ECHA Committee for Risk Assessment:

Evaluation of the Classification and Labelling of Glyphosate

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- **Established in June 2007**
- **Ca 600 staff from 27 EU and EEA countries**

- REACH

Registration Evaluation, Authorisation and Restriction of Chemicals

- CLP

Classification, Labelling & Packaging

- BPR

Authorisation of Biocidal Active Substances and Products

- PIC Prior Informed Consent

Import / Export notifications for dangerous chemicals (UN Rotterdam Convention)

Main activities

- Manage the 4 regulatory processes and deliver opinions and decisions
- Disseminate information on chemicals
- Develop scientific IT tools
- Provide regulatory assistance to industry (helpdesk and guidance), including SME's
- Support enforcement (Hosts the Forum on enforcement)
- Advise EU institutions and Member States on chemical safety with help of scientific committees
- Assist EU's international activities (UNEP and OECD; accession countries)

ECHA's Scientific Committees

- ECHA has four scientific Committees
- **RAC – Committee for Risk Assessment** - composed of independent experts nominated by the EU/EEA countries and appointed by the ECHA Management Board in their personal capacity
- Currently there are 51 RAC members from 26 Member States and 2 EEA countries – on a 3 year renewable term

*The ECHA Management Board has 28 representative from **Member States**, appointed by the Council, three **Commission** representatives, two independents appointed by the **European Parliament** and three **interested parties** representatives*

Transparency

- Eligibility criteria for membership are in place, members are screened upon nomination
- RAC members may not be employed by a private enterprise, industry association or other body with any direct interest in the work of ECHA
- Annual Declarations of Interest and specific declarations to each agenda point at the start of each meeting
- Member States not allowed to brief Committee members but are obliged to support them in their work[1]
- 103 accredited stakeholder organisations (representing industry, academia and civil society including trade unions)
- RAC meetings attended by 7 regular stakeholder organisations as observers: EEB, ETUI, CONCAWE, EuCheMS, CEFIC, ECPA and Eurometaux - occasional stakeholders on request

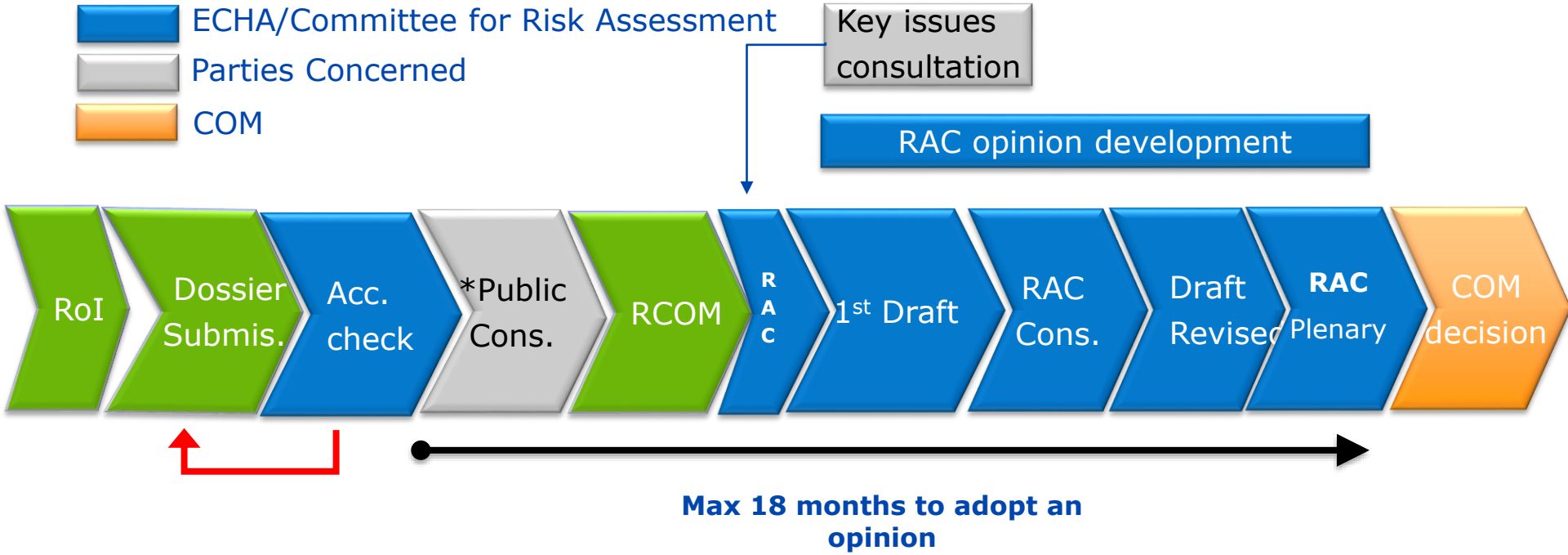
1. REACH Art. 85(7)

CLP

Harmonised C & L process

Main actors

- Dossier submitter
- ECHA/Committee for Risk Assessment
- Parties Concerned
- COM



* The Public Consultation was launched **on 2 June 2016** after the dossier was in **accordance with CLP**

Weight of evidence in the Legislation

- With multiple studies, where the CLP classification criteria cannot be applied directly, e.g. to a single key study, then all the **available information** bearing on the determination of hazard is considered together[1]
- The **quality and consistency** of the data is given appropriate weight
- Both **positive and negative results are assembled together** in a single weight of evidence determination
- Where the information from each single source alone is regarded as insufficient, the weight of evidence from several independent sources may lead to the conclusion that a substance has or has not a particular dangerous property[2]
- The role of epidemiology data is specifically considered[3]

1. CLP Art 9(3) + Annex I: 1.1.1
2. REACH Annex XI, Section 1.2
3. CLP Annex I: 1.1.1.4

About studies……..

- Industry is responsible for generating the required data to demonstrate the safety of their products
- What counts is how reliable the study is and how outsiders can have confidence in that reliability
- Key in this is the use of Internationally standardised OECD guidelines for carrying out animal testing
- Good Laboratory Practice, an OECD developed quality system is mandatory in the EU/EEA, the USA and Japan and is central to credibility
- GLP accredited laboratories undergo regular facility inspections
- The archived study files are open to inspection by the National GLP inspectorate.

Classification and Labelling of glyphosate

Genotoxicity

- A large number of *in vitro* studies including mutation and chromosomal aberration assays using standard protocols
- a broad data set of both unpublished, largely GLP and OECD guideline compliant *in vivo* reports as well as publicly available studies (14 studies, 11 oral)
- Supporting Comet assays (*in vitro* and *in vivo*)
- Studies involving human exposure to GBH

RAC concluded that glyphosate does not result in gene mutations or chromosomal aberrations - there was evidence of transient strand breaks. ***No classification of glyphosate for germ cell mutagenicity is warranted***

Carcinogenicity

Animal studies

- Rats: Total 9 Studies (7 fully considered)
  - 6 studies GLP/ OECD Guideline compliant. 5 were negative, all were considered
    - Evidence for tumours in the pancreas, liver and thyroid seen in one study were considered in detail
  - 3 studies not guideline/GLP compliant: two negative but one had positive findings and **was** considered
    - Evidence for pancreatic adenomas was considered in detail
  - RAC concluded that the rat studies overall did not demonstrate convincing evidence of glyphosate induced tumours
    - Low incidence but statistically significant trend for adenomas. Levels of carcinomas were in general not significantly increased. No progression into malignant forms observed.

Carcinogenicity

Animal studies

- Mice: Total 5 Studies
  - All studies were GLP and OECD Guideline compliant.
  - Evidence of renal tumours, haemangio-sarcomas and malignant lymphoma present at low levels were considered in detail:
    - Malignant lymphomas increased in 4 studies (3 x CD-1). Common tumour type in Swiss mice and high control values in female CD-1
    - Renal tumours at low incidences in 3 studies (2 studies at v. high doses). These tumours are rare in CD-1 mice.
    - Haemangiosarcomas increased in 2 studies at the highest dose.
  - RAC considered: statistical significance (pairwise vs trend tests), dose response, biological relevance and consistency, including comparison with historical control data, differences in findings between the sexes and the high doses used in some studies

Epidemiology

- Cohort study (AHS): prospective, still ongoing - no increased risk identified
- Case-control studies: retrospective, many reviews, re-analyses and meta-analyses show only weak statistically significant associations between exposure to glyphosate-based herbicides and findings of cancer, especially non-Hodgkin's lymphoma.
- Chance, reporting bias and confounding factors could not be ruled out with reasonable confidence
- A causal relationship could not be confirmed
- RAC concluded that the evidence from epidemiological studies was insufficient to demonstrate carcinogenicity in humans.

Carcinogenicity

Conclusions

- Animal studies were of sufficient reliability and relevance to allow a robust evaluation following the requirements of the EU Regulation on classification and labelling (CLP).
- In rats, convincing evidence of glyphosate induced tumours was not demonstrated
- In mice, while effects were observed:
  - the incidences of the findings were generally low,
  - not supported by findings at lower exposure levels
  - were generally seen without a clear dose-response relationship
  - there was no evidence of progression to malignancy
- The evidence from epidemiological studies was considered insufficient to demonstrate carcinogenicity in humans

Taking a weight of evidence approach, no classification for carcinogenicity is warranted for glyphosate according to the CLP criteria.

Thank you for your attention

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RAC track record
(number of opinions delivered to the Commission)

Year	Classification & Labelling	Restriction	Authorisation	Executive Director requests	Derived No Effect Levels	Dose-response analyses	Total
2008	0	0	0	0	0	0	**0**
2009	1	0	0	0	0	0	**1**
2010	15	0	0	1	0	0	**16**
2011	30	4	0	2	0	0	**36**
2012	31	2	0	1	0	0	**34**
2013	34	2	1	3	3	2	**45**
2014	51	5	30	2	0	1	**89**
2015	38	5	25	0	2	3	**73**
2016	35	2	63	0	2	0	**102**
Total	***235***	***20***	***119***	***9***	***7***	***6***	**396**