EUROPEAN CHEMICALS AGENCY
BOARD OF APPEAL

SUMMARY OF DECISION OF 29 AUGUST 2023 OF THE BOARD OF APPEAL OF THE EUROPEAN CHEMICALS AGENCY

Case number: A-006-2022

(Dossier evaluation – Compliance check – Section 8.7.3. of Annex IX – EOGRTS – Investigation of the effects of a substance on the gut microbiome)

Factual background

The appeal concerned a compliance check of the registration for the substance octane-1,2-diol (the Substance).[1]

By the Contested Decision, the Agency required the Appellants to submit by 19 July 2024 information on, among others, an extended one-generation reproductive toxicity study (EOGRTS) under Column 1 of Section 8.7.3. of Annex IX to the REACH Regulation[2] in accordance with OECD TG 443. It also specified that the highest dose level in parental animals must be determined based on clear evidence of an adverse effect on sexual function and fertility without severe suffering or deaths as specified in Appendix 1 to the Contested Decision, or follow the limit dose concept ('EOGRTS Testing Conditions').

The Appellants requested the Board of Appeal to annul the Contested Decision insofar as it required them to conduct the EOGRTS by 19 July 2024. In the alternative, they requested the Board of Appeal to exercise its powers under Article 93(3), for example by amending the Contested Decision to (i) allow for 36 months for them to submit the EOGRTS, and (ii) remove from Appendix 1 to the Contested Decision the following specification: '*Regarding the highest dose level, it is important to ensure that sufficient severity of toxicity in both female and male animals is achieved to ensure that potential effects on sexual function and fertility in either gender is not overlooked*'.

Main findings of the Board of Appeal

In its Decision of 29 August 2023, the Board of Appeal dismissed the appeal as unfounded.

The Board of Appeal rejected the Appellants' first plea that the time limit set in the Contested Decision prevents them from investigating the effects of the Substance on the gut microbiome before starting the EOGRTS. The Appellants argue that the prior investigation of the gut microbiome is necessary both from a legal and scientific point of view.

First, the Board of Appeal held that the Agency was not legally required to extend the time limit set in the Contested Decision as the investigation of the effects of the Substance on the gut microbiome is not a legal prerequisite for conducting the EOGRTS under Column 1 of Section 8.7.3. of Annex IX. The Board of Appeal found that this provision mentions repeated dose toxicity studies as the source of information on concerns which may justify the need to carry out an EOGRTS. It is clear from that provision and also confirmed by the Appellants at the hearing that the investigation of the effects of the Substance on the gut microbiome is not a preliminary dose-range finding study of the Substance and therefore not a standard information requirement for registration purposes. Therefore, the Agency is not obliged to

[1] EC number 214-254-7.

[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.

wait for the generation of information not falling within the scope of the information requirements set out in the testing Annexes.

Second, the Board of Appeal held that on the basis of the facts of the case, contrary to what the Appellants claimed, the preliminary investigation of the effects of the Substance on the gut microbiome is not scientifically necessary for an adequate hazard assessment.

In the present case, the Appellants failed to establish that there could be a direct causation between the effects observed in the available studies – which triggered the requirement to carry out an EOGRTS – and the antimicrobial activity of the Substance. Furthermore, the Board of Appeal found that even assuming that that investigation could be useful to demonstrate a specific maternally-mediated mechanism, it cannot nevertheless exclude on its own that other factors (e.g. the potential palatability effects of the Substance) might have caused the effects observed in the available studies.

The Board of Appeal also found that lowering the doses to a level where no antimicrobial effects are detected, as argued by the Appellants, runs the risk of not achieving sufficient exposure to the Substance for the parental animals and the developing embryo and foetuses and therefore of overlooking potential effects on sexual function and fertility.

The Board of Appeal further found that the Agency correctly limited its examination to the information submitted by the Appellants in their registration and that it remains the Appellants' sole responsibility to generate, gather and submit to the Agency the information that they consider that will fulfil the information requirements of the REACH Regulation. The Appellants, if they so wish, may therefore present an updated registration with information on both the EOGRTS and the effects of the Substance on the gut microbiome.

The Board of Appeal rejected the Appellants' second plea that the Agency, by requesting information on an EOGRTS with the EOGRTS Testing Conditions, committed an error of assessment, failed to take relevant information into account, exceeded its competences, and breached Articles 13(3) and 25, as well as the principles of legal certainty and protection of legitimate expectations.

First, the Board of Appeal held that the Agency committed no errors in requiring in the Contested Decision that the highest dose level must be set on the basis of clear evidence of an adverse effect on sexual function and fertility.

According to the Appellants, the OECD TG 443 merely requires the highest dose to be chosen with the aim to induce 'some systemic toxicity', and not specific toxicity (i.e. developmental or reproductive toxicity). However, the Board of Appeal found that under the OECD TG 443 – read in conjunction with the sixth introductory paragraph to Annex IX, Recital 7 of Commission Regulation (EU) 2015/282[3] and the other relevant provisions of the CLP Regulation[4] – the doses inducing 'some systemic toxicity' have to be set at appropriately high levels so as to ensure adequate identification of a potential hazard of the concerned substance in relation to its effects on sexual function and fertility.

Second, the Board of Appeal held that the Agency did not breach Article 25.

According to the Appellants, the administration of the highest dose will likely cause animal suffering and lead to massive systemic toxicity, as well as the imposition of legally uncertain and undefined dose levels increases the risk of the study having to be duplicated. However, the Board of Appeal held that the consequences of the existence of a data-gap under Column 1 of Section 8.7.3. of Annex IX – not disputed by the Appellants – flow directly from the REACH Regulation, which requires the Appellants to submit either information on an OECD

[3] Commission Regulation (EU) 2015/282 amending Annexes VIII, IX and X to the REACH Regulation as regards the Extended One-Generation Reproductive Toxicity Study (OJ L 50, 21.2.2015, p. 1; 'Regulation 2015/282').

[4] Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (OJ L 353, 31.12.2008, p. 1; 'CLP Regulation').

TG 443 study or, alternatively, an acceptable adaptation in accordance with the specific adaptation rules in Column 2 of Section 8.7.3. of Annex IX or the general adaptation rules in Annex XI. Since neither of these information was provided by the Appellants, the Agency was neither required nor empowered to consider whether it is consistent with Article 25 for the Appellants to be required to submit this information.

Third, the Board of Appeal held that the Agency did not breach the principles of legal certainty and protection of legitimate expectations.

According to the Appellants, the Contested Decision contained vague and entirely undefined terms and deviated from the Agency's guidance document *'Advice on dose-level selection for the conduct of reproductive toxicity studies (OECD TGs 414, 421/422 and 443) under REACH*'.[5] However, the Board of Appeal held that the Contested Decision lays down the requirements for the dose level setting for the EOGRTS by merely replicating the wording of the provisions and test guidelines applicable to this information requirement. The Appellants are able to know, without ambiguity, what their obligations are and to take steps accordingly. The Board of Appeal also found that the guidance document refers to paragraphs of the OECD TG 443 to be read in conjunction with the sixth introductory paragraph to Annex IX, Recital 7 of Regulation 2015/282, and the other relevant provisions of the CLP Regulation, and is therefore consistent with the EOGRTS Testing Conditions.

Finally, the Board of Appeal rejected the part of the second plea by which the Appellants claimed that the Agency exceeded its competences, as it was unsubstantiated.

The appeal was therefore dismissed.

NOTE: The Board of Appeal of ECHA is responsible for deciding on appeals lodged against certain ECHA decisions. The ECHA decisions that can be appealed to the Board of Appeal are listed in Article 91(1) of the REACH Regulation. Although the Board of Appeal is part of ECHA, it makes its decisions independently and impartially. Decisions taken by the Board of Appeal may be contested before the General Court of the European Union.

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[5] European Chemicals Agency, *Advice on dose-level selection for the conduct of reproductive toxicity studies (OECD TGs 414, 421/422 and 443) under REACH*, January 2022, available at https://www.echa.europa.eu/documents/10162/17220/211221_echa_advice_dose_repro_en.pdf/27159fb1-c31c-78a2-bdef-8f423f2b6568?t=1640082455275 (last accessed on 22.09.2023).