EUROPEAN CHEMICALS AGENCY
BOARD OF APPEAL

SUMMARY OF DECISION OF 21 JUNE 2023 OF THE BOARD OF APPEAL OF THE EUROPEAN CHEMICALS AGENCY

Case number: A-004-2022

(Dossier evaluation – Compliance check – Sections 8.7.2. and 8.7.3. of Annex IX – Mode of administration for PNDT study and EOGRTS – Dose level setting – Time limit to submit the requested information)

Factual background

The appeal concerned a compliance check of the registration for the substance (E)-anethole (the Substance).[1]

By the Contested Decision, the Agency required the Appellant to submit under Section 8.7.2. of Annex IX to the REACH Regulation[2] a prenatal developmental toxicity (PNDT) study and under Column 1 of Section 8.7.3. of Annex IX an extended one-generation reproductive toxicity study (EOGRTS), both studies via oral administration by gavage in accordance with OECD test guidelines 414 and 443 respectively. As to the EOGRTS, the Contested Decision stated that the dose level setting shall aim to induce systemic toxicity at the highest dose level. The Contested Decision also required under Column 2 of Section 8.4. of Annex IX information on a transgenic rodent somatic and germ cell gene mutation assays or an *in vivo* mammalian alkaline Comet assay, which has not been challenged by the Appellant.

The Appellant requested the Board of Appeal to annul the Contested Decision insofar as it required (i) oral administration by gavage for the PNDT study and the EOGRTS, (ii) an EOGRTS, and (iii) specific requirements for the dose level setting in the EOGRTS. Furthermore, to annul the Contested Decision for impeding to allow the three requested studies to be carried out in sequence by 21 October 2024.

Main findings of the Board of Appeal

In its Decision of 21 June 2023, the Board of Appeal dismissed the appeal as unfounded.

Request for the PNDT study and the EOGRTS to be carried out via oral administration by gavage

The Board of Appeal rejected the Appellant's plea that the Agency committed an error of assessment, exceeded its competences, breached Sections 8.7.2. and 8.7.3. of Annex IX and Article 25.

First, the Board of Appeal held that the Agency has the competence to require the use of a specific mode of administration (oral administration by gavage in the present case) in the PNDT study and the EOGRTS in accordance with the applicable test guidelines. The Board of Appeal found that when the relevant OECD test guidelines provide for flexibility and allow for specific modifications in individual cases on the basis of specific knowledge on a substance's properties, the Agency may require the registrant to carry out the respective study by using

[1] EC number 224-052-0.

[2] Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (OJ L 396, 30.12.2006, p. 1). All references to Articles and Annexes hereinafter concern the REACH Regulation unless stated otherwise.

a specific mode of administration if this mode of administration is possible under the applicable test guideline and necessary to obtain meaningful information on the intrinsic properties of the substance in question.

Second, the Board of Appeal held that the Appellant did not demonstrate that the Agency committed an error of assessment in requiring the use of oral administration by gavage on the basis of:

(i) the existing studies indicating that oral administration by gavage may cause more severe reproductive and developmental toxicity than oral administration through the diet,

(ii) the reduced palatability of the Substance and the difficulties in achieving and maintaining sufficiently high dose levels via oral administration through the diet, and

(iii) the regulatory means empowering (and requiring) the Agency to ensure that, if a vertebrate animal study cannot be avoided on the basis of existing information, a vertebrate animal study requested in a compliance check decision is carried out in a way that maximises the likelihood of obtaining data that is adequate for hazard and risk assessment, and minimises the risk of having to duplicate that study.

In the present case, the Appellant has not demonstrated that the choice for oral administration by gavage made by the Agency based on existing information is inadequate for hazard and risk assessment, and that that choice would lead to duplication of studies.

The Board of Appeal also held that, contrary to what the Appellant claimed, the Contested Decision does not preclude the Appellant from carrying out the studies by innovative scientific methods, which the Agency could not have assessed yet, insofar as those methods fill the data gaps of its registration and take due account of the objections identified in the Contested Decision.

Request for information on the EOGRTS

The Board of Appeal rejected the Appellant's plea that the Agency committed an error of assessment, exceeded its competences, breached Section 8.7.3. of Annex IX, Article 25 and the Appellant's right to be heard.

First, the Board of Appeal held that the Agency did not commit an error, has not exceeded its competences nor has breached the invoked provisions by observing that the effects in an existing PNDT study on the Substance should not be disregarded only because carried out at high doses, and therefore that the results of that study were relevant to establish a fertility concern and trigger the EOGRTS. Second, when the conditions for triggering an EOGRTS at Annex IX level are fulfilled, the EOGRTS is a standard information requirement irrespective that some of the properties of the Substance might be examined in a PNDT study as well. Third, the Agency did not breach the right to be heard by not requesting the Appellant to provide further information when it considered that the Appellant's claim in its comments on the draft decision was unsubstantiated.

The Board of Appeal further rejected the Appellant's arguments challenging the Agency's request for the dose level setting. The Board of Appeal held that the Agency is competent to define certain elements of the study design within the flexibility allowed by the applicable test guideline and under the conditions set out in that guideline, and that it may be necessary for the Agency to set out requirements for the dose level setting to maximise the likelihood of obtaining useful results from the requested study.

Not allowing to carry out the three studies in sequence by 21 October 2024

Finally, the Board of Appeal rejected the Appellant's plea that the Agency committed an error of assessment and breached the relevant sections of Annex IX and Article 25. The Board of

Appeal held that in line with Article 25 it was for the Appellant to take appropriate measures following the adoption of the Contested Decision to start carrying out one of the two (non-contested) mutagenicity studies or developing an adaptation if it considered that it could lead to the possibility of adapting the PNDT study and the EOGRTS, irrespective of any time limit.

The Board of Appeal also found that the Appellant did not provide supporting evidence to demonstrate the error of assessment.
