

# **Glyphosate and ECHA's "weight of evidence"**

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# Weight of evidence (WoE) – ECHA definition:

- “A combination of information from several independent sources ...”
- Useful when “individual studies provide different or conflicting conclusions”.

# „Sufficient evidence“ according to EU regulation 1272/2008

- significant increase of tumour incidences in (at least) **two or more independent studies in one species**
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- Significant increases in all 5 mouse studies, but not the same tumour types across all studies

## Case of kidney tumours in mice

- 3/5 studies with increased tumour rates
- sufficient evidence exists, but maybe conflicting results → **use WoE**

# WoE - Limit dose

Increased incidence of kidney tumours in the 3 of 5 studies

## ECHA:

**2 of the 3 studies not relevant**, because top dose higher than an alleged limit dose of 1,000 mg/kg bw.

## Reality:

- 1,000 mg/kg limit does not exist at all for carcinogenicity studies.
- False application of the limit dose from chronic toxicity
- **All 3 studies remain relevant**

# WoE - Statistical Method

Statistically significant increase in 3 of 5 studies

## **ECHA:**

Increases statistically significant when using Trend Test, but not in Pairwise Comparisons

**Increases not significant** in Pairwise Comparison = irrelevant

## **Reality:**

### OECD

- recommends the Trend Test for tumor incidences
- also states “Significance in either kind of test is sufficient”
- even non-significant increase may apply, if biologically relevant
- **Increases significant** in all 3 studies by Trend Test

# WoE – Historical Controls (HC)

## ECHA:

„renal tumours in male mice were not likely to be treatment related, because ... the findings were **within** the historical control ranges.“ (Opinion, p. 53)

## Reality:

Findings were **outside** HC ranges in 2 studies, HC range in 3rd study possibly skewed

1983 study 6%  $\leftrightarrow$  3.3% (HCD upper limit)

1997 study 4%  $\leftrightarrow$  2% (HCD upper limit)

2001 study 4%  $\leftrightarrow$  mean 2%; range 0 – **6% (skewed?)**

# WoE – Mechanistic Evidence

## ECHA:

„renal tumours in male mice were not likely to be treatment related, because ... there was **no plausible mechanism**.“

## Reality:

Oxidative stress = plausible mechanism,

- caused by glyphosate (multiple studies)
- shown in kidneys of male mice in a study (Gao et al. 2018) assessed by ECHA as „reliable“
- **plausible mechanism shown** in target organ of target species

# Conclusion

- ECHA dismissed important WoE elements making untrue statements
- Evidence **sufficient for category 1B**
- ECHA: not even category 2, instead: no classification at all

For comparison: ECHA criteria for **category 2**

- evidence of carcinogenicity is **restricted to a single experiment → 5 studies with evidence** (3 with kidney tumours)
- **unresolved questions** regarding the adequacy of the design, conduct or interpretation of the studies;  
**→ ECHA claims unresolved questions w/o explanation**
- the agent increases the incidence **only of benign neoplasms ... → malignant tumours in all 5 studies**