IARC Monograph Evaluation of Glyphosate
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Background and Evidence for Carcinogenicity

How Are the IARC Monograph Evaluations Conducted?

- Procedural guidelines for participant selection, conflict of interest, stakeholder involvement & meeting conduct
- Separate criteria for review of human, animal and mechanistic evidence
- Decision process for overall evaluations

Key epidemiology studies:
Case-control studies from Canada, Sweden and the US
- Positive association that persisted after adjustment for other pesticides
- No additional support for association, but does not contradict other studies

Cancer biosassays (oral exposure):
Male mouse (CD-1), "pure" glyphosate:
  - Rare tumours in two studies:
    - Renal tubule carcinoma [P=0.037]; adenoma/carcinoma (combined) [P=0.034]; Haemangiosarcoma [P=0.001]
  - Rat, "pure" glyphosate:
    - Benign tumours in SD rats (male pancreatic islet cell adenoma in 2 studies; male hepatocellular adenoma and female thyroid C-cell adenoma in 1 study)
    - No increases in 2 other studies (SD, Wistar)
    - One study (Wistar) was inadequate (short duration)

Evaluation Timeline and Publications

Volume 112 Results

Evidence in Experimental Animals

- Glyphosate (GLY), Malathion (MAL), Diazinon (DZN), Tetrachlorvinphos (TCVP)
  - Based on limited evidence in humans and experimental animals, and strong mechanistic evidence
  - For GLY and MAL, mechanistic evidence provided independent support of the 2A classification based on evidence in humans and in experimental animals

Evidence in Humans

- Group 1: Sufficient
  - GLY
- Group 2A: Limited
  - DZN
- Group 2B: Inadequate
  - TCVP

Overall evaluation of glyphosate: Group 2A Probable carcinogenic to humans

Carcinogenicity of trichlorfon, parathion, malathion, diatox, and glyphosate

Mechanistic and other data: 10 Key characteristics of carcinogens

- Key characteristic
  - Oncogenetic
  - Genotoxic
  - Proliferation
  - Differentiation
  - Inflammation
  - Carcinogenesis
  - Cytotoxicity
  - Electrophilicity
  - DNA-reactivity
  - Epigenetic alterations

- Strength of Evidence
  - Weak evidence
  - Moderate evidence
  - Sufficient evidence
  - Limited evidence
  - No data

- Operation in Humans?
  - Can operate in humans
  - Can operate but not in humans
  - Cannot operate

Overall evaluation of glyphosate:

- Glyphosate is the most commonly used herbicide worldwide.
- In humans, evidence for carcinogenicity was limited; case-control studies of occupational exposures in Canada, Sweden and the USA reported increased NHL risks.
- In experimental animals, evidence for carcinogenicity was sufficient; glyphosate induced rare tumours in mice (renal tubule carcinoma, haemangiosarcoma).
- Strong mechanistic data (for genotoxicity, and for oxidative stress) supported the Group 2A cancer hazard classification of glyphosate.