RAC-60

16 March 2022

CLH Dossier: Glyphosate

Assessment Group on Glyphosate
(AGG, consisting of authorities in France, Hungary, The Netherlands and Sweden)

Background

The current opinion on classification and labelling of glyphosate was adopted in 2017.

Why a new proposal for classification and labelling?

The current approval of glyphosate for use in plant protection products expires in December 2022.

A decision on renewal of approval requires an assessment made in accordance with the requirements set out in Regulation (EC) No 1107/2009 and associated legislation.

In agreement with Commission implementing Regulation (EU) No 844/2012, the assessment includes a proposal for classification and labelling:

"*The draft renewal assessment report shall also include […] where relevant, a suggestion for the classification or reclassification of the active substance in accordance with Regulation (EC) No 1272/2008*"

The assessment is made in agreement with:

- Data requirements specified in Regulation (EU) No 283/2013 and relevant guidance documents
- Criteria for classification and labelling specified in Regulation (EC) No 1272/2008 and the Guidance on the Application of the CLP Criteria

Differences compared to the previous CLH dossier: Toxicology 1(3)

- **Acute toxicity, irritation, sensitization, STOT-SE, STOT-RE, Reproductive toxicity**
  - In line with current harmonized classification: H318 (eye damage)

- **Mutagenicity:**
  - New data: 2 negative Ames, 1 negative *in vitro* micronucleus (MN) assay, 2 negative *in vitro* mammalian cell gene mutation (MCGM) assays, 1 negative *in vivo* MN, public literature studies (mainly *in vitro* Comet assays, methodological shortcomings – unclear toxicological relevance).
  - Full data package provided containing studies performed according to latest OECD guidelines.
  - Proposal in line with current harmonized classification: no classification for mutagenicity.

Differences compared to the previous CLH dossier: Toxicology 2(3)

- **Carcinogenicity:**
  - No change in classification proposal: in a weight of evidence approach, no hazard classification for carcinogenicity is warranted for glyphosate according to the CLP criteria.
  - Re-assessment of all animal studies (six acceptable studies in rat, five acceptable studies in mouse) and all public literature including the publication by Portier (see next slide).
  - Re-assessment of tumours in the **testis**, **pancreas** and **thyroid gland** in rats and **kidney** tumours, **haemangiosarcomas** and **malignant lymphomas** in mice: no major differences compared to the previous assessment (except that historical control data has been added or updated). Overall conclusions not changed from the previous review.
  - The current assessment of **liver** tumours in rats includes a second study in which liver tumours were observed. Conclusion on liver tumours not changed from the previous review.
  - New assessments of **pituitary gland tumours, skin basal cell tumours** and **skin keratoacanthomas** in rats: increased tumour incidences highlighted in publication by Portier (2020). Assessments of these tumours provided in the RAR.

Differences compared to the previous CLH dossier: Toxicology 3(3)

- **Carcinogenicity (continued):**
- Publication by Portier (2020)
  - The author provides a statistical evaluation including a trend test analysis of all carcinogenicity studies.
  - The tumour types showing statistically significant trends in the analysis by Portier (2020) were further taken into consideration (refer to previous slide).
  - Portier (2020) used one-sided testing with a significance level of 0.05, whereas in the original study reports two-sided testing was presented. Where relevant, AGG presented both one-sided and two-sided results in the RAR.
  - AGG statistical analyses based on values of original study reports, statistical in previous CLH report (2016) and/or by AGG own statistical analysis. However, both one- or two-sided significance can be calculated, depending on the hypothesis to test.
  - Statistical analysis is only a part of the interpretation of the biological importance of a particular finding.
  - Tumour incidence data of Portier analysis compared with AGG analysis: few minor differences were observed

- Epidemiological studies
  - Studies have been (re-)assessed; most studies already included during the previous assessment; two new studies assessed (Andreotti 2018 and Pahwa 2019); data gap for two other studies (Zhang 2019 and Leon 2019; refer to RCOM table for preliminary conclusion).

Differences compared to the previous CLH dossier: Phys/chem and Ecotoxicology

Hazardous to Physical Chemical properties

- No classification proposal as for the previous CLH dossier.

Hazardous to the Aquatic Environment

- No change in classification proposal for hazard to aquatic environment: Glyphosate is considered not rapidly degradable, not acutely toxic and classified as aquatic chronic 2 (H411).
- Statistical re-analysis of data do not impact proposed classification.
- Further consideration of literature data is needed, including new data used for setting of Environmental Quality Standards (EQS). Impact on classification can not be excluded (available mid-April 2022, see next slide).
- New standard studies will be submitted on aquatic organisms that may impact the classification (i.e. sediment dwelling organisms, rooted macrophytes,…) (available mid-April 2022, see next slide).

Literature search, criticism and requests for additional data

- The applicant presented a literature search in accordance with legislation and EFSA guidance (2011). Ca 4800 articles were found in sections toxicology, ecotoxicology, environmental fate, or residues in food/feed.
  Of these ca 4000 were considered as ‘non-relevant’ for the data requirements by the applicant. Of the remaining, ca 200 were presented in detail (i.e. with study summaries).

- AGG’s review of the literature search resulted in requests for articles/study summaries for additional >300 references.

- In comments submitted in the public consultation, AGG’s assessment of the literature search was criticized for inconsistency and for dismissing too many published studies (see next slide).

- Based on comments received during public consultation additional studies have been requested from the applicant by EFSA. These data will be submitted by mid-April. AGG understands that data relevant for classification will also be submitted to ECHA.

How AGG will address the criticism related to published studies

- AGG will address the criticism in the revised RAR:
  - explain the approach used for the assessment of the applicant's literature search,
  - clarify criteria and terminology used to classify studies,
  - check that all studies in the revised RAR are consistently classified,
  - clarify the number of articles/study summaries requested by AGG.

- AGG aims to present a document which, in general terms, explains the procedures and AGG's assessment of published studies. The document will be available Q2 2022 and can be submitted to ECHA.

- The revised RAR with evaluation of additional studies and detailed clarifications with respect to open literature can be finalised by Q3 2022.