GRG Position on Grass Residue Decline Data for Chronic Wild Mammal Risk Assessment

Introduction: In the 2021 dRAR for glyphosate, the RMS requested that the grass residue decline data, used to refine the level of residues anticipated on dietary items for the chronic wild mammal risk assessment, may need to be re-assessed using current kinetics analysis approaches.

In the chronic mammal risk assessment, a refined residue decline DT_{50} value of 2.8 days is used to replace a default DT_{50} value of 10 days that is used in the calculation of a time weighted average value (fTWA) and applied in the chronic risk assessment, principally for the small herbivorous mammal (common vole - *Microtus arvalis*).

The GRG performed a kinetics re-analysis of the data from 22 sets of grass residue trials on which the mean DT50 value of 2.8 days is based as presented in the EFSA (2015) conclusion on glyphosate. This historical data set comprises 18 non-GLP and 4 GLP sets of data. The non-GLP trials were conducted before GLPs were implemented. The re-analysis of the residue decline data was conducted according to the kinetics analysis requirements highlighted by the RMS in the 2021 dRAR.

The GRG have concluded that there are sufficient robust data that provide a strong weight of evidence, to support the use of a DT_{50} of 2.8 days to refine the chronic wild mammal risk assessment. All 22 trials are considered to support a DT_{50} < 10 days. The four GLP trials were considered the most reliable for DT_{50} determination, with a worst maximum DT_{50} value of 2.6 days and a range of DT_{50} values of between 0.41 to 2.6 days.

Detail: In the 2015 RAR, the DT_{50} and r^2 values (a measure of goodness of fit) for each trial were cited and judged to be acceptable by the RMS. However, the newly revised criteria since the previous submission to assess model fit were not evaluated (e.g., visual fit, chi², t-test probability, confidence intervals, and residual scatter). Each of these new criteria were evaluated in the re-analysis for the grass residue decline data.

The 22 residues trials cited in the 2015 RAR, have now been re-examined, with each trial analysed using a 3-step process:

- *Step 1*: general suitability for modern kinetic analysis - GLP/non-GLP, quality of reporting, number of data points, timing of data points, rainfall.

- *Step 2*: kinetic analysis using CAKE (computer assisted kinetic evaluation) version 3.4, and evaluation of modern fit criteria.

- *Step 3*: expert judgement.

Of the 22 trials, four were GLP (reported in 1994) and 18 were non-GLP (reported in 1976-1988, conducted before GLPs were implemented). Thirteen of the non-GLP trials were considered to have either too few sampling timepoints for re-analysis or the sampling points were not appropriately spaced. However, all trials were generally found to support a shorter DT_{50} than the default value of 10 days.

The remaining non-GLP trials were considered for kinetics re-analysis. Although not all of the new kinetics criteria were met, these trials strongly support DT_{50} values < 10 days. The remaining five non-GLP and four GLP trials were kinetically analysed at Step 2. Only the GLP trials showed potentially good model fit based on the new standards. Applying a bi-phasic kinetics model did not result in more acceptable fits.

At Step 3 an expert judgement was made, with the following observations:

- Rainfall occurred in all but one trial. In the non-GLP trials, daily rainfall amounts could not be determined.

- In the four GLP trials, rainfall was recorded on Day 0 or Day 1 but this was very light, with a maximum rainfall amount of ≤3.4 mm/day.

- The four sampling timepoints in the GLP trials were early (D0, 1, 3, 5 post application) and highly relevant to accurate determination of an expected short DT_{50} value. The non-GLP trials had one or two early sampling time points, close to the expected DT_{50} (D0, 3, 7, 9, 10, 14; or D0, 3, 7, 10, 14) that gave a reasonable level of certainty in DT_{50} estimates.

- Residues in samples from earlier timepoints are considered more relevant for dietary consumption as the action of glyphosate on plants leads to wilting shortly after application (typically within 6-9 days post application), so plant material would be less palatable to voles and would provide a less suitable habitat / refuge.

- Despite the age of the studies (20 – 40 years) the quality of the reported non-GLP trials is considered to support the relevance of a short DT_{50}, that fits with the EU environmental / climatic conditions.

- Overall, 21 of the 22 trials indicate DT_{50} <10 days. Multiple 'non-GLP' studies 'visually' support a DT_{50} value much shorter than 5 days but are not considered in the re-analysis due to a low number of timepoints. These older studies were not conducted specifically for determining residues in vole diet to refine wild mammal risk assessment. Despite this fact, the trials absolutely do inform on the behaviour of glyphosates residues in foliage following spray applications at rates relevant to the proposed GAP for use in European countries, that do reflect a range of anticipated climatic conditions.

- The GRG believe that a shorter DT_{50} value (< default DT_{50} of 10 days) is relevant to apply at the refinement step of the chronic mammal risk assessment. The assumptions around the use of a 10 day DT_{50} in the EFSA (2009) guidance include consideration of more persistent substances no longer on the EU market and non-EU data; and therefore, arguably, is not representative of the relevant environmental variability in the EU (Ebeling & Wang, 2018)[1].

- Based on the Step 3 expert analysis, the four GLP trials were considered the most reliable for DT_{50} determination, with the remaining non-GLP trials also strongly supporting a DT_{50} < 10 days.

The worst case DT_{50} from the four GLP trials is estimated to be 2.6 days. In conjunction with the weight of evidence provided by the whole dataset including the non-GLP trials, a DT_{50} of 2.8 days is supported by the existing residue decline data. Furthermore, to reference a much larger data set, Ebeling and Wang (2018), examined foliage residue dissipation trials covering 30 compounds and 396 field residue trials from a range of crops. Across all trials, for all compounds, covering multiple zones and crops, the

[1] Ebeling M, Wang M. Dissipation of plant protection products from foliage. Environ Toxicol Chem. 2018 37:1926-1932. doi: 10.1002/etc.4148.

geometric mean foliar DT_{50} was 3.2 days. These data provide further evidence to support a short DT_{50} value as being representative of the EU climatic situation.

In conclusion, the available GLP trials support a DT_{50} of 2.6 days (i.e. the worst case from the 4 GLP trials; a little shorter than the DT_{50} value used in the risk assessment based on the previous analysis). However, further studies can be conducted to further support the conclusions of the chronic wild mammal risk assessment for glyphosate, if requested.