Fenamidone: 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's last submission for reapproval of fenamidone to EU authorities was made in 2014 in accordance with EU law governing the approval of pesticidal substances (Regulation (EC) No 1107/2009) at the time. Based on the toxicological profile of the active substance, a DNT study was not required under the applicable requirements. This was confirmed by EFSA. A DNT study was performed and submitted to US authorities upon their request and Bayer informed the EU authorities of the existence of this study. All studies were passed on to Gowan when the active ingredient was divested in 2019.

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 Fenamidone:

***1999**: Bayer submits application for approval of fenamidone to EU authorities, which is granted in 2003*

In September 1999, Rhone Poulenc Agro (now Bayer) submitted an application for approval of a new compound (fenamidone) in the EU under Directive 91/414/EEC. At the time, **there was no requirement at EU level to submit a Developmental Neurotoxicity (DNT) study and no such study was thus conducted**. The **approval** was granted in **2003**, until 2013 (later extended to 2019 due to delays).

***2002-2004**: Following a fenamidone application in the US, Bayer initiated a DNT study which did not indicate a potential for developmental neurotoxicity*

In 2002, Bayer applied to register fenamidone in the US (link). Because the US-EPA had established test guidelines for DNT in 1998, they required a DNT study. Hence, **Bayer initiated such DNT study[1] (M-253958-01-1) in 2004 and completed it in 2005**.

After finalization in 2005, Bayer experts reviewed the DNT study results and concluded that they **did not contain any new safety information that suggested an impact on the EU risk assessment**. This because the already submitted toxicological data did not show a DNT effect; and the new DNT study (M-253958-01-1) showed even less sensitivity to the offspring (compared to the parent) and thus did not show additional safety information besides the already submitted toxicological studies.

For this reason, in accordance with EU requirements[2], the study was **not submitted to EU authorities at that time. Please note however, that Bayer notified the study to the EU authorities in the following renewal process that started in 2014 (see details below).**

[1] 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).
[2] There was no notification requirement in light of the approval effective since 2003. The Fenamidone DNT study (M-253958-01-1) was not notified as the data did not qualify as so-called "adverse data". Such notification requirement was stipulated in Art. 7 Directive 91/414/EEC:

2007-2009: US-EPA evaluates the fenamidone DNT study and confirms the absence of a potential for developmental neurotoxicity

When reviewing the fenamidone DNT study, US authorities initially (in 2007) asked for additional data, i.e. an abbreviated DNT study using a different rat strain. When concluding their scientific assessment in 2009, however, they decided that the available data already demonstrated a safe use, and no additional data was needed to complete the assessment. The requirement for an abbreviated DNT study was dropped. Bayer never carried out such additional study.

***2012-2014**: During the (new) EU renewal process, Bayer informs the RMS of the existence of this DNT study and proactively added reference of such a study to the renewal dossier*

Bayer held a pre-submission meeting in December 2012 with the 'Rapporteur' Member State (RMS) to prepare for the renewal submission of fenamidone. During this meeting, **Bayer informed the RMS of the existence of the 2004/2005 DNT study (M-253958-01-1), its design and key findings**.

In January 2014, Bayer submitted its renewal dossier for fenamidone to the EU authorities (including the RMS, EFSA, Commission and all Member States), which **included a reference to said DNT study in what Bayer called a 'reference list of studies with no dossier relevance for fenamidone'**. It should be noted that it was Bayer's decision to include this reference list in their renewal dossier, and that this was not a requirement at the time.

***2016-2018**: The EFSA concludes there is no need for additional DNT studies. Fenamidone is not renewed due to other (not-DNT-related) critical areas of concern*

In February 2016, the EFSA conclusion is made public (link), stating that after review of the submitted acute and repeated neurotoxicity study, additional studies such as developmental neurotoxicity were not required.

In 2018, the European Commission decided to not renew the approval of fenamidone due to other reasons,[3] not related to DNT.

2019: *Further developments*

In December **2019**, **Bayer divested fenamidone to Gowan**.

[3] The main reason for the EU non-approval of fenamidone in 2018 was because it was not possible to conclude on the genotoxic potential of fenamidone and no health-based reference values could be set. DNT was thus not the reason for the non-renewal of the substance.