 2010; FSANZ, 2009a,b; HCB, 2009; Doull et al., 2007).

The authors also presented clinical pathology data in Fig. 5 and
Table 3 which they interpreted to show changes in serum and
urine electrolytes supporting their hypothesis of kidney damage.
However, as stated earlier, the presentation of the data does not
permit comparison of the actual measured values to controls since
control data were not presented. No actual mean data for the urine
and serum electrolytes were provided to compare comparisons
between test and control groups as well as historical control
ranges for these parameters from the testing laboratory.

3.4. Glyphosate safety

Since a number of the changes observed in this study were not
dose related, the authors conjectured that these findings were hor-
monal and sex dependent, and exhibited a threshold response at a
single dose, which happened to be the lowest dose tested. They
state categorically that Roundup is a “sex endocrine disruptor”
that contributed to the tumors and other pathologies observed in
their study, with no scientific basis for this statement.

To respond to these allegations, it is necessary to review what is
known about the potential toxicology of Roundup and its active
ingredient, glyphosate. WEATHER MAX® herbicide is a typical
commercial Roundup formulation that is essentially the potas-
sium salt of glyphosate with 10% surfactant in water. The category
of surfactant in this Roundup™ formulation was evaluated by the
US EPA in 2009 and was considered acceptable for this use in
pesticide products based on the results of multiple repeat dose
studies, including reproductive and developmental toxicology
(US EPA, Federal Register, 2009a). It should further be noted that
consumers have regular exposure to surfactant materials in the
form of shampoos, soaps, and cleaning products. These are simi-
larly not believed to present reproductive/endocrine risks, but in
any event, exposure to surfactant residues as a result of pesticide
exposure represents a very small portion of human surfactant
exposure. There is no evidence that the surfactant categories used
in Roundup are endocrine disruptors (Williams et al., 2012).

Glyphosate is a structural analog of the amino acid glycine, it
has a methylphosphonate group at the amino terminus instead of
carbonyl group. Amino acids are not endocrine disruptors.
Extensive in vitro (test-tube) and animal data indicate glyphosate
is not an endocrine disruptor. Although glyphosate was included
in the EPA’s initial substances for the endocrine disrupter
screening program, EPA has stated “This list should not be con-
strued as a list of known or likely endocrine disruptors. Nothing
in the approach for generating the initial list provides a basis to
infer that by simply being on this list these chemicals are sus-
pected to interfere with the endocrine systems of humans or other
species, and it would be inappropriate to do so.” (US EPA, Federal
Register, 2009b). Furthermore, the EPA specifically rejected the
assertions presented in Richard et al. (2005) that glyphosate was
an endocrine disruptor based on (i) exceedingly high doses, over
40 times the maximum acceptable concentration for this study
type, (ii) failure to actually meet the criteria for a positive result
in this assay, despite the high dosing, and (iii) lack of demonstrated
study proficiency including no concurrent positive controls to
demonstrate assay validity (US EPA, 2011).

The cited in vitro studies conducted by the Séralini laboratory
have repeatedly been reviewed and considered irrelevant to
in vivo exposures by numerous authoritative bodies. In vitro test
systems are not appropriate for evaluating surfactants due to their
physico-chemical properties impairing cell membrane integrity,
including mitochondrial membranes. The selective use of literature,
without consideration of research (Levine et al., 2007) demonstrating
that the effect is the result of surfactant impacts
on mitochondrial membranes and occurs with a range of surfa-
tants, including those with much greater consumer exposure,
demonstrates consistent and undeterred bias in the authors’ pub-
lication record. Numerous authoritative body reviews have dis-
counted the relevance of the Seralinii team’s research to human
health risk assessment; such as, French Ministry of Agriculture
and Fish, Committee for Study of Toxicity (2005), French Agency
for Food Safety, AFSSA (2009), and BfR (2009).

The safety of glyphosate has been assessed in numerous
chronic/carcinogenicity studies conducted by various registrants
over the years, as glyphosate has gone off-patent, and none of
these studies have found any evidence that glyphosate causes
mammary cancer or any other kind of cancer. The WHO/FAO Joint
meeting on Pesticide Residues reviewed several glyphosate
toxicology data sets including five chronic rat and two chronic
mouse studies in 2004, concluding no evidence of carcinogenicity
(WHO/FAO, 2004a,b). The US EPA’s classification as “Group E car-
cinogen (signifies evidence of non-carcinogenicity in humans)” is
based on review of two chronic rat and one chronic mouse study
(US EPA, 1993) and the EU Commission conclusion of “no evidence
of carcinogenicity” is based on review of four chronic rat and four
chronic mouse studies (EC, 2002). The dosages used covered a
broad range of exposures, and the highest dosages used were much
greater than those tested by the authors and many, many times
higher than human potential exposures since glyphosate can be
dosed at high levels in animals as it is not very toxic. Thus, the
overwhelming weight of evidence indicates glyphosate is not an
animal carcinogen.

In the authors’ chronic study, there were 20 control and 180
test rats (sexes combined) divided into 9 different groups. In
contrast, the FAO/WHO (2004b) review of glyphosate referenced
above included a total of 2330 rats in 5 chronic rat studies.
Included in this number were 540 control rats. In the recent EU An-
nex 1 Renewal dossier submitted in Europe for glyphosate, there
were 9 chronic rat studies with a total of 3938 rats (additional
studies from new manufacturers of glyphosate) of which 942 were
control rats. The new chronic studies also reported no evidence of
carcinogenicity. The authors failed to mention the many toxicology
studies carried out on glyphosate that confirm it does not cause
cancer or liver and kidney pathologies as reported by the authors.
The authors did not acknowledge that there was another
chronic rat study carried out with glyphosate tolerant soybeans
where the investigators reported no evidence of treatment-related
adverse effects including cancer. This was a more robust study as it
contained 50 rats/sex/group (Sakamoto et al., 2008).

The authors also reported blood hormonal analyses (estradiol,
testosterone), although no specified times during the day were gi-
ven for blood sampling. Hormonal parameters exhibit significant
diurnal variations. For this reason, proper analysis must include
the historical variation observed in the performing laboratory,
but no information was provided in this study – a very significant
omission. Secondly, the results of hormone analysis on just one day
are not representative of what is going on throughout the study,
especially for hormones characterized by episodic secretion. No
dose–response relationship in hormone levels was observed. It is
not possible to correlate the hormone levels observed at one time
point in this study with the development of mammary tumors as
proposed by the authors. Further, in rats, the main mode of action
for development of mammary tumors is an increase of prolactin ac-
tivity and then an increase in pituitary tumors. Thus, we question
the increase of tumor incidence with concomitant decrease of estradiol
and increase of testosterone. It is not logical.

The authors also propose another hypothesis to explain their
data, that the introduction of the CP4 EPSPS enzyme that imparts
tolerance to topically applied glyphosate caused metabolic
disturbances in secondary metabolites. In particular, they report
a statistically significant reduction in the levels of secondary
metabolites caffeic and ferulic acid in the NK603 diet. The levels
of ferulic acid in the NK603 diet (exact diets not specified) were re-
ported to be from 735 to 889 ppm compared to 1057 ppm in the
control. Since they report differences in the diets, it is unclear
whether other ingredients in the diet could have contributed
to these differences. No details were provided on the dietary com-
ponents in the formulated diets except the level of NK603 and control
grain that were added.

In a published study summarizing compositional analysis of
NK603 grain, Ridley et al. (2004) reported no differences in ferulic
acid levels between NK603 and its control comparator. The range
of grain ferulic acid was 1500–2500 ppm (mean 2000 ppm) for
glyphosate sprayed NK603 maize. Control maize levels ranged from
1700 to 2300 ppm (mean 2000 ppm). Ferulic acid levels can vary
considerably in non GM maize ranging from 174 to 3540 ppm (fw)
with a mean of 1950 ppm (ILSI Crop Composition Data Base, v4.2).

3.5. Questions on EM methods

The authors reported finding glycogen dispersion or appearance
of lakes, etc. following electron microscopic (EM) examination
of livers from animals fed NK603 (sprayed) or animals administered
Roundup in drinking water. Manuela Malatesta, who performed
the EM work described in this publication, has been previously
criticized for technical deficiencies regarding EM work carried
out in mice fed presumably glyphosate tolerant soybeans
(Williams and DeSesso, 2010).

The authors do not describe the fed/fast state of the animals at
the time of terminal killing. The liver is a dynamic organ that stores
and releases glycogen quickly. Different feeding states of animals
in the same treatment/control group could give samples that look
like all three micrographs in Fig. 4.

The authors’ statements regarding the quality of the methods
used are not backed up by the description in the publication.
The electron microscopy is based on an unknown number of samples
from one control, one low dose and one mid dose animal. These
animals were reported to exhibit the greatest degree of liver
pathology yet the authors report no procedures to ensure a bal-
anced investigation of treated versus control samples. The micro-
ograph of the control portion of a hepatocyte shows tissue from an
area 13 × 13 μ. The total area is of the picture is the area is
about the size of 3 red blood cells. This is a very small amount of
tissue on which to draw a conclusion.

The most significant issues with the limited amount of selective
microscopy used to support the authors’ contentions relate to the
anatomy of the liver. The liver is a large organ (the largest internal
organ in the body) that has great diversity in its anatomy. If a
sample were taken from the edge of the liver and were compared
to a sample from the middle of the same liver near the entry of the
portal vein, the cells would look different. The fact that the tissue
was diced and not put in fixative precludes knowing whether the
samples were taken from the same section of organ across all
treatment groups.

Not only is the liver diverse across the organ, but also within
its internal structure. One of the ways histologists describe the
organization of the liver is by speaking about the liver lobule. For
the purpose of this discussion, the method that describes a liver
lobule as liver cells surrounding the central vein of the lobule will
be used. In that description, the lobule is conceptualized as consist-
ing of three concentric layers of cells that surround the central vein
in a hexagonal shape. (There are thousands of these lobules in a
lobe of the liver.) The arterial supply to the liver lobules is derived
from arteries at the angles of the hexagon. In the fed state, glucose
arrives via the arteries and is processed into glycogen by the hepa-
tocytes. The outer layer takes up glycogen first; later the middle
layer will take up glycogen; and finally, if sufficient glucose is left, glycogen will be found in the inner layer. Glycogen stores are depleted in reverse order. Consequently, the innermost layer tends to look glycogen-depleted most of the time; under fed conditions the outer layer has many glycogen granules; and the middle layer is intermediate in appearance. One could find all three of the conditions illustrated in Fig. 4 by looking within a single (or several) lobules from the same tissue sample. Mitochondria also have various appearances depending on their proximity to the oxygen rich arteries or oxygen depleted central vein.

In the absence of rigorous morphometric analysis that also accounts for the anatomy of liver lobules, the photographs in Fig. 4 have neither context nor toxicological meaning.

In Fig. 3, necrotic foci are considered to be either clear focus or basophilic focus: which is scientifically wrong as these foci are neoplastic entities. Moreover basophilic focus with atypia is not part of the international microscopic nomenclature. Furthermore, microscopic pictures cannot be interpreted properly (bad quality and low magnification). Macroscopic pale spots cannot be correlated to a necrotic focus.

3.6. Questions regarding materials and methods, missing data

No information was provided regarding the identification of the near isoline to confirm that it had similar genetic background. The location, growing conditions, watering and agrochemical treatments of crops were not detailed. This could have had an impact on the composition of crops and then on the outcome of the study. No information was provided on the potential mycotoxins that might be found in the control and NK603 treated crops and might have impacted the study. Was the grain stored adequately during the 2 years of the study to minimize mold growth and mycotoxin contamination? How often were batches made, were they checked periodically by qPCR methods to confirm that the control diets contained only control and not test maize and visa versa. How were the diets stored?

No information was provided regarding (a) detailed diet formulation and manufacturing processes as well as nutrient composition of the diets (b) drinking water contaminant analysis methods or results (c) homogeneity, stability or concentration of ROUNDUP in drinking water formulations. How often were drinking water solutions produced?

The control group was reported to contain 33% non-GM maize in the diet. Low and mid dose NK603 groups (sprayed, unsprayed) reportedly contained 11% and 22% NK603 maize grain. Results from the low and mid dose groups cannot be compared to the control group if they had lower levels of corn grain added to the diets.

There was no drinking water control group for comparison to the treatment groups fed different concentrations of Roundup in drinking water.

3.7. Missing data

In Table 1, the study design represents that behavioral studies were conducted twice. There is no mention of behavioral studies in methods and no results were presented.

Ophthalmology was reported to be conducted twice. There is no mention of ophthalmology evaluations in the methods and no results were presented.

Microbiology was to be conducted in feces and urine. There is no mention of microbiology evaluations in the methods and no results were presented.

Evaluation of glyphosate residues in tissues was reported to be performed, but no information on methods or data generated was provided. Tissue residues are usually evaluated after administration of radiolabelled test materials under toxicokinetic testing guidelines such as OECD 417 (OECD, 2010). For glyphosate, the results of such studies have been evaluated by the WHO/FAO Joint Meeting on Pesticide Residues (2004a,b) and other regulatory agencies around the world.

Evaluation of the transgene in tissues was reported. There was no mention of transgene analysis in methods or results sections, with the exception of confirmation NK603 in maize grain and formulated diets by qPCR.

Food, water consumption and body weights were reported to be measured in the study, but the data were not presented in the manuscript. This is basic information that should be provided for a chronic feeding study to assess potential adverse effects.

Clinical pathology data was reported to be measured at eleven different intervals during the study but only data from month 15 was summarized, and not in a manner it could be easily reviewed. Further, data from the two sexes was presented differently. No historical control information from the testing laboratory for measured parameters was presented.

4. Conclusion

As a result of methodological failures, incomplete data presentation, and lack of proper statistical analysis, Seraili et al.’s conclusions regarding NK603 and/or Roundup cannot be supported by the presented data. Indeed, the fundamental flaw in regards to the number of animals employed makes it highly unlikely that any of the purported findings can be statistically supported using standard approaches to analysis even if more data were to be provided by the authors.

Conflict of Interest

The authors declare that there are no conflicts of interest.

5. United references

(EFSA (2008); EFSA (2011); Ministere De L’Agriculture et de la Peche (2007); Hammond et al. (2004); ILSI (2011); OECD (2009); WHO/FAO (2004); Williams et al. (2012)).


Ministere De L’Agriculture et de la Peche (29 Janvai), 2007) Instruction de la saisine de la Commission d’étude de la toxicité par la DGAL sur l’article “Differential effects of glyphosate and Roundup on human placental cells and aromatase”.


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