EUROPEAN CHEMICALS AGENCY
BOARD OF APPEAL

DECISION OF THE BOARD OF APPEAL OF THE EUROPEAN CHEMICALS AGENCY

29 April 2021

(Testing proposal – Pre-natal developmental toxicity study on a second species – Extended one-generation reproductive toxicity study – UVCB and multi-constituent substances – Duties of the Agency – Third-party consultation – Animal welfare – Proportionality)

Case number	A-014-2019
Language of the case	English
Appellant	LG Chem Europe GmbH, Germany
Representative	Claudio Mereu Fieldfisher (Belgium) LLP, Belgium
Contested Decision	TPE-D-2114465664-40-01/F of 5 July 2019 adopted by the European Chemicals Agency (the 'Agency') pursuant to Article 40 of 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; the 'REACH Regulation')

THE BOARD OF APPEAL

composed of Antoine Buchet (Chairman and Rapporteur), Uta Jensen-Korte (Technically Qualified Member) and Ekaterina Georgieva (Legally Qualified Member)

Registrar: Alen Močilnikar

gives the following

Decision

Background to the dispute

1. The Appellant is a registrant of the substance 1,4-Benzenedicarboxylic acid, mixed Bu and 2-ethylhexyl diesters (EC number 946-149-3, CAS number 1571954-81-8; the 'Substance'). The Appellant registered the Substance at the 1 000 tonnes or more per year tonnage band.

2. The Appellant's registration dossier included two testing proposals: one for a pre-natal developmental toxicity ('PNDT') study on a second species, and one for an extended one-generation reproductive toxicity study ('EOGRTS').

3. In the testing proposal for an EOGRTS, the Appellant considered that a pre-mating treatment of two weeks for both sexes is adequate '*as [the Substance] has no effects on spermatogenesis or sperm integrity*' and '*no effects on the oestrous cycle*'. The Appellant suggested that the dose level setting of the EOGRTS should be based on a 90-day sub-chronic toxicity study (OECD TG 408), a PNDT study in a first species, and a combined repeated dose toxicity study and reproductive/developmental toxicity screening test (OECD TG 422) that were available in its registration dossier.

4. The Appellant proposed to conduct the EOGRTS without extension of Cohort 1B to mate the Cohort 1B animals to produce the F2 generation and without Cohorts 2A and 2B and/or Cohort 3. The Appellant considered that the extension of Cohort 1B and the inclusion of Cohorts 2A and 2B and/or Cohort 3 in the study design were not necessary as the 90-day sub-chronic toxicity study and the OECD 422 screening study showed that the Substance has no effect on reproductive organs and is not expected to cause developmental neurotoxicity or developmental immunotoxicity.

5. Between 21 May and 5 July 2018, the Agency conducted a public consultation on the Appellant's testing proposals for the PNDT study on a second species and the EOGRTS, in accordance with Article 40(2) of the REACH Regulation (all references to Articles and Annexes hereinafter concern the REACH Regulation unless stated otherwise).

6. During the public consultation, the Agency received the following contribution from a third party:

   'In EOGRTS, based on certain criteria or triggers, selected offspring are assigned at weaning to different cohorts for further investigation of sexual maturation, reproductive organ integrity and function, neuropathological and behavioural endpoints, and/or immune function. If the proposed study by the Registrant is confirmed by ECHA; the basic study design (Cohorts 1A, and 1B without extension) is considered to be appropriate in the absence of any triggers or conditions necessitating the inclusion of additional cohorts or a further generation. The results from 90-day repeated dose studies with the test material has not effect on reproductive organs. No changes in the weight and no findings were found in macroscopy or histopathology of related tissues. In the combined Repeated Dose Toxicity Study and Reproductive/Developmental Toxicity Screening and Estrous cycles, pre-coital interval, mating performance, fertility and gestation length were unaffected by treatment. The clinical condition of the offspring, their survival, sex ratio, ano-genital distance and male nipple counts showed no adverse effects of parental treatment. Litter size was slightly affected by treatment. When compared with the controls, the mean number of implantations in females treated at 330 or 1 000 mg/kg/day was slightly low (84 and 86 %, respectively) and this resulted in a lower total litter size on Day 1 in these groups. However, this effect on number of implantations was not observed in the embryo fetal developmental toxicity study. Therefore an extension of cohort 1 is not necessary. The substance is not considered to be genotoxic based on the study data and does not meet the criteria for classification as a mutagen (Category 2) according to CLP. There is no indication (based on the structure of the substance or from the existing toxicological dataset) of an endocrine-related mode of action. There is no indication (either from

structural alerts or from the existing toxicological dataset) of (developmental) neurotoxicity or (developmental) immunotoxicity.'

7. On 23 August 2018, the Agency notified the draft decision to the Appellant pursuant to Article 50(1), informing the Appellant of its right to comment. According to the draft decision:

'Your testing proposal is accepted and you are requested to carry out:

1. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) in a second species (rabbit), oral route using the registered substance.

Your testing proposal is modified and you are requested to carry out:

2. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: EU B.56/OECD TG 443) in rats, oral route with the registered substance specified as follows:

- *Ten weeks premating exposure duration for the parental (P0) generation;*
- *Dose level setting shall aim to induce some systemic toxicity at the highest dose level;*
- *Cohort 1A (Reproductive toxicity);*
- *Cohort 1B (Reproductive toxicity) with extension to mate the Cohort 1B animals to produce the F2 generation;*
- *Cohorts 2A and 2B (Developmental neurotoxicity).'*

8. In the letter by which the draft decision was notified to the Appellant, the Agency stated, *inter alia*, the following:

'For the purpose of the abovementioned decision making, ECHA does not take into account any dossier updates after 31 October 2018, i.e. 30 calendar days after the end of the commenting period under Article 50(1) of the REACH Regulation. Any such updates will be examined by ECHA after the deadline set in the adopted decision has passed. […]

Possibility for an informal discussion with ECHA

In addition to the opportunity to provide formal comments through the webform, ECHA would like to offer you a possibility to informally and without delay discuss the scientific rationale behind the current draft decision.

To establish such a scientific exchange with ECHA staff, we invite you to contact us within 10 working days from the date of this letter […].

Please specify the points of the draft decision you would like to discuss, your contact details, and your availability for the informal discussion. After receipt of this information ECHA will contact you. […]'

9. On 27 September 2018, the Appellant submitted comments on the draft decision. In its comments the Appellant stated that the Substance is a multi-constituent substance, '*not a UVCB as detailed previously in the test proposal*'. The Appellant argued that a '*considerable volume of in vivo testing data*' on one of the three constituents and the common metabolite of all constituents of the Substance, terephtalic acid, was available. The Appellant submitted that, instead of performing a PNDT study on a second species, the information requirement of Section 8.7.2. of Annex X could be fulfilled by '*using a combination of study data, publicly available data and also QSAR [quantitative structure-activity relationship] assessments*'. The Appellant submitted that, instead of performing an EOGRTS, the information requirement of Section 8.7.3. of Annex X could be fulfilled by '*using a combination of information already available on [the Substance], information from structurally related substance, publicly available data and QSAR assessment*'.

10. On 5 July 2019, as no proposals for amendment were submitted by the competent authorities of the Member States, the Agency adopted the Contested Decision in accordance with Article 51(3).

11. According to the Contested Decision:

'*Your testing proposal is accepted and you are requested to carry out:*

1. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method: OECD TG 414) in a second species (rabbit), oral route using the registered substance.

Your testing proposal is modified and you are requested to carry out:

2. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) in rats, oral route with the registered substance specified as follows:

- *Ten weeks premating exposure duration for the parental (P0) generation;*
- *Dose level setting shall aim to induce some systemic toxicity at the highest dose level;*
- *Cohort 1A (Reproductive toxicity);*
- *Cohort 1B (Reproductive toxicity) with extension to mate the Cohort 1B animals to produce the F2 generation;*
- *Cohorts 2A and 2B (Developmental neurotoxicity).*

You have to submit the requested information in an updated registration dossier by 12 January 2022. You also have to update the chemical safety report, where relevant. The timeline has been set to allow for sequential testing.'

Procedure before the Board of Appeal

12. On 4 October 2019, the Appellant lodged this appeal.

13. On 9 December 2019, the Agency lodged its Defence.

14. On 15 May 2020, the Appellant lodged its observations on the Defence and replied to written questions from the Board of Appeal.

15. On 3 September 2019, the Agency lodged its observations on the Appellant's observations on the Defence.

16. On 15 October 2020, Ekaterina Georgieva and Uta Jensen-Korte were designated to act, respectively, as legally and technically qualified members of the Board of Appeal in this case, in accordance with the second subparagraph of Article 3(2) of Commission Regulation (EC) No 771/2008 laying down the rules of organisation and procedure of the Board of Appeal of the European Chemicals Agency (OJ L 206, 2.8.2008, p. 5; the 'Rules of Procedure').

17. On 27 January 2021, a hearing took place at the Appellant's request. The hearing was held by video-conference in accordance with Article 13(7) of the Rules of Procedure. At the hearing, the Parties made oral submissions and answered questions from the Board of Appeal.

Form of order sought

18. The Appellant requests the Board of Appeal to annul the Contested Decision. In the alternative, the Appellant requests the partial annulment of the Contested Decision insofar as it requires the EOGRTS to be conducted with the following parameters:

    (a) ten weeks premating exposure duration for the parental (P0) generation;

    (b) dose level setting which shall aim to induce systemic toxicity at the highest dose level;

    (c) Cohort 1B (reproductive toxicity) with extension to make the Cohort 1B animals to produce the F2 generation; and

    (d) Cohorts 2A and 2B (developmental neurotoxicity).

19. The Appellant also requests the Board of Appeal to order the Agency to pay the costs of the appeal proceedings.

20. The Agency requests the Board of Appeal to dismiss the appeal as unfounded.

Reasons

21. The Appellant raises the following pleas in law:

    1. The Agency breached Columns 1 and 2 of Section 8.7.2. of Annex IX and Section 8.7.2. of Annex X by requiring the Appellant to carry out a PNDT study on a second species (first plea);
    2. The Agency breached Article 40(1), (3) and (4) by adopting the Contested Decision '*prematurely and unlawfully*' (second plea);
    3. The Agency breached Article 40(2) regarding the public consultation on the Appellant's testing proposal (third plea);
    4. The Agency failed to take into account all the available information (fourth plea);
    5. The Agency breached Article 13 of the Treaty on the Functioning of the European Union ('TFEU'), Article 25 of the REACH Regulation, and '*the principle of proportionality/animal welfare/sound administration*' (fifth plea).

22. It is appropriate to examine together the second and the fourth plea. Therefore, the pleas will be examined in the following sequence: first plea, second and fourth plea together, third plea, and fifth plea.

1. First plea: The Agency breached Columns 1 and 2 of Section 8.7.2. of Annex IX and Section 8.7.2. of Annex X by requiring the Appellant to carry out a PNDT study on a second species

Relevant legislation

23. Column 1 ('*standard information required*') of Section 8.7.2. of Annex IX provides:

    '*Pre-natal developmental toxicity study, one species, most appropriate route of administration, having regard to the likely route of human exposure (B.31 of the Commission Regulation on test methods as specified in Article 13(3) or OECD 414).*'

24. Column 2 ('*specific rules for adaptation from Column 1*') of Section 8.7.2. of Annex IX provides:

    '*The study shall be initially performed on one species. A decision on the need to perform a study at this tonnage level or the next on a second species should be based on the outcome of the first test and all other relevant available data*.'

25. Column 1 ('*standard information required*') of Section 8.7.2. of Annex X provides:

    '*Developmental toxicity study, one species, most appropriate route of administration, having regard to the likely route of human exposure (OECD 414).'*

26. Column 2 ('*specific rules for adaptation from Column 1*') of Section 8.7. of Annex X provides:

    '*The [reproductive toxicity studies set out in Sections 8.7.2. and 8.7.3.] need not be conducted if:*

    — the substance is known to be a genotoxic carcinogen and appropriate risk management measures are implemented, or

    — the substance is known to be a germ cell mutagen and appropriate risk management measures are implemented, or

    — the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit

using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure.

If a substance is known to have an adverse effect on fertility, meeting the criteria for classification as toxic for reproduction category 1A or 1B: May damage fertility (H360F), and the available data are adequate to support a robust risk assessment, then no further testing for fertility will be necessary. However, testing for developmental toxicity must be considered.

If a substance is known to cause developmental toxicity, meeting the criteria for classification as toxic for reproduction category 1A or 1B: May damage the unborn child (H360D), and the available data are adequate to support a robust risk assessment, then no further testing for developmental toxicity will be necessary. However, testing for effects on fertility must be considered.'

Arguments of the Parties

27. By its first plea the Appellant argues that the Agency erred in considering that there was a data gap in the Appellant's registration dossier as regards the information on a PNDT study on a second species.

28. The Appellant argues that it had fulfilled the standard information requirement as regards the pre-natal developmental toxicity under Annexes IX and X by providing a PNDT study in one species. The conditions for requesting a PNDT study on a second species under Column 2 of Section 8.7.2. of Annex IX were not met.

29. The Agency disputes the Appellant's arguments.

Findings of the Board of Appeal

30. By its first plea the Appellant argues, in essence, that a PNDT study on a second species is not a standard information requirement under Column 1 of Section 8.7.2. of Annex X.

31. The argument of the Appellant must be rejected for the following reasons.

32. The information requirements set out in Columns 1 of Annexes VII to X (the 'testing Annexes') are cumulative. This principle is set out in the first introductory paragraph to Annex VI. The introduction to each of the testing Annexes, including the second paragraph of Annex X, repeats this principle.

33. The Appellant registered the Substance at the 1 000 tonnes or more per year tonnage band. The Appellant was therefore required to fulfil the information requirements of Annex X. In accordance with the second paragraph of Annex X, *'the information required in column 1 of this Annex is additional to that required in column 1 of Annexes VII, VIII and IX'*.

34. As a result of the cumulative information requirements set out in Column 1 of the testing Annexes, registrants at the level of Annex X are required to perform a PNDT study in a species other than the species used in the PNDT study under Column 1 of Section 8.7.2 of Annex IX, unless one or more of the adaptations in Section 8.7. of Annex X or Annex XI apply (see Case A-004-2012, *Lanxess Deutschland*, Decision of the Board of Appeal of 10 October 2013, paragraph 73).

35. Column 1 of Section 8.7.2. of Annex IX requires registrants to perform a PNDT study on one species. Pursuant to Column 2 of Section 8.7.2. of Annex IX the registrants at the level of Annex IX may be required also to perform a PNDT study on a second species depending on the outcome of the PNDT study on the first species and all other relevant available data.

36. The adaptation rule set out in Column 2 of Section 8.7.2. of Annex IX is not applicable at the level of Annex X. Indeed, as provided for in the second paragraph of Annex X, '*Column 2 of <u>this</u> Annex lists specific rules according to which the registrant may propose to omit the required standard information, replace it by other information, provide it at a later stage or adapt it in another way*' (emphasis added).

37. Column 2 of Section 8.7.2. of Annex X does not contain a specific adaptation rule with respect to the standard information requirement for a PNDT study on a second species set out in Column 1 of Section 8.7.2. of Annex X.

38. It follows that registrants at the level of Annex X are required to submit information on PNDT studies on two different species unless one or more of the specific adaptation rules in Section 8.7. of Annex X or of the general adaptation rules in Annex XI apply.

39. Contrary to the Appellant's arguments, the Agency was therefore correct in finding, in the Contested Decision, that '*[p]re-natal developmental toxicity studies on two species are part of the standard information requirements for substances registered for 1000 tonnes or more per year*'.

40. As a result, the Appellant's plea that the Agency breached Columns 1 and 2 of Section 8.7.2. of Annex IX and Section 8.7.2. of Annex X must be rejected.

2. Second and fourth pleas: The Agency breached Article 40(1), (3) and (4) by adopting the Contested Decision '*prematurely and unlawfully*' and failed to take all the available information into account

Relevant legislation

41. Article 40(1) provides:

'*1. The Agency shall examine any testing proposal set out in a registration or a downstream user report for provision of the information specified in Annexes IX and X for a substance.*

[…].'

42. Article 40(3) provides:

'*On the basis of the examination under paragraph 1, the Agency shall draft one of the following decisions and that decision shall be taken in accordance with the procedure laid down in Articles 50 and 51:*

(a) a decision requiring the registrant(s) or downstream user(s) concerned to carry out the proposed test and setting a deadline for submission of the study summary, or the robust study summary if required by Annex I;

(b) a decision in accordance with point (a), but modifying the conditions under which the test is to be carried out;

(c) a decision in accordance with points (a), (b) or (d) but requiring registrant(s) or downstream user(s) to carry out one or more additional tests in cases of non-compliance of the testing proposal with Annexes IX, X and XI;

(d) a decision rejecting the testing proposal;

(e) a decision in accordance with points (a), (b) or (c), if several registrants or downstream users of the same substance have submitted proposals for the same test, giving them the opportunity to reach an agreement on who will perform the test on behalf of all of them and to inform the Agency accordingly within 90 days. If the Agency is not informed of such agreement within such 90 days, it shall designate one of the registrants or downstream users, as appropriate, to perform the test on behalf of all of them.'

43. Article 40(4) provides:

'*The registrant or downstream user shall submit the information required to the Agency by the deadline set.*'

44. The first and second subparagraphs of Column 2 of Section 8.7.3. of Annex X provide:

'*An [EOGRTS] with the extension of cohort 1B to include the F2 generation shall be proposed by the registrant or may be required by the Agency in accordance with Article 40 or 41, if:*

(a) the substance has uses leading to significant exposure of consumers or professionals, taking into account, inter alia, consumer exposure from articles, and

(b) any of the following conditions are met:

- *the substance displays genotoxic effects in somatic cell mutagenicity tests in vivo which could lead to classifying it as Mutagen Category 2, or*
- *there are indications that the internal dose for the substance and/or any of its metabolites will reach a steady state in the test animals only after an extended exposure, or*
- *there are indications of one or more relevant modes of action related to endocrine disruption from available in vivo studies or non-animal approaches.*

An [EOGRTS] including cohorts 2A/2B (developmental neurotoxicity) and/or cohort 3 (developmental immunotoxicity) shall be proposed by the registrant or may be required by the Agency in accordance with Article 40 or 41, in case of particular concerns on (developmental) neurotoxicity or (developmental) immunotoxicity justified by any of the following:

- *existing information on the substance itself derived from relevant available* in vivo *or non-animal approaches (e.g. abnormalities of the [central nervous system], evidence of adverse effects on the nervous or immune system in studies on adult animals or animals exposed prenatally), or*
- *specific mechanisms/modes of action of the substance with an association to (developmental) neurotoxicity and/or (developmental) immunotoxicity (e.g. cholinesterase inhibition or relevant changes in thyroidal hormone levels associated to adverse effects), or*
- *existing information on effects caused by substances structurally analogous to the substance being studied, suggesting such effects or mechanisms/modes of action.'*

Arguments of the Parties

45. By its second and fourth pleas the Appellant argues that the Agency erred in the conduct of the decision-making procedure and failed to take all the available information into account in the Contested Decision.

46. First, the Appellant argues that in its registration dossier, it erroneously described the Substance as a substance of unknown or variable composition, complex reaction products or biological materials ('UVCB'). In its comments on the draft decision, the Appellant '*re-visited its position*' as regards the need for a PNDT study on a second species and an EOGRTS because it realised that the Substance is a multi-constituent substance, not a UVCB substance.

47. The Appellant argues that, after having corrected the error in the description of the Substance type, it became possible to fulfil the information requirements of Sections 8.7.2. and 8.7.3. of Annex X by a combination of read-across from the constituents of the Substance under Section 1.5. of Annex XI, a weight of evidence approach under Section 1.2. of Annex XI, and QSAR predictions under Section 1.3. of Annex XI. The Appellant argues that such adaptations cannot be applied for a UVCB substance but are relevant for a multi-constituent substance.

48. The Appellant argues that the Agency should have raised on its own motion the '*inaccuracies*' of the Appellant's registration dossier as regards the description of the Substance type. The Appellant argues that the Agency should have considered the '*critical new information*' on the description of the Substance type before the adoption of the Contested Decision and should have given the Appellant an opportunity to update its registration dossier once the Appellant had changed its position on the description of the Substance type in its comments on the draft decision.

49. Second, the Appellant argues that the Agency failed to take into account all the available information as regards the availability of alternative methods for fulfilling the contested information requirements.

50. The Appellant argues that the Agency '*willingly or negligently omitted to consider*' the information that was available in the registration dossiers of two of the three constituents of the Substance and is published on the Agency's website. The Appellant argues that this information shows '*individually and collectively that [the Substance] is not a reproductive or/and developmental toxicant*'.

51. The Appellant argues that the Agency therefore breached its duties under Article 40(1), (3) and (4) and adopted the Contested Decision '*prematurely and unlawfully'*.

52. The Appellant argues that, as a result of these failures, the Agency erred in requesting the Appellant to provide information on a PNDT study on a second species and on an EOGRTS, and at least when it required the EOGRTS to be performed with '*additional parameters*' (see paragraph 18 above).

53. The Agency disputes the Appellant's arguments.

Findings of the Board of Appeal

2.1. Failure in the conduct of the decision-making procedure

54. By its second plea the Appellant argues, in essence, that before adopting the Contested Decision the Agency should have raised on its own motion the '*inaccuracies*' of the Appellant's registration dossier as regards the description of the Substance type. The Agency should have given the Appellant the opportunity to update its registration dossier following the '*critical new information*' on the description of the Substance type which the Appellant provided in its comments to the draft decision.

55. The arguments of the Appellant must be rejected for the following reasons.

56. First, the relevant provisions that apply to the decision-making procedure in the examination of testing proposals are Articles 40, 50 and 51. Under those provisions, the Agency does not have a legal obligation to wait for registrants to improve their justification for an adaptation beyond what the specific provisions of the REACH Regulation and the requirements of principle of good administration require (see, to this effect, Case A-005-2016, *Cheminova*, Decision of the Board of Appeal of 30 January 2018, paragraph 49; see also Case A-016-2019 to A-029-2019, *Lubrizol France and Others*, Decision of the Board of Appeal of 23 February 2021, paragraph 76).

57. In the present case, the Appellant was provided with an opportunity to update its registration dossier within 30 days following the end of the 30-day timeline prescribed to provide comments on the draft decision in Article 50(1). This possibility was explicitly mentioned in the letter by which the Agency notified the draft decision to the Appellant (see paragraph 8 above). The Appellant did not update the registration dossier to withdraw its testing proposals or to propose an adaptation within that timeframe. It was not until 24 October 2019, which is after the adoption of the Contested Decision, that the Appellant submitted an update to its registration dossier.

58. In the letter by which the draft decision was notified to the Appellant, the Agency also offered the Appellant the possibility of an informal dialogue to '*discuss the scientific rationale behind*' the draft decision. The letter also clearly informed the Appellant that the Agency will contact it '*after receipt of [the] information*' indicated therein, i.e. the '*points of the draft decision you would like to discuss, your contact details, and your availability for the informal discussion'* (see paragraph 8 above). However, the Appellant chose not to use the possibility to have such an informal dialogue in which it could have clarified also the issues related to the description of the Substance type in its testing proposals.

59. Second, it is the sole responsibility of registrants to generate, gather and submit to the Agency information that will substantiate an adaptation in accordance with the requirements of the REACH Regulation. Article 40 does not empower the Agency to require

registrants to generate, gather and submit information to substantiate an adaptation (see *Lubrizol France and Others*, cited in paragraph 56 above, paragraphs 125 and 126 of the Decision).

60. Third, in the registration dossier of the Appellant the Substance type was primarily described as a multi-constituent substance. The reference to the Substance type as a UVCB substance only appeared in the testing proposals. The fact that the Agency did not comment on this discrepancy in the Contested Decision once it had been raised by the Appellant does not have any bearing on the fact that in the registration dossier the Substance type was primarily described as a multi-constituent substance.

61. Therefore, the Appellant's comments on the draft decision as regards the Substance type cannot be considered to be a substantial new information that would have required the Agency to re-start, or repeat certain steps of, the decision-making process (see, to this effect, Case A-001-2018, *BrüggemannChemical, L. Brüggemann*, Decision of the Board of Appeal of 9 April 2019, paragraph 72).

62. Fourth, nothing in Section 1.5. of Annex XI ('*Grouping of substances and read-across approach*') or elsewhere in the REACH Regulation precludes the use of read-across adaptations for UVCB substances. The possibility to apply read-across adaptations for multi-constituent substances and for UVCB substances is explicitly mentioned in the relevant guidance document of the Agency (*Read-Across Assessment Framework (RAAF) – Considerations on multi-constituent substances and UVCBs*, March 2017, p. 29). Therefore, even if the Appellant had considered that the Substance is a UVCB substance, that, in itself, would not have prevented it from seeking to rely on a read-across adaptation for the Substance.

63. In view of paragraphs 56 to 62 above, the Appellant's plea that the Agency erred in the conduct of the decision-making procedure must be rejected.

2.2. Failure to take all the available information into account

64. By its fourth plea the Appellant argues, in essence, that when considering the need for a PNDT study on a second species and an EOGRTS the Agency failed to take into account the information in the registration dossiers of two of the three constituents of the Substance. According to the Appellant, it can be concluded from this information, which is publicly available on the Agency's website, that the Substance '*is not a reproductive or/and developmental toxicant'* and therefore a PNDT study in second species and an EOGRTS are not necessary.

65. The argument of the Appellant must be rejected for the following reasons.

66. In the conduct of its decision-making procedures the Agency is required to examine carefully and impartially all the relevant facts of the cases and to gather all the factual and legal material necessary for the exercise of its discretion, and to ensure the proper conduct and the efficiency of the procedures it implements (see judgment of 3 October 2019, *BASF and REACH & Colours* v *ECHA*, T-806/17, EU:T:2019:724, paragraph 75).

67. Checking the dossiers of other registrants of the same substance for relevant information in the course of a testing proposal decision-making procedure under Article 40 is good practice and one practical way for the Agency to help ensure that testing on vertebrate animals is undertaken only as a last resort as required by Article 25(1) (see Case A-001-2014, *CINIC Chemicals Europe*, Decision of the Board of Appeal of 10 June 2015, paragraph 75). However, the Agency cannot be required to consider information available in the registration dossiers of any other substances and publicly available information for other substances that has not been specifically raised by the registrant.

68. The Agency was therefore required to take into account the data available in the registration dossiers of the constituents of the Substance only to the extent that such information was specifically raised by the Appellant during the decision-making procedure leading to the Contested Decision (see, to this effect, Case A-006-2018, *Emerald Kalama Chemical and Others*, Decision of the Board of Appeal of 24 March 2020, paragraph 107).

69. It is for the registrant who submits an adaptation to set out clearly the relevant provision of Annexes VII to XI on which the adaptation is based, the grounds for the adaptation, and the scientific information which substantiates those grounds (see Case A-011-2018, *Clariant Plastics & Coatings (Deutschland)*, Decision of the Board of Appeal of 4 May 2020, paragraph 35).

70. In its comments on the draft decision, the Appellant stated that a '*considerable volume of in vivo testing data*' on one of the three constituents of the Substance, and on the common metabolite of the constituents of the Substance, terephtalic acid, was available. According to the Appellant, the information requirement for endpoint 8.7.2. of Annex X on the Substance could be fulfilled by '*using a combination of study data, publicly available data and also QSAR assessments*' and the information requirement of Section 8.7.3. of Annex X could be fulfilled by '*using a combination of information already available on [the Substance], information from structurally related substance, publicly available data and QSAR assessment*' (see paragraph 9 above).

71. The Appellant argues that the information requirement set out in Section 8.7.2. of Annex X could be fulfilled by an adaptation under Column 2 of Section 8.7. of Annex X, and that both of the contested information requirements could be fulfilled by a combination of adaptations under Sections 1.2. (weight of evidence), 1.3. (QSAR predictions) and 1.5. (read-across) of Annex XI.

72. However, the Appellant has not substantiated those claims in its registration dossier or during the decision-making process leading to the Contested Decision.

73. First, the Appellant did not establish that any of the conditions set out in the specific adaptation rule of Column 2 of Section 8.7. of Annex X would be fulfilled in the present case (see paragraph 26 above).

74. Second, whilst the Appellant argues that the contested information requirements can be fulfilled by using a combination of weight of evidence, QSAR and read-across adaptations, it did not provide, in its registration dossier or during the decision-making process leading to the Contested Decision, any evidence on the weight of evidence or the QSAR adaptations.

75. Third, the Appellant submitted a read-across adaptation under Section 1.5. of Annex XI only after the Contested Decision had been adopted. During the decision-making procedure leading to the Contested Decision, the Appellant only referred to a possibility to rely on read-across from the constituents of the Substance, without substantiating this hypothesis.

76. Therefore, in its registration dossier and in the course of the decision-making procedure leading to the Contested Decision, the Appellant failed to substantiate its hypothesis that the information requirements for a PNDT on a second species and an EOGRTS could be fulfilled by a combination of read-across, weight of evidence and QSAR adaptations.

77. As the Appellant had not substantiated the adaptations, the Agency had no other option but to require the Appellant to fulfil the data gaps in the registration dossier by submitting information on a PNDT study on a second species and an EOGRTS (see *Clariant Plastics & Coatings (Deutschland)*, cited in paragraph 69 above, paragraphs 49 to 51 and 96 of the Decision).

78. In view of the paragraphs 66 to 77 above, the Appellant's plea that the Agency has failed to take all the available information into account must be rejected.

2.3. Failure in defining the study design of the EOGRTS

79. The Appellant argues that if the EOGRTS is required, the '*basic study design*' is sufficient (see paragraphs 3 and 4 above). The Appellant argues that the Agency erred in requiring the EOGRTS to be performed with a ten weeks pre-mating exposure duration for the parental (P0) generation and with a dose level that shall aim to inducing some systemic toxicity at the highest dose level. Moreover, the Appellant argues that the extension of Cohort 1B animals to produce the F2 generation and the inclusion of Cohorts 2A and 2B in the study design are unnecessary.

80. According to the Contested Decision, the standard length of the pre-mating exposure duration in an EOGRTS is ten weeks, which allows '*to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility*'. The Contested Decision also states that ten weeks pre-mating exposure duration is required, unless the available substance-specific data supports a shorter pre-mating exposure duration. The Contested Decision further states that ten weeks premating exposure duration is also supported by the lipophilic nature of the Substance.

81. The Appellant has not provided any argument to refute those reasons.

82. The Appellant has also not provided any arguments capable of demonstrating that the Agency erred in requiring that the dose level setting of the EOGRTS shall aim to induce some systemic toxicity at the highest dose level.

83. The conditions for the extension of Cohort 1B to produce the F2 generation are set out in the first subparagraph of Column 2 of Section 8.7.3. of Annex X (see paragraph 44 above).

84. In the Contested Decision the Agency found that those conditions are fulfilled. The Substance has uses which lead to significant exposure of consumers and professionals. Based on its water octanol-partition coefficient value, the Substance is expected to reach a steady state in test animals only after an extended exposure. In addition, the results of the available 90-day sub-chronic toxicity study indicate endocrine-disrupting modes of action.

85. In its comments on the draft decision and in the course of these appeal proceedings the Appellant argued that the endocrine disruption effects displayed in the 90-day sub-chronic toxicity study would be irrelevant for humans. However, the Appellant has not disputed the Agency's finding that the Substance has uses leading to a significant exposure of consumers or professionals and that, based on its water octanol-partition coefficient value, the Substance is expected to reach a steady state in test animals only after an extended exposure.

86. Therefore, it is undisputed that the condition set out in letter (a) and at least one of the independent conditions set out in letter (b) of the first subparagraph of Column 2 of Section 8.7.3. of Annex X that trigger the extension of Cohort 1B to produce the F2 generation are fulfilled in the present case.

87. The conditions for the extension to include Cohorts 2A and 2B are set out in the second subparagraph of Column 2 of Section 8.7.3. of Annex X (see paragraph 44 above).

88. In the Contested Decision the Agency found that the Substance fulfils those conditions. The available 90-day sub-chronic toxicity study shows hypertrophy of follicular epithelium in thyroid glands in both sexes, in the mid and high-dose groups (300 and 1000 mg/kg bw/day), which is '*evidence on specific mode(s) of action with an association to (developmental) neurotoxicity*'. Such a morphological change of the thyroid gland creates a particular concern for developmental neurotoxicity.

89. The Appellant argues that the thyroid effect was secondary to and a consequence of an adaptive response of the liver, that the thyroid effect was not adverse and that the finding was clearly identified as being rodent specific and irrelevant to humans. However, the Appellant has failed to provide any supportive data to substantiate these claims.

90. Therefore, the Appellant has not demonstrated that the Agency erred in concluding that the thyroid findings are indication for a specific mechanisms/modes of action of the substance with an association to developmental neurotoxicity.

91. In view of paragraphs 80 to 90 above, the Appellant has not established that the Agency erred in requiring the EOGRTS to be performed with a ten weeks pre-mating exposure duration for the parental (P0) generation and with a dose level that shall aim to inducing some systemic toxicity at the highest dose level, as well as in requiring the EOGRTS with the extension of Cohort 1B and the Cohorts 2A and 2B.

2.4. Conclusion on the Appellant's second and fourth pleas

92. It follows from the reasons set out in Sections 2.1. to 2.3. above that the Agency did not breach Article 40(1), (3) or (4) when it accepted the Appellant's testing proposal for the PNDT on a second species as such, and the Appellant's testing proposal for the EOGRTS as modified pursuant to Column 2 of Section 8.7.3. of Annex X. The Agency also did not fail to take into account the information provided by the Appellant in its registration dossier and in its comments to the draft decision.

93. As a result, the Appellant's pleas that the Agency breached Article 40(1), (3) and (4) and failed to take all the available information into account must be rejected.

3. Third plea: The Agency breached Article 40(2) as regards the public consultation on the Appellant's testing proposal

Relevant legislation

94. Article 40(2) provides:

'*Information relating to testing proposals involving tests on* vertebrate *animals shall be published on the Agency website. The Agency shall publish on its website the name of the substance, the hazard end-point for which vertebrate testing is proposed, and the date by which any third party information is required. It shall invite third parties to submit, using the format provided by the Agency, scientifically valid information and studies that address the relevant substance and hazard end-point, addressed by the testing proposal, within 45 days of the date of publication. All such scientifically valid information and studies received shall be taken into account by the Agency in preparing its decision in accordance with paragraph 3.*'

Arguments of the Parties

95. By its third plea the Appellant argues that the Agency breached Article 40(2) '*by ignoring information submitted by a third party'* in a public consultation on the Appellant's testing proposals and *'by requiring that scientific information submitted by third parties "fulfils" information requirements in a registration dossier'*.

96. The Agency disputes the Appellant's arguments.

Findings of the Board of Appeal

97. In response to the public consultation held pursuant to Article 40(2), the Agency received the third-party comments set out in paragraph 6 above.

98. According to the Contested Decision, the third party used '*similar scientific reasoning*' as the Appellant when it considered in its comments that the basic study design of the EOGRTS (Cohorts 1A and 1B without extension) is appropriate. The Contested Decision states that the third party '*did not provide any scientific data which would fulfil this information requirement'*.

99. Under Article 40(2), third parties may submit scientifically valid information and studies that address the relevant substance and hazard endpoint within 45 days of the date of publication of the testing proposal. The Agency must take into account any such scientifically valid information and studies received. Contrary to the wording used in the Contested Decision, this does not mean that the information received from the third-party consultation under Article 40(2) must '*fulfil*' the information requirement (see Case A-015-2019, *Polynt*, Decision of the Board of Appeal of 9 February 2021, paragraph 81). A requirement that the information provided by the third party is to '*fulfil*' the information requirement would go beyond the conditions set out in Article 40(2). However, the Agency did not breach Article 40(2) in the present case for the following reasons.

100. The third party provided observations in which it considered that '*the basic study design*' of the EOGRTS is sufficient as the Substance '*has not effect on reproductive organs'* and as '*[t]here* is *no indication (either from structural alerts or from the existing toxicological dataset) of (developmental) neurotoxicity or (developmental) immunotoxicity'.* These observations raised by the third party were based on the data used by the Appellant in its registration dossier. Therefore, the Agency was correct when it found that the third party's comments as regards the EOGRTS study design were based on '*similar scientific reasoning*' that was used by the Appellant.

101. The substance of all the observations made by the third party is therefore addressed in the parts of the Contested Decision which examine the duration of the pre-mating exposure, the extension of Cohort 1B, and the inclusion of Cohorts 2A and 2B in the study design. The Appellant has not demonstrated that the Agency failed to take into account the third party's observations as required by Article 40(2).

102. Insofar as the observations made by the third party all relate to the modifications of the study design of the EOGRTS, they have all been addressed in Section 2.3. above.

103. As a result, the Appellant's plea that the Agency breached Article 40(2) must be rejected.

4. Fifth plea: The Agency breached Article 13 of the TFEU, Article 25 of the REACH Regulation, and '*the principle of proportionality/animal welfare/sound administration*'

Arguments of the Parties

104. By its fifth plea the Appellant argues that the Agency breached Article 13 of the TFEU, Article 25 of the REACH Regulation, and '*the principle of proportionality/animal welfare/sound administration*' as it failed to consider alternatives to animal testing.

105. The Agency disputes the Appellant's arguments.

Findings of the Board of Appeal

106. Article 13 of the TFEU provides, amongst other things, that in formulating and implementing certain policies, *'the Union and the Member States shall, since animals are sentient beings, pay full regard to the welfare requirements of animals'*. The REACH Regulation contains a number of provisions which take into account the welfare of animals. This includes, for example, Article 25(1) (see, for example, Case A-006-2012, *Momentive Specialty Chemicals*, Decision of the Board of Appeal of 13 February 2014, paragraph 96).

107. In order to respect the principle of proportionality, measures adopted by the European Union institutions and agencies must not exceed the limits of what is appropriate and necessary in order to achieve the objectives legitimately pursued by the measure in question. When there is a choice between several appropriate measures recourse must be had to the least onerous, and the disadvantages caused must not be disproportionate to the aims pursued (judgment of 21 July 2011, *Etimine*, C-15/10, EU:C:2011:504, paragraph 124; *Polynt*, cited in paragraph 99 above, paragraph 94 of the Decision).

108. The right to good administration is enshrined in Article 41 of the Charter of Fundamental Rights of the European Union. The right to good administration entails, in particular, a duty for the administration to examine carefully and impartially all the relevant aspects of an individual case and the right of the person concerned to be heard and to receive an adequately reasoned decision (see Case A-004-2019, *Arkema*, Decision of the Board of Appeal of 24 November 2020, paragraph 45).

109. To support its pleas based on Article 13 of the TFEU, Article 25 of the REACH Regulation as well as the '*the principle of proportionality/animal welfare/good administration'*, the Appellant raises similar arguments to those raised to support its second, third and fourth pleas which were examined in Sections 2 and 3 above. In essence, the Appellant argues that, since the PNDT study on a second species and the EOGRTS are not necessary, the

Agency breached Article 13 of the TFEU, Article 25 of the REACH Regulation as well as the '*the principle of proportionality/animal welfare/sound administration*'.

110. Since the Appellant's first, second and third pleas, and the arguments presented by the Appellant to support them, have been rejected, the Appellant's plea that the Agency breached Article 13 of the TFEU, Article 25 of the REACH Regulation as well as the '*the principle of proportionality/animal welfare/good administration*' must also be rejected for the same reasons.

111. In view of paragraphs 106 to 110 above, the Appellant's plea that the Agency breached Article 13 of the TFEU, Article 25 of the REACH Regulation, and *'the principle of proportionality/animal welfare/sound administration'* must be rejected.

Conclusion on the appeal

112. As all the Appellant's pleas have been rejected, the appeal must be dismissed.

Claim for the reimbursement of costs

113. In the Notice of Appeal, the Appellant requests the Board of Appeal to order the Agency to pay the costs of these proceedings.

114. The Rules of Procedure do not provide for the reimbursement of costs that are not, as provided in Articles 17 and 21(1)(h) thereof, related to the taking of evidence. Furthermore, Article 17a of the Rules of Procedure provides that the parties shall bear their own costs.

115. Consequently, and as in the present case no costs arose in relation to the taking of evidence, the Appellant's request for reimbursement of costs is rejected.

Refund of the appeal fee

116. Pursuant to Article 10(4) of Commission Regulation (EC) No 340/2008 on the fees and charges payable to the European Chemicals Agency pursuant to the REACH Regulation (OJ L 107, 17.4.2008, p. 6), if an appeal is dismissed, the appeal fee is not refunded. As this appeal is dismissed, the appeal fee is not refunded.

Effects of the Contested Decision

117. The Contested Decision, upheld in the present case, required the Appellant to submit information on a PNDT study on a second species and on an EOGRTS by 12 January 2022 which is two years, six months and seven days from the date of that Decision.

118. Pursuant to Article 91(2), an appeal has suspensive effect. The deadline to provide the information at issue must therefore be calculated starting from the date of notification of the present decision of the Board of Appeal to the Parties.

119. The Appellant must therefore provide information on a PNDT study on a second species and on an EOGRTS in the form required by the Contested Decision by 6 November 2023.

On those grounds,

THE BOARD OF APPEAL

hereby:

1. **Dismisses the appeal.**

2. **Decides that the PNDT study on a second species and the EOGRTS in the form required by the Contested Decision must be submitted by 6 November 2023.**

3. **Rejects the claim for the reimbursement of costs incurred in these proceedings.**

4. **Decides that the appeal fee is not refunded.**

Antoine Buchet
Chairman of the Board of Appeal

Alen Močilnikar
Registrar of the Board of Appeal