Fenamiphos: Timelines, actions and decision taken by Bayer

On June 1, 2023, an article by Mie and Rudén was published in the journal Environmental Health, in which crop protection product manufacturers are accused of having allegedly withheld studies on developmental neurotoxicity from the EU approval process and thus having hindered the evaluation of various active substances. Bayer is mentioned in connection with three active ingredients.

Bayer's position in this regard can be also found in this public statement: Transparency in Crop Protection | Bayer Global

Bayer, along with other companies, made a submission for fenamiphos to EU authorities in 2002 in accordance with EU law governing the approval of pesticidal substances (Directive 91/414/EEC) at the time. A DNT study required by US authorities was started in parallel and completed in 2004, after the start of the EU evaluation process. Effects seen in this study only occurred at higher doses compared with the low thresholds set by EU regulators for the amount of fenamiphos that e.g. consumers, operators and the environment could be safely exposed to. Thus, it did not provide additional information which could have an impact on the assessment. Consequently, based on the studies already available, EU regulators were able to carry out a complete risk assessment, including developmental neurotoxicity. This was confirmed in a later review by EU authorities. All studies were passed on to AMVAC when the active ingredient was divested in 2010

In this context and in line with Bayer's commitment to transparency, the following overview provides further information with regards to timelines as well actions and decision taken by Bayer for the active ingredient fenamiphos:

***2002**: IRVITA (and Bayer) submits application for approval of fenamiphos to EU authorities*

In April 2002, IRVITA Plant protection submitted an application for approval of fenamiphos in the EU under Directive 91/414/EEC. IRVITA was considered as the main applicant, and Bayer was regarded as additional applicant. At the time, **there was no EU requirement to submit a DNT study, and no such study was thus conducted**.

***2004**: Fenamiphos DNT study is finalised, as requested by the US-EPA, after the draft Renewal Assessment Report is issued under the EU process*

In August 1999, the **US Environmental Protection Agency (EPA) had issued a broad data call-in[1] for developmental neurotoxicity ('DNT') studies[2]** for 140 substances (link), including fenamiphos.

In **January 2004[3]**, this requested **DNT study[4] for fenamiphos (M-002519-01-1) was finalized and made available to the US-EPA**.

After finalization in 2004, Bayer experts reviewed the DNT study results and concluded that this study did not contain any new safety information that suggested an impact on the EU risk assessment**.**

[1] The US system uses a **data call-in** approach. Here, the US-EPA would define the scientific area that needs further investigation, foster a discussion with stakeholder from academia, industry and civil society on how to support such objective and the US-EPA would then decide on the exact requirements. Industry would then get a specified time to generate and submit the requested data, followed by an evaluation and decision by US-EPA. This process is different from the EU approval process.
[2] The US-EPA had recently (in August 1998) established new test guidelines for DNT (link), hence the data call-in process for DNT followed shortly after that.
[3] At this point in time, in the EU approval process of fenamiphos, the draft assessment report (dRAR) from the Rapporteur Member State (RMS) was already published (November 2003). This dRAR from the RMS set very strict reference values to conduct the risk assessment and also noted that "no primary neurotoxic effects were found for fenamiphos".
[4] Developmental neurotoxicity (DNT) investigates potential toxic effects of a specific substance on the developing nervous system. DNT studies investigate if the offspring (young animals) is more sensitive than their parents (adult animals).

Regulators' assessment of all submitted studies (e.g. NL assessment report first version of 2003, confirmed by later versions and EFSA conclusion of 2006) had already set low thresholds for the amount of fenamiphos that e.g. consumers, operators and the environment could be safely exposed to (so-called toxicity reference values, TRVs). The effects seen in the DNT study (M-002519-01-1) occurred at higher doses only, hence the TRVs were already low enough to protect against potential DNT effects. Thus it did not show additional safety information besides the already submitted toxicological studies.

For this reason, in accordance with EU requirements5, it was not submitted to EU authorities.

2006: *Fenamiphos is renewed in the EU*

In March 2006, the EFSA conclusion is finalized (link), and subsequently Member States voted for a renewal of fenamiphos in the Standing Committee (SCoPAFF, July 2006) **until July 2017** (link; later extended until 2019).

2010: *Further developments: EFSA confirming that there are no DNT effects*

In December 2010, Bayer divested fenamiphos to AMVAC. Bayer can therefore not comment on the subsequent application for renewal done in 2016. It should however be noted that the **EFSA conclusion from 2019 (link) states that "there were no developmental neurotoxicity (DNT) effects"** in the conducted DNT study[6]; thus, confirming that it would not have impacted the EU risk assessment back in 2004.

[5] **Directive 91/414/EEC did not contain any provision for data submission during the pending approval process**. In practice, the EU process prerequisites that the dossier contains all required data. The period between submission of the dossier (and its completeness check) and approval lacks any regulation for submission of regular data to complement the dossier, which is only possible in exceptional cases. The current and also earlier EU pesticide regulations require, however, that after the approval decision any information which "suggests" that the approval criteria are not met any longer, i.e. potential harmful effects on human ("adverse data"), has to be notified immediately and do not impose requirements to provide unnecessary information not meeting these criteria. Comparable provisions for the period between dossier submission and approval decision do not exist. It is and was always without doubt for Bayer, however, that the same standard must apply also during this period to safeguard an appropriately efficient but under all circumstances robust safety evaluation process. Bayer has fully complied with these standards.

[6] This point was also recognised by Mie & Rudén in their Article.