TIME-WEIGHTED AVERAGE FACTOR (fTWA) ASSESSMENTS FOR BIRDS AND MAMMALS UNDER THE NEW BIRD AND MAMMAL GUIDANCE: EXPERIENCES TO DATE

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fTWA: what is it and what has changed?

- Once applied, pesticides degrade over time, resulting in decreasing residues on bird and mammal food items e.g. crop leaves, weeds, insects. The time-weighted average factor (fTWA) represents residue decline in the risk assessment.
- Default fTWA of 0.53 (DT_{50} of 10 days and averaging period of 21 days) can be applied in reproductive risk assessments for foliar applications **under EFSA (2009)**, providing there is no evidence of long-term effects arising from short-term exposure.
- **Under EFSA (2023)**, although the default fTWA of 0.53 remains, the appropriateness of using an fTWA with the lowest ecologically relevant endpoint must be made based on the available toxicity data (Figure 7 and 8 in EFSA 2023, see below).
- If an fTWA cannot be used for mammals, it also cannot be used for birds, with only rare exceptions expected. No additional data should be generated to refine this aspect of the assessment.
- Even when an fTWA is appropriate, the risk assessment may also need to be performed without it using the next highest toxicity endpoint → risk assessment #1: lowest ecologically relevant NOAEL/BMD10 with fTWA; risk assessment #2: higher ecologically relevant NOAEL/BMD10 without fTWA

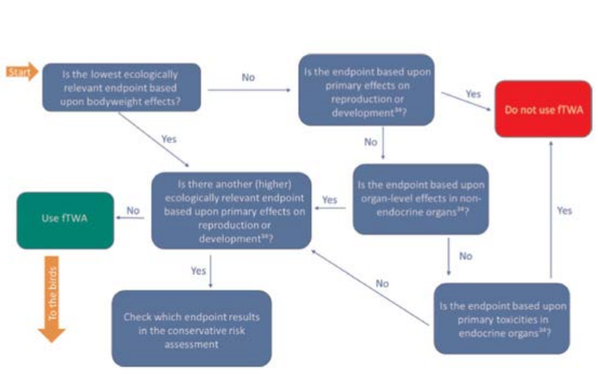
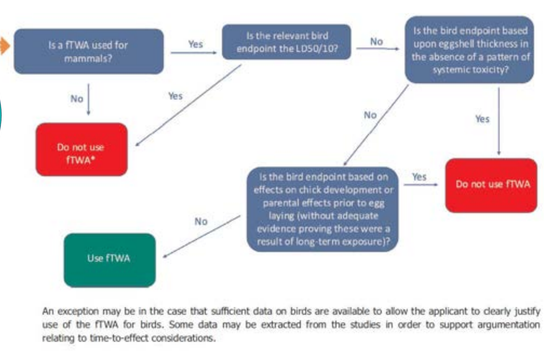


Figure 7: Flowchart for deciding if fTWA can be used in the risk assessment for mammals



An exception may be in the case that sufficient data on birds are available to allow the applicant to clearly justify use of the fTWA for birds. Some data may be extracted from the studies in order to support argumentation relating to time-to-effect considerations.

Figure 8: Flowchart for deciding if fTWA can be used should be used in the risk assessment for birds

Implications?

- Default fTWA of 0.53 in EFSA (2009) reduced TER by ~2x
- Between 2017-2022, 15 out of 63 actives used residue decline data to further refine fTWA in EU evaluations (Pers. Obvs.)
- If fTWA not deemed appropriate for an active substance, risk assessments may now fail that previously passed with either default or refined fTWA; alternative refinement options will be required e.g. ecological refinements (NB. These will also be more challenging under ESFA (2023) due to changes in study design recommendations)
- Final decision on use of fTWA will be made by regulatory authorities/EFSA after residue decline data already generated and risk assessment constructed and submitted; conversely, residue decline refinements might not be attempted by Notifiers in case finally not accepted, resulting in less crop uses being proposed

Observations so far on using EFSA (2023) approach to fTWA

- No evidence presented in EFSA (2023) that the approach taken under EFSA (2009) was underprotective
- Assessments are time consuming as all relevant toxicity studies for birds and mammals must be examined in detail to determine the nature of the effects observed; best done alongside ecorelevant endpoint assessments; required data not always easy to find
- Not currently possible to easily enter a predetermined fTWA into the EFSA bird and mammal calculator tool
- fTWA can only be used for birds if deemed appropriate for mammals, so mammal assessment is always required if fTWA is to be used in the risk assessment, even if fTWA refinement is only required for the bird risk assessment
- Assessment for mammals requires decision on whether the lowest ecorelevant endpoint is based on primary effects on reproduction or development, but this is not always an easy decision to make
- Toxicity dataset very limited for birds, with often only one reproductive toxicity study available, and studies are often challenging to interpret due to 'noisy' data from less-than-ideal study design
- Not considered appropriate for birds when effects on egg-shell thickness, but not clear whether effects of <18% could be deemed not ecorelevant (based on evidence presented in EFSA 2009) and thus whether fTWA could be used in such instances
- Guidance indicates fTWA not appropriate for chick development effects (not clearly defined in the guidance but are considered to cover effects on eggs, developing embryos and chicks, based on pers. comm. with EFSA WG) or parental body weight effects prior to egg laying; use therefore very limited for bird risk assessments

RECOMMENDATIONS

- Perform fTWA assessments, and ideally discuss them with regulators, before commissioning residue decline studies.
- EFSA have already indicated in the EFSA (2023) guidance that the avian reproductive toxicity study could be redesigned to generate more useful data for BMD modelling – could it also capture more data useful for fTWA assessments?
- Research into time-critical exposure windows for birds could be useful – can we make predictions using modes of action, effect type, etc?

References
European Food Safety Authority (EFSA). 2009. Risk assessment for birds and mammals. https://doi.org/10.2903/j.efsa.2009.1438
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