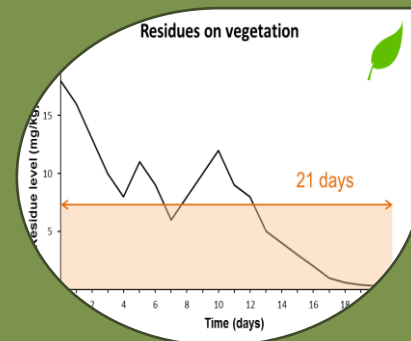


# 3rd Virtual Workshop on the revised EFSA Birds and Mammals Guidance Document

Background, Regulatory hurdles, Ambiguities, Lines of evidence, Modelling – How best to approach the new fTWA assessment.

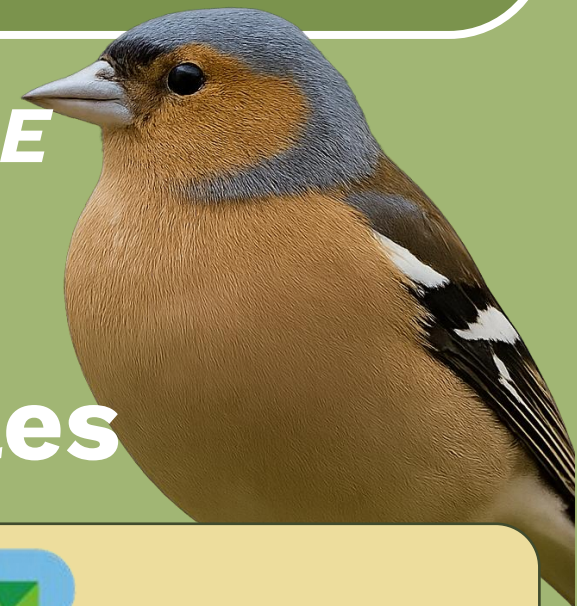


April 28, 2026



10 am – 3 pm CET

***Manousos Foudoulakis - CLE***  
**Topic 1: Background  
and regulatory hurdles**



**RIFCON**



**CropLife**  
EUROPE

# Assessing the Regulatory Impact: The Critical Role of fTWA



- Is there an impact of the TWA justification to the EU portfolio? Can we quantify the impact?
- How does this impact the refinement strategies?

# Impact assessment - Als



## Industry assessed the potential impact at EU level under the assumption of fTWA = 1, using three complementary approaches

1. Review of EFSA conclusion-Key findings
  - CLE reviewed EFSA conclusions for **51** Als (evaluation available upon request).
  - Without applying fTWA **52.9%** substances would have failed the Tier 1 RA for one or both B&M species in one or more representative uses.
2. CLE evaluation of higher tier refinements for B&M
  - CLE evaluated 58 Als at EU level.
  - 12 out of 58 (**20.7%**) Als reviewed used residue decline data to refine. Residue decline was the most frequently used refinement option.
3. Review of recent projects, presentations and publications from external sources
  - CEA evaluated 63 Als at EU level (Brooks et al., SETAC 2023).
  - About half passed at screening or tier I.
  - 15 out of 63 (**24%**) Als used residue decline data to refine (2017-2022). In case no fTWA can be applied, alternative or additional refinement options will be required e.g. ecological refinements if there is still room for refinements.



**For product submissions, residue refinement is most often used as the primary, and usually the first refinement option with data** 3

# Regulatory hurdles - metabolites



- Under new EFSA B&M chronic risk assessment needed for both Als & metabolites.
  - Long term screening RA required for metabolites more toxic than parent **or** for persistent metabolites that meet P criteria **or** the metabolite is found to be relevant based on rotational crop metabolism studies.
- Usually, only limited toxicity data are available for metabolites. No chronic toxicological data are available for metabolites for both birds & mammals as it is not required under Regulation 283/2013 and 284/2013.
- **Due to data limitations, the applicability of fTWA can not be assessed for metabolites in case long term RA is required.**
- More difficult to discuss metabolites in product submissions than in the EU process as this challenge has not been identified during the data development.
- 10x approach

# CLE concern to PAI on fTWA for PPP



- PAI decision (Sep 2025):
- Toxicity endpoint: “*until the BMD for the active substance concerned has been derived at EU level (in particular as part of the approval or renewal of approval of the active substance) **the NO(A)EL will be used***”.
- TWA: “*The decision, if the TWA may be used, is to be made/assessed **by one MS** on behalf of the other MS of the EU. To set the fTWA, **the procedure described** in the GD on the evaluation of new data on an active substance submitted post (renewal of) approval (GD SANCO/10328/2004-rev 10) **is to be followed***”.
- **Request to PAI to re-discuss and reconsider the approach on fTWA assessments**

# CLE concern to PAI on fTWA for PPP



- List of fTWA evaluation options:
- 1. Evaluate **only** the study (-ies) from which the ecotox chronic endpoint was derived.
  - Aligns with PAI decision for the endpoint selection as well – no tox endpoint reevaluation.
  - When applying the “3x higher” rule cannot be applied.
- 2. Evaluate **all studies** which were **considered** in the most recent EFSA conclusion and RAR for deriving the ecotox chronic endpoint - aligned with PAI for the endpoint selection (?)
  - Aligns with PAI decision for the endpoint selection–no tox endpoint reevaluation (?)
  - When applying the “3x higher” rule, the ecologically relevant endpoints of these studies should be compared (EFSA 2023), **not the endpoints for human health.**
  - Which studies should be evaluated vs dataset proposed in the EFSA B&M GD?

# General points – 3x higher EP

## Example (real active substance):

Ecologically relevant NOAELs were only evaluated for the reproduction and developmental studies during the previous EU-level review and are within 3x. Which study or studies should be included in an fTWA evaluation for a product submission?

Study type	Guideline	Relevance according to EFSA 2023	Studies considered/concluded in RAR/EFSA conclusion for deriving ecotox-relevant chronic mammal endpoint
2-generation reproduction toxicity	OECD 416	X	X
Extended 1-generation reproduction toxicity	OECD 443	X	
Prenatal developmental toxicity	OECD 414	X	X
Repro/dev toxicity screening test	OECD 421	Supportive info only	
Combined repeated dose toxicity study with repro/dev screening test	OECD 422	Supportive info only	
Developmental neurotoxicity	OECD 426	X	
90-day neurotoxicity study in rodents	OECD 424	X	
Carcinogenicity	OECD 451	X (limited relevance)	
Chronic toxicity	OECD 452	X (limited relevance)	
Combined chronic toxicity/carcinogenicity	OECD 453	X (limited relevance)	
Repeated dose 28-day oral toxicity	OECD 407	X (lower relevance than studies above)	
Subchronic 90-day oral toxicity	OECD 408 (rodents) OECD 409 (non-rodents)	X (lower relevance than studies above)	

# CLE concern to PAI on fTWA for PPP



- List of fTWA evaluation options:
- 3. Evaluate all studies considered relevant under EFSA 2023 for deriving an ecotox chronic endpoint - **review ecotox and tox.**
  - Not aligned with PAI for the endpoint selection.
  - Challenge: Ecotox-relevant endpoints aren't available for many tox studies and it's likely that some will have lower human health NOAELs than the current ecotox-relevant endpoint in the EFSA conclusion.
- 4. Evaluate **only at EU level** (in particular as part of the approval or renewal of approval of the active substance) **as for BMD.** Until then the TWA should be used as in the last EU review.



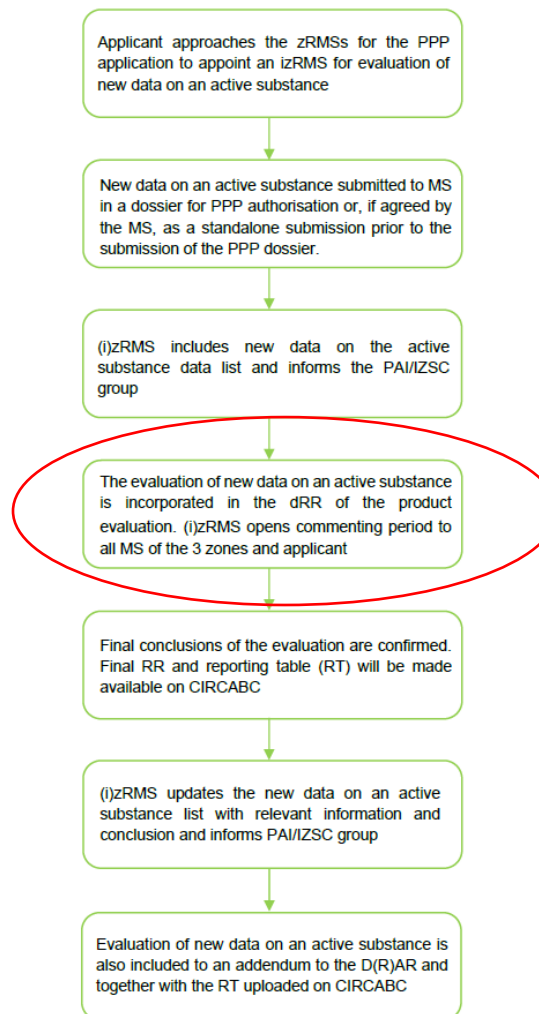
# CLE concern to PAI on fTWA for PPP



- The SANCO document (SANCO/10328/2004-rev 10) is not fit for purpose to evaluate fTWA as it is assumed for new data- no new AI data will be used.
- Data access-protected data: existing AI data not accessible to 3<sup>rd</sup> party.
- Data access-non-protected data:
  - 3<sup>rd</sup> parties still unlikely to have access to the full studies reports.
  - 3<sup>rd</sup> parties may lack access to additional information required, e. g. where expert judgement or contextual study details are needed.

- The SANCO document (SANCO/10328/2004-rev 10) **is not fit for purpose to evaluate fTWA**
- For the fTWA assessment, existing active substance data, but no new active substance data will be used
- **If the fTWA evaluation is challenged during the evaluation process can the applicant submit additional information/data? How?**

Appendix 3: The evaluation procedure new data on an active substance - zonal level



# CLE concern to PAI on fTWA for PPP



- Assessing the fTWA within a zonal procedure triggered by any product evaluation is not transparent as no official peer review may happen and the notifier might not be involved.
- The fTWA outcome generated by one MS would be visible only when the evaluation is finalized, without the possibility for the original data owner (Annex I notifier) or other applicants to contribute in the evaluation. This lack of transparency poses a risk of inconsistent assessments, duplicated efforts and legal concerns.

# CLE concern to PAI on fTWA for PPP



- In Public CIRCABC product evaluation is not visible. Access to existing evaluations does not imply that they must influence the zonal decision

A.S.	Evaluating zRMS	Product name / code	Context of the submission of new AS data	Date of submission	Data point	Author(s)	Year	Title	Company report No.	GLP or GEP status	Owner	Expected date of finalisation of the evaluation	Data point sufficiently addressed Y/N	Conclusion of the evaluation vs context of the submission	Link to CIRCABC for the dRR/RR	Link to Circabc for the addendum according to SANCO/10328/2004	Remarks
name of the active substance	name of the MS who does the evaluation	Product name and code as product name can be different among MSs	e.g. Member States shall pay particular attention to: — the protection of	date where the data are submitted to the evaluating zRMS	information that can be found in appendix 1 of the dRR: Lists of data considered in support of the evaluation	information that can be found in appendix 1 of the dRR: Lists of data considered in support of the evaluation	information that can be found in appendix 1 of the dRR: Lists of data considered in support of the evaluation	information that can be found in appendix 1 of the dRR: Lists of data considered in support of the evaluation	information that can be found in appendix 1 of the dRR: Lists of data considered in support of the evaluation	information that can be found in appendix 1 of the dRR: Lists of data considered in support of the evaluation	information that can be found in appendix 1 of the dRR: Lists of data considered in support of the evaluation	to be added by the evaluating zRMS when starting the evaluation (with date of last update if needed)	in relation to columns D and F	in relation to columns D and F	to be added after finalisation of the evaluation	the document has to be completed after finalisation of the evaluation	
	AT		Member States shall pay particular attention to: - the assessment of consumer intake from the diet	July 2024	KCA 6.2.1		2022			Y		Finalised (09/Y		Acceptable	<a href="https://circabc.europa.eu/sf/file/10328/2004">https://circabc</a>	<a href="https://circabc.europa.eu/sf/file/10328/2004">https://circabc</a>	
					KCA 6.2.3		2022										
					KCA 6.5.1		2004										
					KCA 6.5.1		2008										
					KCA 6.5.1		2012										
					KCA 6.5.3		2006										
					KCA 6.5.3		2010										
					KCA 6.3		2016										
					KCP 7.1.7		2012										
					KCP 7.1.7/1		2024										
	AT		Member States shall pay particular attention to: - the assessment of consumer intake from the diet	March 2024	KCP 10.2.1/01		2021			Y		Draft available			<a href="https://circabc.europa.eu/sf/file/10328/2004">https://circabc</a>	<a href="https://circabc.europa.eu/sf/file/10328/2004">https://circabc</a>	
					KCP 10.2.1/02		2021										
					KCP 10.2.1/03		2021										
					KCP 10.2.1/04		2021										
					KCP 10.2.1/05		2021										
					KCP 10.2.1/06		2021										
					KCP 10.2.1/09		2022										
					KCP 10.2.2/01		2023										
					KCA 6.2.1/01		2021										
					KCA 6.2.1/02		2022										
	FR		New active substance	Nov 25	KCA 6.2.1 / 01		2024			Y		Q3 2026					
					KCA 6.2.1 / 03		2022										
					KCA 6.2.1 / 02		2024										
	FR		New active substance	Nov 25	KCA 6.2.1 / 02		2024			Y		Q2-Q3 2026					

- Two case studies are provided in the following slides

# CLE concern to PAI on fTWA for PPP



**Case study 1: Three companies submit a product renewal dossier in parallel. All three product dossiers contain “Active Substance A”.**

- *Company X submits a solo-formulation to the Central Zone only (zRMS Austria).*
- *Company Y submits a mixture formulation containing “Active Substance A” and “Active Substance B” to all regulatory zones (zRMS Sweden, Poland, Spain).*
- *Company Z submits a mixture formulation containing “Active Substance A”, “Active Substance C” and “Active Substance D” to one MS in the Northern Zone, (zRMS Latvia).*
- For other AIs as mixing partners fTWA assessment is also triggered in various cases.
- Different companies & zRMSs will be involved. It is unclear how PAI/MS envisions the alignment between the different zRMSs for the fTWA assessment as well as the transparency of the evaluations for the different submitting companies.
- **For one AI there is one applicant or Task Force (= data owner/notifier). How will the TWA evaluation be managed?**

# CLE concern to PAI on fTWA for PPP



## Case study 2 (Real case): Transparent peer review process

Post-AIR process	AI data owner/notifier	Other companies with PPP registrations for this AI
Applicants	1	10+
Formulations	29	50+
zRMS	18	?
Mixing partner	8	10+

- Following the currently proposed procedure, fTWA review be done by one MS and review will only be visible for the submitting company + MSs
- The data owner, other registration holders and EFSA will not be included in review, even though the outcome will have EU-wide implications
- As the outcome would not be visible for many registration holders, they cannot adjust their risk assessment if needed
- For mixture partners this process is even more complex and unclear
- **For one AI there is one applicant or Task Force (= data owner/notifier). How will the TWA evaluation be managed?**

# CLE concern to PAI on fTWA for PPP



- **The fTWA assessment should eliminate unnecessary debates around endpoint selection by providing a consistent basis for evaluation.**
- **It is essential that the fTWA assessment is applied consistently across the EU. Inconsistent use among Member States can lead to divergent evaluations, especially because the interpretation of fTWA inputs and data can itself vary if not harmonized.**

# CLE concern to PAI on fTWA for PPP



- **The fTWA should be evaluated as part of the process on the approval or renewal of approval of active substances, in alignment with the approach proposed for the evaluation of Benchmark Dose (BMD) modelling, allowing a transparent process for authorities and applicants.**
- Conducting fTWA assessments at EU level will further.
  1. ensure that the assessment will be based exclusively on EU agreed endpoints,
  2. ensure a transparent and harmonized review process and
  3. avoid unnecessary complexity in case of several simultaneously submitted product submissions.
- **For the interim period, prior to a new EU level assessment, CLE proposes product risk assessments should rely on the most recent EFSA conclusion, including the decision on whether fTWA is applicable, together with the relevant NOEL.**



# CLE concern to PAI on fTWA for PPP



CLE will organise a Sponsored Lunch Seminar during SETAC Europe 2026 (**19th of May 2026**) in Maastricht, during which this topic will also be discussed:

1. Navigating B&M Regulatory hurdles in evolving Regulatory Environments
2. Benchmark Dose “Cookbook” Decision Scheme
3. Outcome of the workshop “Background, Regulatory hurdles, Ambiguities, Lines of evidence, Modelling - How best to approach the new fTWA assessment
4. Challenges around criteria for higher tier field studies
5. HSE CRD update on bird and mammal risk assessment in Great Britain
6. From Guidance to Practice: Lessons learned from the new Birds & Mammals Framework – An Industry Reality Check

Weblink:

[Sponsored Lunch Seminar: The new EFSA Birds and Mammals Guidance Document: Ready for take off?](#)

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# Thank You

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