

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**