# Reliability of industrial studies that were used for the classification of glyphosate

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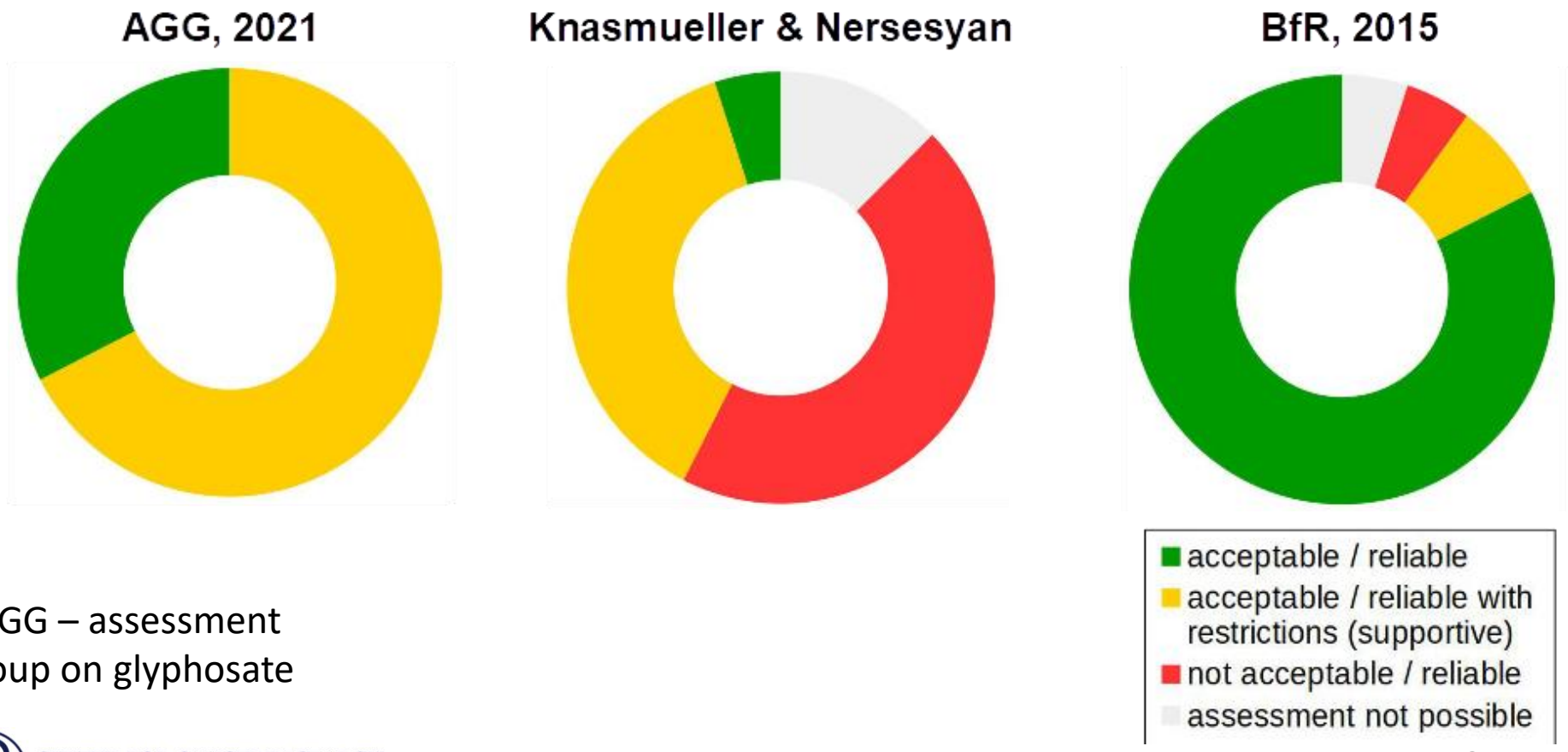
# 64 studies were available from EFSA

- 27 Salmonella/microsome assays
- 2 Rec A assays
- 5 HPRT tests in vitro
- 7 Chromosomal Aberration tests in vitro
- 2 Micronucleus tests in vitro
- 17 Micronucleus studies with bone marrow cells in vivo
- 2 Chromosomal Aberration studies with bone marrow cells in vivo
- 2 Dominant Lethal tests with rodents

# A large fraction of the studies is not reliable as the methods used are not in agreement with international guidelines (e.g. OECD guidelines)

## Differences in the Assessment of 40 Manufacturers's Genotoxicity Studies




*AGG – assessment group on glyphosate

# Most relevant shortcomings and mistakes

(details for 53 studies https://www.global2000.at/sites/global/files/Analyse-Glyphosat-Studien.pdf

https://actions.sumofus.org/a/glyphosate-genotox)

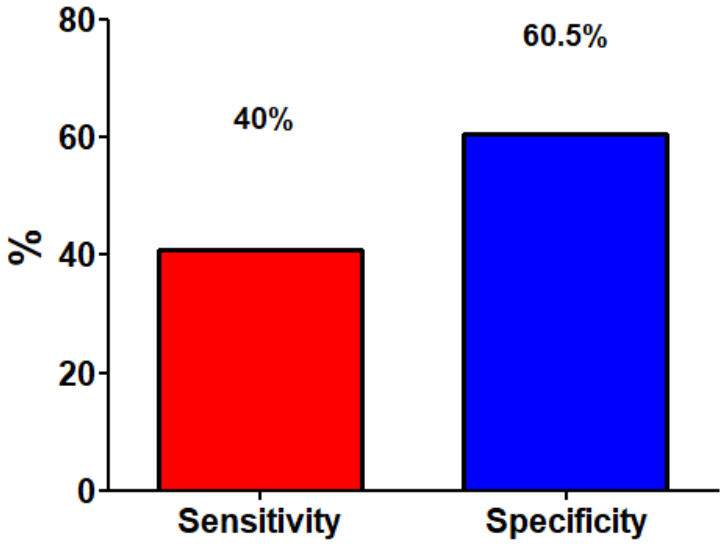
- Salmonella tests: not all mandatory strains included
- Outdated tests: UDS, RecA
- Background rates of bacterial test are sometimes not OK
- Number of cells not sufficient
- Positive controls are sometimes not acceptable
- No adequate statistical analyses
- No repetition experiments
- In some cases studies are in agreement with older regulation but not with the actual ones

# Are there reasons to believe that glyphosate is genotoxic? DEFINITELY YES !!!!!!

The classification of glyphosate as non mutagenic is mainly based on the use of methods that are more than 30 years old, predominately on results of micronucleus and chromosomal aberration tests with bone marrow cells and Salmonella/microsome assays.

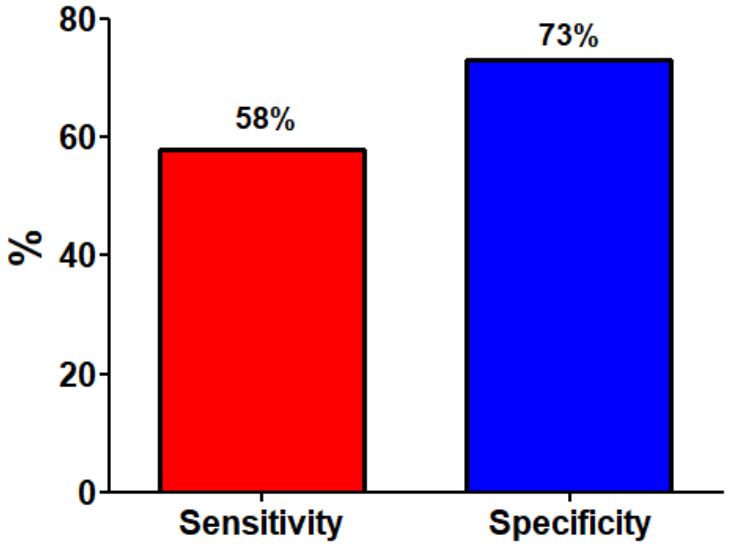
**MN bone marrow test**
Morita et al. 2016

328 chemicals*




**Salmonella/microsome assay**
Kirkland et al. 2005

717 chemicals*




***detection of carcinogens/non-carcinogens**

**Results of Dominant lethal tests; not relevant for the detection of DNA damage in somatic cells.**

**Earlier findings indicate that glyphosate causes DNA damage in organs other than the bone marrow. Results of these experiments were not included in the EFSA evaluation (the results may be due to acute toxicity).**

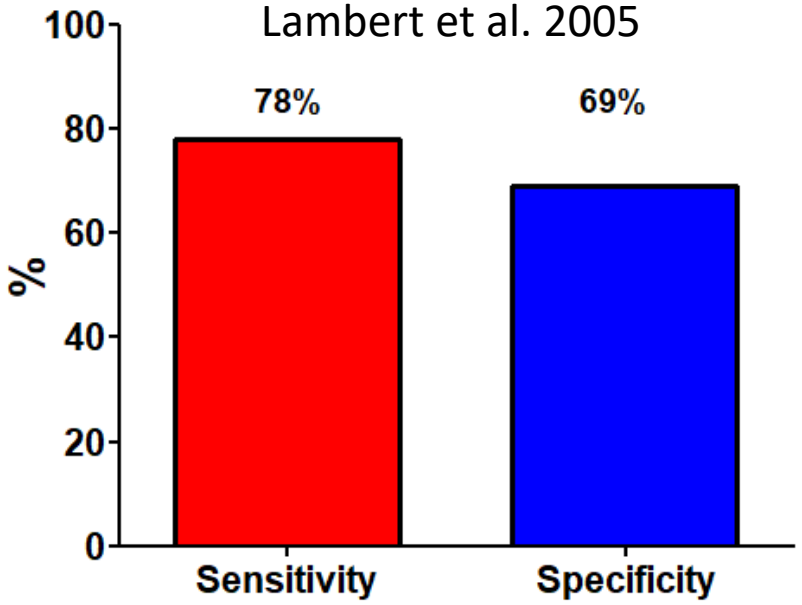
- Kasuba et al. (2017) Positive in human derived liver cells (HepG2)
- Manas et al. (2009) Positive in human derived liver cells (HepG2)
- Manas et al. (2013) Positive in vivo in the liver of mice (SCGE)
- Milic et al. (2018) Positive in vivo in the liver of mice (SCGE)

Several methods are available that allow measurement of DNA damage in various inner organs (experiments with transgenic animals, SCGE experiments). For these tests validated OECD guidelines are available (#489, #488).

**Transgenic rodents**

105 chemicals*

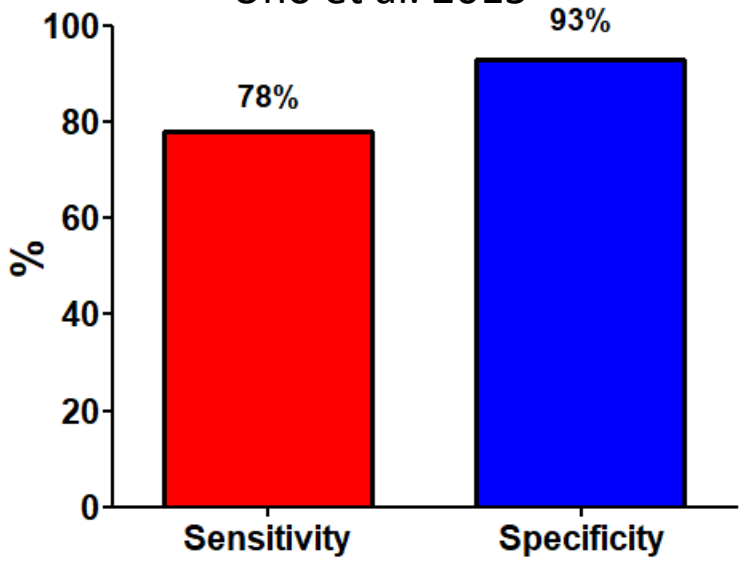
Lambert et al. 2005




**Comet in vivo**

34 chemicals*

Uno et al. 2015




**Numbers indicate detection of rodent genotoxins and non-genotoxins**

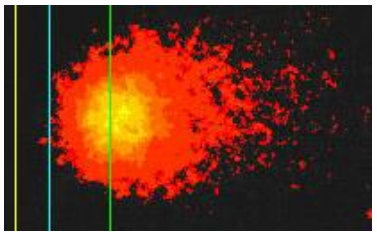
**These methods are known to detect many compounds which give false negative results in bone marrow micronucleus experiments: Kirkland et al. 2008**

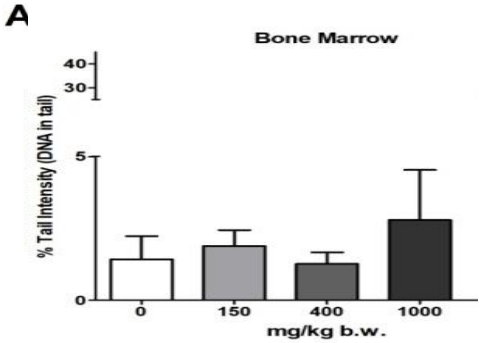
# Additional back-up slides

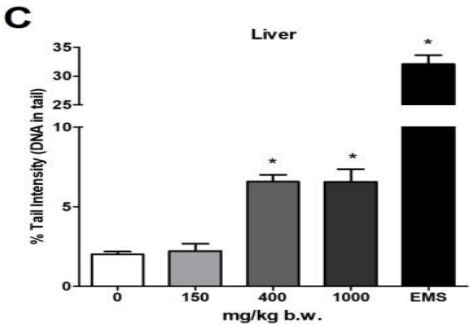
**Our experiments (Knasmueller et al. – not published - not GLP)**

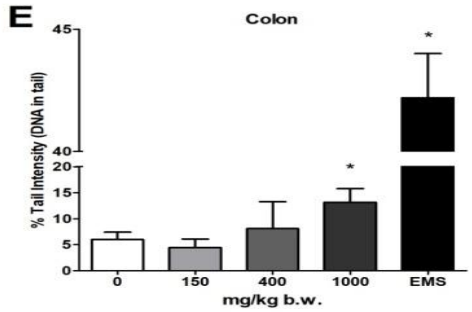
Glyphosate in drinking water (14 days, 150, 400 and 1000 mg/kg bw. per day).

male BALB/c





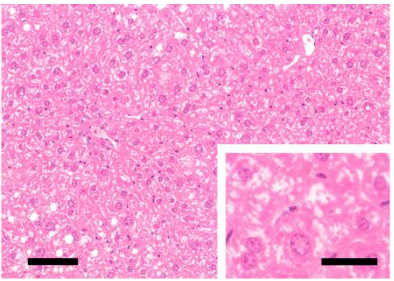




Histology

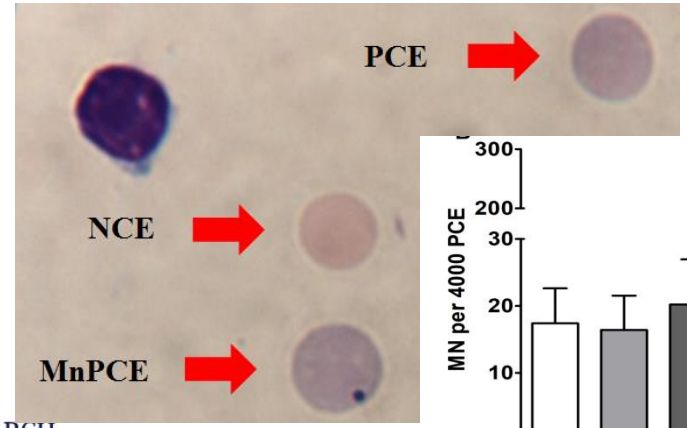
– **No acute cytotoxicity**

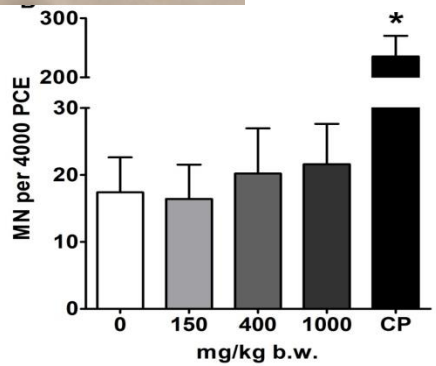
HE-stained sections of liver



MN in bone marrow in PCE after glyphosate

**– No effect**



# Conclusions

- There is an urgent need to provide results from experiments which concern induction of DNA damage in inner organs. Several findings point in this direction.