EUROPEAN CHEMICALS AGENCY
BOARD OF APPEAL

DECISION OF THE BOARD OF APPEAL OF THE EUROPEAN CHEMICALS AGENCY

19 September 2023

(Dossier evaluation – Compliance check – Requirements of Columns 1 and 2 of Section 8.7.3. of Annex IX – EOGRTS – Basic study design – Cohorts 2A and 2B – Powers of the Agency – No assessment of proportionality – Additional investigations on learning and memory function)

Case number	A-009-2022
Language of the case	English
Appellants	Nouryon Functional Chemicals B.V., the Netherlands Arkema GmbH, Germany PERGAN Hilfsstoffe für Industrielle Prozesse GmbH, Germany United Initiators GmbH, Germany Represented by Ruxandra Cana, Eléonore Mullier, Hannah Widemann, and Tom Gillett Steptoe and Johnson LLP, Belgium
Contested Decision	Decision of 8 June 2022 on a compliance check of the registration for the substance di-tert-butyl 1,1,4,4-tetra-methyltetramethylene diperoxide, adopted by the European Chemicals Agency under Article 41 of the REACH Regulation

THE BOARD OF APPEAL

composed of Antoine Buchet (Chairman and Rapporteur), Nikolaos Georgiadis (Technically Qualified Member), and Marijke Schurmans (Legally Qualified Member)

Registrar: Alen Močilnikar

gives the following

Decision

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1. Background to the dispute

1. This appeal concerns a compliance check of the registration for the substance di-tert-butyl 1,1,4,4-tetramethyltetra-methylene diperoxide (the **Substance**).[1]

2. All the Appellants registered the Substance between 2011 and 2013 at the tonnage band of 100 to 1 000 tonnes per year, which corresponds to the volume of manufacture or import referred to in Annex IX to the REACH Regulation.[2]

3. On 1 February 2021, the Agency initiated a compliance check under Article 41.

4. On 27 August 2021, the Agency notified to the Appellants a draft decision in accordance with Articles 41(3) and 50(1). The draft decision required the Appellants to submit information on numerous information requirements concerning both human health and the environment. In particular, the draft decision required the Appellants to submit information on an extended one-generation reproductive toxicity study (**EOGRTS**) under Column 1 of Section 8.7.3. of Annex IX, including cohort 1A, cohort 1B without extension to mate the animals to produce the F2 generation, and cohorts 2A and 2B.

5. On 4 October 2021, the Appellants submitted comments on the draft decision in accordance with Article 50(1). In particular, the Appellants submitted comments on the need to perform an EOGRTS and on the design of that study. The Agency took those comments into account and revised the draft decision by responding to the Appellants' comments but did not modify the request for the EOGRTS.

6. On 3 March 2022, the Agency notified the revised draft of the decision to the competent authorities of the Member States in accordance with Articles 50(1) and 51(1).

7. On 30 March 2022, the competent authority of the Netherlands submitted a proposal for amendment to the Agency in accordance with Article 51(2). According to that proposal, cohorts 2A and 2B of the EOGRTS should include additional investigations on learning and memory function as described in paragraph 37 of test guideline (**TG**) 426 of the Organisation for Economic Co-Operation and Development (**OECD**), which is equivalent to European Union (**EU**) test method B.53 as set out in the Annex to the Test Methods Regulation.[3]

8. On 10 May 2022, the Appellants submitted comments on the proposal for amendment in accordance with Article 51(5). The Appellants' comments were submitted, together with the revised draft of the decision, to the Member State Committee.

9. On 8 June 2022, following the unanimous agreement of the Member State Committee, the Agency adopted the Contested Decision in accordance with Article 51(6).

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1 EC No 201-128-1; CAS No 78-63-7.

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.

3 Commission Regulation (EC) No 440/2008 laying down test methods pursuant to the REACH Regulation (OJ L 142, 31.5.2008, p. 1). All references to EU test methods hereinafter concern test methods set out in the Annex to the Test Methods Regulation.

2. Contested Decision

10. The Contested Decision requires the Appellants to submit, by 15 September 2025, *inter alia* information on an EOGRTS under Section 8.7.3. of Annex IX including:

- cohort 1A (reproductive toxicity),
- cohort 1B (reproductive toxicity) without extension to mate the cohort 1B animals to produce the F2 generation,
- cohorts 2A and 2B (developmental neurotoxicity), and
- investigations on learning and memory function as described in paragraph 37 of OECD TG 426, corresponding to EU test method B.53.

3. Procedure before the Board of Appeal

11. On 8 September 2022, the Appellants filed their appeal.

12. On 9 November 2022, the Agency submitted its Defence.

13. On 29 November 2022, PETA Science Consortium International e.V. was granted leave to intervene in these proceedings in support of the Appellants.

14. On 9 January 2023, the Appellants submitted their observations on the Defence.

15. On 8 February 2023, PETA Science Consortium International e.V. stated that it no longer wished to intervene in the proceedings.

16. On 20 February 2023, the Agency submitted its observations on the Appellants' observations on the Defence.

17. On 7 June 2023, a hearing was held on the Appellants' request. The hearing was held at the Agency's premises. At the hearing, the Parties made oral submissions and responded to questions from the Board of Appeal.

4. Form of order sought

18. The Appellants request the Board of Appeal to:

- annul the Contested Decision in as far as it requires them to submit information on the EOGRTS,
- order the refund of the appeal fee, and
- take such other or further measures as justice may require.

19. The Agency requests the Board of Appeal to dismiss the appeal.

5. Assessment of the case

5.1. Admissibility of the request to take such other or further measures as justice may require

20. As part of the form of order which they seek, the Appellants request the Board of Appeal to take such other or further measures as justice may require. The Agency objects to the admissibility of that request on the ground that it lacks precision.

21. Article 6(1)(d) of the Rules of Procedure[4] provides that the notice of appeal must contain the remedy sought by the appellant. The remedy sought defines the scope of the dispute and must be set out clearly in the notice of appeal.[5] However, a lack of precision in that regard does not lead to inadmissibility if the remedy sought can be discerned from the entirety of the arguments put forward by the party in question.[6]

22. At the hearing, the Appellants stated that their request to take such other or further measures as justice may require should be understood as meaning that, if the Board of Appeal considers the appeal to be well-founded, it could amend the Contested Decision to request a study in accordance with OECD TG 421 as part of a tiered approach instead of the EOGRTS.

23. However, that interpretation is not supported by any of the Appellants' written submissions. The notice of appeal provides no detail on the Appellants' request and does not explain the meaning of that request in any way. The Appellants also failed to clarify their request in their observations on the Defence which were submitted after the Agency's objection of inadmissibility. In their written submissions, the Appellants refer to a study in accordance with OECD TG 421 only to argue that the Agency's assessment was vitiated by error.

24. The Appellants' request to take such other or further measures as justice may require is therefore too imprecise to comply with Article 6(1)(d) of the Rules of Procedure as its meaning cannot be discerned from the entirety of the arguments put forward during the proceedings.

25. The appeal must consequently be dismissed as inadmissible to that extent.

5.2. Substance of the case

26. The Appellants raise two pleas in law in their Notice of Appeal, each consisting of three parts. The arguments of the Appellants will be examined in the following order:

- arguments relating to the requirement to submit information on an EOGRTS with the basic study design (Column 1 of Section 8.7.3. of Annex IX),[7]
- arguments relating to the requirement for the EOGRTS to include cohorts 2A and 2B (Column 2 of Section 8.7.3. of Annex IX),[8] and
- arguments relating to the investigations on learning and memory function (paragraph 37 of EU test method B.53).[9]

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[4] 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)

[5] See, by analogy, judgment of 15 September 2016, *European Dynamics Luxembourg and Evropaïki Dynamiki* v *EIT*, T-481/14, EU:T:2016:498, paragraph 460.

[6] See, by analogy, judgment of 28 June 2011, *Verein Deutsche Sprache* v *Council*, C-93/11 P, EU:C:2011:429, paragraph 18.

[7] First part of the first plea and first part of the second plea.

[8] Second part of the first plea and second part of the second plea.

[9] Third part of the first plea and third part of the second plea.

5.2.1. The requirement to submit information on an EOGRTS with the basic study design (Column 1 of Section 8.7.3. of Annex IX)

27. The Appellants raise two lines of argument against the finding in the Contested Decision that they are required to submit information on an EOGRTS with the basic study design under Column 1 of Section 8.7.3. of Annex IX.

(a) Requirements of Column 1 of Section 8.7.3. of Annex IX

Arguments of the Parties

28. The Appellants argue that the Agency breached Column 1 of Section 8.7.3. of Annex IX and the principle of proportionality by failing to assess in the Contested Decision whether requiring an EOGRTS with the basic study design is proportionate.[10]

29. Specifically, according to the Appellants, in deciding whether to require information on an EOGRTS with the basic study design the Agency should have applied the test developed in the case-law concerning the necessity of requests for further information under substance evaluation (potential risk, need to clarify the potential risk, and realistic possibility of improved risk management measures).[11]

30. Furthermore, according to the Appellants, carrying out a study in accordance with OECD TG 421 as part of a tiered approach would constitute a less onerous measure as it would show that an EOGRTS with the basic study design is not required by Column 1 of Section 8.7.3. of Annex IX in this case and be consistent with Article 25.

31. The Agency disputes the Appellants' arguments.

Findings of the Board of Appeal

32. The Appellants argue that when requiring an EOGRTS with the basic study design under Column 1 of Section 8.7.3. of Annex IX the Agency must examine whether requiring that study is justified by a potential risk relating to reproductive toxicity, whether that risk needs to be clarified, whether there is a realistic possibility that the study may lead to improved risk management measures, and whether the study is the least onerous option. All those arguments relate to the requirements of the principle of proportionality.[12]

33. In order to assess the merits of that argument it is necessary to examine the extent of the Agency's discretion when carrying out a compliance check under Article 41 in relation to Column 1 of Section 8.7.3. of Annex IX. Where the Agency has a power of discretion as to the measure to be taken, it must ensure that the measure it chooses is proportionate.[13] Where it has no such power of discretion, because the measure to be taken has been determined by the legislature, the

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[10] First part of the second plea.

[11] Judgment of 20 September 2019, *BASF Grenzach* v *ECHA*, T-125/17, EU:T:2019:638, paragraph 276; see also decision of the Board of Appeal of 27 October 2015, *International Flavors & Fragrances*, A-006-2014, paragraph 76.

[12] See judgment of 20 September 2019, *Germany* v *ECHA*, T-755/17, EU:T:2019:647, paragraph 287; see also, for example, decision of the Board of Appeal of 10 May 2022, *Lanxess Deutschland and Schirm*, A-002-2021, paragraphs 88 and 89.

[13] See, for example, decisions of the Board of Appeal of 29 April 2013, *Honeywell*, A-005-2011, paragraphs 65 to 71 and 93 to 97; and of 18 August 2020, *Symrise*, A-010-2018, paragraphs 188 to 190.

Agency is neither required nor empowered to examine the proportionality of the measure, that assessment being reserved to the EU Courts in accordance with Article 277 of the Treaty on the Functioning of the European Union (**TFEU**).[14]

34. Column 1 of Section 8.7.3. of Annex IX sets out the '*[s]tandard information required*' for a registration. At the time of adoption of the Contested Decision, that provision stated:

'*Extended One-Generation Reproductive Toxicity Study ([EU test method B.56] or OECD 443), basic test design (cohorts 1A and 1B without extension to include a F2 generation), one species, most appropriate route of administration, having regard to the likely route of human exposure, if the available repeated dose toxicity studies (e.g. 28-day or 90-day studies, OECD 421 or 422 screening studies) indicate adverse effects on reproductive organs or tissues or reveal other concerns in relation with reproductive toxicity*' (emphasis added).

35. An EOGRTS with the basic study design is therefore a standard information requirement for registration if the available information shows at least one of the following: (1) adverse effects on reproductive organs, (2) adverse effects on reproductive tissues, or (3) other concerns in relation to reproductive toxicity.

36. When carrying out a compliance check under Article 41 in conjunction with Column 1 of Section 8.7.3. of Annex IX, it therefore falls to the Agency to assess whether at least one of the conditions referred to in the previous paragraph is fulfilled. If at least one of those conditions is fulfilled, the Agency is obliged to require information on an EOGRTS with the basic study design as standard information. The Agency has no power of discretion as regards the measure to be taken.

37. It follows that, contrary to the Appellants' arguments, the Agency was not required to examine whether requesting information on an EOGRTS with the basic study design as standard information is consistent with the principle of proportionality or with Article 25.

38. In any event, the Appellants' argument that carrying out a study in accordance with OECD TG 421 as part of a tiered approach would show that the conditions of Column 1 of Section 8.7.3. of Annex IX are not met in this case, must also be rejected for the following reasons. The Agency's assessment is based on information which is currently available. No OECD TG 421 study is currently available on the Substance as the Appellants adapted the information requirement corresponding to that study under Annex VIII. If the information which is currently available is sufficient to meet at least one of the conditions of Column 1 of Section 8.7.3. of Annex IX – which will be examined in detail in Section (b) below – the Agency does not have the obligation to wait for a registrant to generate further information before adopting its decision.[15]

39. In conclusion, the Agency did not breach Column 1 of Section 8.7.3. of Annex IX or the principle of proportionality by failing to assess, in the Contested Decision, whether requiring an EOGRTS with the basic study design is proportionate. The Appellants' line of argument to that effect must be rejected.

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[14] See judgments of 28 June 2023, *Polynt* v *ECHA*, T-207/21, EU:T:2023:361, paragraph 110; and of 29 March 2023, *Nouryon Industrial Chemicals and Others* v *Commission*, T-868/19, EU:T:2023:168, paragraphs 69, 70 and 174; see also decisions of the Board of Appeal of 29 August 2023, *Symrise and Others,* A-006-2022, paragraphs 75 and 76; and of 4 May 2020, *Clariant Plastics and Coatings (Deutschland)*, A-011-2018, paragraphs 94 to 96.

[15] See, by analogy, decisions of 30 January 2018, *Cheminova*, A-005-2016, paragraph 49; of 9 February 2021, *Polynt*, A-015-2019, paragraph 85; and of 29 April 2021, *LG Chem Europe*, A-014-2019, paragraph 56.

(b) Errors in the Agency's scientific assessment under Column 1 of Section 8.7.3. of Annex IX

Arguments of the Parties

40. The Appellants argue that, in requiring an EOGRTS with the basic study design under Column 1 of Section 8.7.3. of Annex IX, the Agency committed several errors in its scientific assessment, failed to take all relevant available information into account and breached the principles of legal certainty and of the protection of legitimate expectations.

41. First, the Appellants argue that the Agency made an error of assessment in relying on the results of a 90-day oral toxicity study carried out according to OECD TG 408 (the **OECD TG 408 study**)[16] which is included in the Appellants' registration.

42. In the first place, according to the Appellants, the effects observed in the OECD TG 408 study (reduced epididymal spermatid count in the high-dose group) were incidental and of no toxicological relevance. Although the study showed a reduction in spermatid count in the cauda epididymis in the high dose-group, the spermatid count in the caput epididymis and in the testes, which were also examined in the study, was unchanged or even slightly higher.

43. In the second place, according to the Appellants, the Agency reversed the burden of proof by stating that, in the absence of information on the spermatid count in the mid-dose and low-dose groups, a possible dose dependency of the effects observed in the OECD TG 408 study cannot be ruled out. According to the Appellants, the spermatid count was carried out only in the high-dose group, and not in the low- and mid-dose groups, in accordance with paragraph 41 of OECD TG 408, because the effect was not considered adverse by the contract research organisation which carried out the study.

44. Second, the Appellants argue that the Agency made an error of assessment in relying on the results of a repeated-dose 28-day oral toxicity study carried out according to OECD TG 407 (the **OECD TG 407 study**),[17] which is included in the Appellants' registration. According to the Appellants, the findings in that study (evidence of testicular tubular degeneration/atrophy in all dose groups) are not relevant as they were observed in a limited number of animals and at limited severity, including occurrence in one male animal in the control group, and a dose-response relationship could not be established.

45. Third, the Appellants argue that the Agency committed an error of assessment and failed to comply with its own guidance[18] by assessing only the existence of effects in the OECD TG 408 study and in the OECD TG 407 study, whilst failing to assess whether those effects are adverse and/or due to the administration of the Substance.

46. The Agency disputes the Appellants' arguments.

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[16] Harlan Laboratories Ltd/[confidential], *Di-tert-butyl 1,1,4,4-tetramethyltetramethylene diperoxide: Ninety Day Repeated Dose Oral (Gavage) Toxicity Study in the Rat* (study report), 2014.

[17] Harlan Laboratories Ltd/[confidential], *28-Day Oral (Gavage) Toxicity Study with di-tert-butyl 1,1,4,4-tetramethyltetra-methylene diperoxide* (study report), 2011.

[18] European Chemicals Agency, *Guidance on Information Requirements and Chemical Safety Assessment*, Chapter R.7a: Endpoint specific guidance, Version 6.0, July 2017, pp. 487-488 and 544-550.

Findings of the Board of Appeal

47. Column 1 of Section 8.7.3. of Annex IX requires an EOGRTS with the basic study design as a standard information requirement for registration if the available information shows at least one of the following: (1) adverse effects on reproductive organs, (2) adverse effects on reproductive tissues, or (3) other concerns in relation with reproductive toxicity.

48. According to the Contested Decision, these conditions are fulfilled in the present case due to the results of two studies contained in the Appellants' registration:

- The OECD TG 408 study shows a statistically significant and biologically relevant reduction of 40% in caudal epididymis sperm count in the highest dose group (150 mg/kg bw/day) compared to the control group. This effect constitutes the main reason for finding that an EOGRTS is required under Column 1 of Section 8.7.3. of Annex IX.
- The OECD TG 407 study shows testicular tubular degeneration/atrophy at all dose levels (20, 60 and 200 mg/kg bw/day). This effect supports the finding that an EOGRTS is required under Column 1 of Section 8.7.3. of Annex IX.

49. First, with regard to the OECD TG 408 study, the Appellants raise two arguments to support their claim that the Agency's assessment is vitiated by two errors.

50. The Appellants' first argument, according to which the effects observed in the OECD TG 408 study were incidental and of no toxicological relevance, must be rejected for the following reasons.

51. The OECD TG 408 study – the robust study summary and the full study report of which were both submitted to the Board of Appeal in these proceedings – shows a reduction of 40% in spermatid count in the cauda epididymis in the high-dose group (150 mg/kg bw/day) compared to the control group.

52. That effect does not constitute an adverse effect on reproductive organs or tissues as sperm is neither a reproductive organ nor a reproductive tissue. However, as the Agency explained, the spermatid count reduction in question is considerable and raises an '*other concern in relation with reproductive toxicity*', which is the third of the conditions set out in Column 1 of Section 8.7.3. of Annex IX.[19]

53. It is true that the spermatid count in the caput epididymis and in the testes, which was also examined in the OECD TG 408 study, was unchanged or even slightly higher in the high-dose group compared to the control group. However, this does not mean that the sperm count reduction in the cauda epididymis can be disregarded. As the Agency explained at the hearing, spermatid count in the cauda epididymis is the most relevant parameter with regard to the male reproductive performance. It represents the number of mature spermatids capable of fertilising the egg and reflects potential effects during the spermatogenic cycle and in particular during epididymal sperm maturation.

54. The Appellants' second argument, according to which the Agency reversed the burden of proof and failed to establish that the effects observed in the OECD TG 408 study were dose-dependent, must be rejected for the following reasons.

55. The assessment of the conditions set out in Column 1 of Section 8.7.3. of Annex IX must be based on the available information. In the present case, the OECD TG 408 study shows a reduction of 40% in the spermatid count in the cauda epididymis in the highest dose group compared to the control group. The effects in the mid-dose and low-dose groups are unknown as no spermatid count measurement was carried out in those groups.

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[19] See paragraphs 35 and 47 above.

56. Furthermore, it is not necessary for the Agency to establish the dose-dependency of observed effects in order to find that a substance may raise a concern in relation to reproductive toxicity.

57. Therefore, the Agency's statement in the Contested Decision that a possible dose dependency of the spermatid count effects cannot be ruled out does not constitute a reversal of the burden of proof. That statement merely conveys the fact that it is unknown whether the effect occurred in the mid-dose and low-dose groups as – whatever the reason for the omission may have been – those effects were not examined in those groups.

58. Second, with regard to the OECD TG 407 study, the Appellants' argument that the findings in that study (evidence of testicular tubular degeneration/atrophy at all dose-levels) are not relevant must be rejected for the following reasons.

59. The reduction of 40% in spermatid count in the cauda epididymis observed in the high-dose group in the OECD TG 408 study is sufficient on its own to raise an '*other concern in relation with reproductive toxicity*', which is the third of the three conditions set out in Column 1 of Section 8.7.3. of Annex IX.[20] The Appellants' arguments concerning the OECD TG 407 study are consequently inoperative.

60. In any event, the OECD TG 407 study – the robust study summary and the full study report of which were both submitted to the Board of Appeal in these proceedings – shows testicular tubular degeneration/atrophy at all dose levels (20, 60 and 200 mg/kg bw/day) compared to the control group. As the Agency explained, those effects constitute adverse effects on reproductive tissues, which is the second of the three conditions set out in Column 1 of Section 8.7.3. of Annex IX.[21]

61. It is true that it is not clear from the OECD TG 407 study whether the effects observed were statistically significant and whether there was a dose-response relationship. However, the relatively low absolute number of animals in each group which showed those effects results from the low statistical power of the study, i.e. the fact that the group size only included five males per treatment group. Similarly, the fact that some effects also occurred in one animal in the control group does not mean that the effects observed in all the affected animals in all the other groups should be disregarded.

62. Third, with regard to both the OECD TG 408 study and the OECD TG 407 study, the Appellants' argument that the Agency committed an error of assessment and failed to comply with its own guidance must be rejected for the following reasons.

63. In the first place, as regards the argument that the Agency failed to assess whether the effects observed in the two studies are adverse, it must be underlined that the effects observed in the two studies fall under two of the three conditions set out in Column 1 of Section 8.7.3. of Annex IX. Specifically:

- The effects observed in the OECD TG 408 study (reduction of 40% in spermatid count in the cauda epididymis in the high-dose group) raise an 'other concern in relation to reproductive toxicity' (third condition).[22] Column 1 of Section 8.7.3. of Annex IX does not state that the effects on which such a concern is based must necessarily be established as being adverse, provided that they raise a concern for reproductive toxicity.
- The effects observed in the OECD TG 407 study (testicular tubular degeneration/atrophy at all dose levels) constitute adverse effects on

[20] See paragraphs 51 to 53 above.

[21] See paragraphs 35 and 47 above.

[22] See paragraphs 51 to 53 above.

reproductive tissues (second condition).[23] Although the Contested Decision does not expressly use the term 'adverse' in this regard, it states adequate and correct reasons as to why those effects are considered to meet the threshold of the second condition in Column 1 of Section 8.7.3. of Annex IX.[24]

64. In the second place, as regards the argument that the Agency failed to demonstrate that the effects observed in the OECD TG 407 and OECD TG 408 studies are dose-related, it is not necessary for the Agency to establish the dose-dependency of observed effects in order to find that one or more of the conditions set out in Column 1 of Section 8.7.3. of Annex IX are met. Whether the substance actually causes reproductive toxicity effects and whether those effects are dose-dependent is to be examined through the conduct of the EOGRTS. Under Column 1 of Section 8.7.3. of Annex IX, such an assessment would be premature.

65. In the third place, the Agency's guidance, to which the Appellants refer, does not contradict those findings. That guidance cannot and does not supplant Column 1 of Section 8.7.3. of Annex IX. It merely provides general examples of effects which the Agency considers to be capable of fulfilling the conditions set out in that provision. In particular, the Agency's guidance does not state that only adverse and dose-dependent effects can trigger the requirement for an EOGRTS.[25]

66. Fourth, and in addition to the reasons set out above, the OECD TG 408 study and the OECD TG 407 study were carried out using 150 and 200 mg/kg bw/day as the respective highest dose. Those dose levels were not sufficient to induce toxicity short of death or severe suffering.[26] As the Agency explained at the hearing, the fact that effects were observed with the dose setting described above reinforces the concern that the Substance may raise a concern in relation to reproductive toxicity.

67. In conclusion, the Agency did not commit errors in its scientific assessment, fail to take all relevant available information into account or breach the principles of legal certainty and of the protection of legitimate expectations in requiring the EOGRTS under Column 1 of Section 8.7.3. of Annex IX.

(c) Conclusion on the requirement to submit information on an EOGRTS with the basic study design (Column 1 of Section 8.7.3. of Annex IX)

68. It follows from the reasons set out above that the Appellants' arguments concerning the requirement to submit information on an EOGRTS with the basic study design (Column 1 of Section 8.7.3. of Annex IX) must be rejected.

5.2.2. The requirement for the EOGRTS to include cohorts 2A and 2B (second paragraph of Column 2 of Section 8.7.3. of Annex IX)

69. The Appellants raise two lines of argument against the finding in the Contested Decision that the EOGRTS on which they must provide information must include cohorts 2A and 2B under the second paragraph of Column 2 of Section 8.7.3. of Annex IX.

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[23] See paragraphs 59 to 61 above.

[24] See pages 11 and 12 of the Contested Decision.

[25] European Chemicals Agency, *Guidance on Information Requirements and Chemical Safety Assessment*, Chapter R.7a: Endpoint specific guidance, Version 6.0, July 2017, pp. 487-488, 544 et seq.

[26] See paragraphs 15 and 18 of OECD test guideline 408, and paragraphs 18 and 19 of OECD test guideline 407.

(a) Requirements of the second paragraph of Column 2 of Section 8.7.3. of Annex IX

Arguments of the Parties

70. The Appellants argue that the Agency breached the second paragraph of Column 2 of Section 8.7.3 of Annex IX and the principle of proportionality by failing to assess in the Contested Decision whether requiring cohorts 2A and 2B as part of the EOGRTS is proportionate.[27]

71. Furthermore, the Appellants argue that the Agency breached the principle of the protection of legitimate expectations by failing to examine, in accordance with its own guidance, whether the effects observed in the OECD TG 408 study and in the OECD TG 407 study are serious or severe.

72. The Agency disputes the Appellants' arguments.

Findings of the Board of Appeal

73. The Appellants raise two arguments to support their claim that the Agency committed errors of law in its application of the second paragraph of Column 2 of Section 8.7.3. of Annex IX.

- *Compliance with the principle of proportionality*

74. The Appellants argue that when conducting a compliance check concerning the second paragraph of Column 2 of Section 8.7.3. of Annex IX the Agency must examine whether requiring registrants to include cohorts 2A and 2B in an EOGRTS is consistent with the principle of proportionality.

75. In order to assess the merits of that argument it is necessary to examine the extent of the Agency's discretion when carrying out a compliance check under Article 41 in relation to Column 1 of Section 8.7.3. of Annex IX. Where the Agency has a discretion as to the choice of the measure to be taken, it must ensure that the measure it chooses is proportionate. Where is has no such discretion, it is neither required nor empowered to examine the proportionality of the measure, that assessment being reserved to the EU Courts in accordance with Article 277 TFEU.[28]

76. Insofar as is relevant for this case, the second paragraph of Column 2 of Section 8.7.3. of Annex IX ('*Specific rules for adaptation from Column 1*') provides:

'*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 case of particular concerns on (developmental) neurotoxicity or (developmental) immunotoxicity justified by any of the following:*

[…]

- *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) […]*' (emphasis added).

[27] Second part of the second plea.

[28] See paragraph 33 above.

77. That provision must be interpreted as meaning that registrants who are required to submit information on an EOGRTS as standard information are also required to include cohorts 2A and 2B in the EOGRTS if the available information gives reasonable grounds for considering that a substance may cause effects related to (developmental) neurotoxicity,[29] and cohort 3 if the available information gives reasonable grounds for considering that a substance may cause effects related to (developmental) immunotoxicity.

78. When carrying out a compliance check under Article 41 in conjunction with the second paragraph of Column 2 of Section 8.7.3. of Annex IX, it therefore falls to the Agency to assess whether one or more of the conditions of that provision are fulfilled. If one or more of those conditions are fulfilled, the Agency is obliged to require the registrants of the substance to include cohorts 2A and 2A, and/or cohort 3, in their EOGRTS. The Agency has no power of discretion as regards the measure to be taken.

79. If the available information gives reasonable grounds for considering that a substance may cause effects in relation to – in particular – (developmental) neurotoxicity, the Agency is therefore not required to assess whether the inclusion of cohorts 2A and 2B complies with the principle of proportionality.

80. It follows that the Agency was not required to examine whether including cohorts 2A and 2B in the EOGRTS is consistent with the requirements of the principle of proportionality.

81. The Appellants' first argument is therefore unfounded.

- *Compliance with the Agency's guidance*

82. The Appellants argue that the second paragraph of Column 2 of Section 8.7.3. of Annex IX requires the effects at issue to be serious or severe. They refer, in that context, to guidance issued by the Agency.

83. The second paragraph of Column 2 of Section 8.7.3. of Annex IX states that the effects must be 'particular' or 'specific' in the sense that they must relate to (developmental) neurotoxicity or (developmental) immunotoxicity, and not merely to reproductive or systemic toxicity in general.[30] However, contrary to the Appellants' arguments, that provision does not state that the effects observed in the available studies must be especially serious or severe.[31]

84. Furthermore, it is true that the Agency's guidance states that '*[a] particular concern means that the concern should be specific to (developmental) neurotoxicity but also that the concern needs to reach a certain level of severity'*, and that '*a particular concern may be indicated, [sic] such as by serious or severe effects*'.[32] Those statements cannot, however, be read on their own but must be placed in their proper context. Thus, the same guidance refers to serious or severe effects as only one example of a particular concern, other examples being specific types of effects or specific mechanisms/modes of action.[33] Similarly, the guidance refers to signs of thyroid toxicity as a specific mechanism/mode of action that has

[29] See, with regard to the identical provision in Annex X, judgment of 29 March 2023, *Nouryon Industrial Chemicals and Others* v *Commission*, T-868/19, EU:T:2023:168, paragraph 103.

[30] See Recital 9 to Commission Regulation (EU) 2015/282 amending Annexes VIII, IX and X to the REACH Regulation as regards the EOGRTS (OJ L 50, 21.2.2015, p. 1).

[31] Judgment of 29 March 2023, *Nouryon Industrial Chemicals and Others* v *Commission*, T-868/19, EU:T:2023:168, paragraph 105.

[32] European Chemicals Agency, *Guidance on Information Requirements and Chemical Safety Assessment*, Chapter R.7a: Endpoint specific guidance, Version 6.0, July 2017, pp. 528-529.

[33] *Idem*, pp. 544 and 545.

been closely linked to (developmental) neurotoxic effects through relevant changes in thyroid hormone levels, and may justify the inclusion of cohorts 2A and 2B.[34]

85. Contrary to the Appellants' argument, therefore, it is clear that the guidance refers to serious or severe effects as one possible kind of effect which may lead to the inclusion of cohorts 2A and 2B in an EOGRTS. The guidance does not state that the Agency will not require cohorts 2A and 2B to be included in an EOGRTS unless the effects observed in the animals in a study are serious or severe.

86. The Appellants' second argument is therefore also unfounded.

- *Conclusion on the requirements of the second paragraph of Column 2 of Section 8.7.3. of Annex IX*

87. It follows from the reasons set out above that the Appellants' arguments concerning the requirements of the second paragraph of Column 2 of Section 8.7.3. must be rejected.

(b) Errors in the Agency's scientific assessment under the second paragraph of Column 2 of Section 8.7.3. of Annex IX

Arguments of the Parties

88. The Appellants argue that, in requiring the EOGRTS to include cohorts 2A and 2B under the second paragraph of Column 2 of Section 8.7.3. of Annex IX, the Agency committed errors in its scientific assessment, failed to take all relevant available information into account and breached the principles of legal certainty and of the protection of legitimate expectations.

89. First, the Appellants agree that the studies on which the Agency based its findings – namely the OECD TG 408 study, and a repeated dose 28-day oral toxicity study carried out in Japan (the **JECDB study**)[35] – show, respectively, (i) a greater incidence of minimal or diffuse hypertrophy of the follicular epithelium at all dose levels compared to the control, and (ii) significantly increased absolute and relative thyroid weights, and follicular thyroid hyperplasia in males and females, at the high dose. However, the Appellants argue that those findings do not suffice to trigger the requirement for cohorts 2A and 2B because they did not measure thyroid hormone levels.

90. Second, the Appellants argue that the Agency made an error in finding that the OECD TG 408 study shows that the conditions set out in the second paragraph of Column 2 of Section 8.7.3. of Annex IX are met.

91. In the first place, the Appellants argue that the Agency's assessment of the OECD TG 408 study is erroneous as regards whether the thyroid effects observed in that study (greater incidence of minimal or diffuse hypertrophy of the follicular epithelium at all dose levels compared to the control) are serious or severe. According to the Appellants, the effects observed in the study were not clearly dose-related and were also seen in one animal in the control group. Furthermore, minimal or diffuse hypertrophy of the follicular epithelium on its own cannot be considered to be an intrinsically adverse effect. The Appellants refer, in that regard, to a report by the European Society of Toxicologic Pathology (the **ESTP**

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[34] *Ibidem*, p. 529.

[35] Research Institute for Animal Science in Biochemistry and Toxicology (Japan)/N.N., *The 28-day repeated oral administration toxicity test using the rat of 2,5-dimethyl- 2,5-di(tert-but,* JECDB study report.

report).[36] Therefore, according to the Appellants, the effects observed in the OECD TG 408 study are not sufficiently serious or severe to require the inclusion of cohorts 2A and 2B in the EOGRTS.

92. In the second place, the Appellants argue that the Agency's assessment of the OECD TG 408 study is erroneous as regards the human relevance of the thyroid effects observed. According to the Appellants, the rat thyroid gland has been shown to be markedly more sensitive than the human thyroid gland in its response to xenobiotics.

93. Third, the Appellants argue that the Agency made an error in finding that the JECDB study shows that the conditions set out in the second paragraph of Column 2 of Section 8.7.3. of Annex IX are met. According to the Appellants, the JECDB study is of unknown reliability (Klimisch score 4) as the interpretation of the text of the robust study summary, which was translated from Japanese, is not always clear; there is a considerable difference in the highest dose used in the JECDB study compared to the other available repeated dose studies; there is no statement of compliance with rules on good laboratory practice contained within the body of the report; and the year in which the study was conducted is not stated in the report.

94. Fourth, the Appellants argue that the Agency committed an error by requiring cohorts 2A and 2B in order to investigate the potential thyroid mode of action of the Substance. In order to achieve that objective, the Agency should have required a study in accordance with OECD test guideline 421 as part of a tiered approach.

95. Fifth, the Appellants argue that the Agency failed to take into account the results of the OECD TG 407 study in which only minimal thyroid effects were observed.

96. Sixth, the Appellants argue that the Agency failed to take into account the fact that no findings were noted on the thyroid of the pups in a pre-natal developmental toxicity study carried out in accordance with OECD TG 414 (the **OECD TG 414 study**).[37]

97. The Agency disputes the Appellants' arguments.

Findings of the Board of Appeal

98. Under the second paragraph of Column 2 of Section 8.7.3. of Annex IX, registrants who are required to submit information on an EOGRTS as a standard information are also required to include cohorts 2A and 2B and/or 3 in that study if the available information gives reasonable grounds for considering that a substance may cause (developmental) neurotoxicity and/or (developmental) immunotoxicity effects, as the case may be.[38]

99. According to the Contested Decision, that condition is fulfilled as regards cohorts 2A and 2B (developmental neurotoxicity) due to the results of two studies contained in the Appellants' registration:

- The OECD TG 408 study shows a greater incidence of minimal or diffuse hypertrophy of the follicular epithelium at all dose levels compared to the control.

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[36] Huisinga M. *et al*., *Adversity Considerations for Thyroid Follicular Cell Hypertrophy and Hyperplasia in Nonclinical Toxicity Studies: Results From the 6th ESTP International Expert Workshop*, Toxicologic Pathology 2020 48(8) 920-938.

[37] Harlan Laboratories Ltd/[confidential], *Di-tert-butyl 1,1,4,4-tetramethyltetramethylene diperoxide, CAS# 78-63-7: Oral (Gavage) Pre-Natal Development Toxicity Study in the Rat* (study report), 2014.

[38] See paragraph 77 above.

- The JECDB study shows significantly increased absolute and relative thyroid weights, and follicular thyroid hyperplasia in males and females, at the highest dose (1 000 mg/kg bw/day).

100. Specifically, according to the Contested Decision, the effects referred to in the previous paragraph show that the Substance may affect the functioning of the thyroid, and consequently thyroid hormone levels and the neurological development of the foetus.

101. The Appellants' first argument, according to which neither the OECD TG 408 study nor the JECDB study measured the levels of thyroid hormones in the test animals, must be rejected for the following reasons.

102. The second paragraph of Column 2 of Section 8.7.3. of Annex IX refers to '*relevant changes in thyroidal hormone levels associated to adverse effects*' merely as one example of a concern based on specific mechanisms/modes of action with an association to (developmental) neurotoxicity. There is no obligation for the Agency to base its assessment exclusively on existing hormone level measurements. On the contrary, it is sufficient that the available information gives reasonable grounds to consider that a substance might have (developmental) neurotoxicity effects.[39]

103. Furthermore, neither the OECD TG 408 study (which is a 90-day repeated dose toxicity study) nor the JECDB study (which is a 28-day repeated dose toxicity study) measured thyroid hormone levels.

104. In the absence of direct thyroid hormone level measurements, the Agency was therefore entitled to consider that it can reasonably be inferred from histopathological changes in the thyroid that the functioning of the thyroid may be affected; that an impaired functioning of the thyroid may lead to changes in thyroid hormone levels in the dam; and that those changes in hormone levels may cause (developmental) neurotoxicity effects in the foetus.

105. The Appellants' second argument, according to which the Agency made an error in finding that the OECD TG 408 study shows that the conditions set out in the second paragraph of Column 2 of Section 8.7.3. of Annex IX are met, must be rejected for the following reasons.

106. In the first place, contrary to the Appellants' argument, the Agency did not commit an error by failing to assess whether the thyroid effects observed in the OECD TG 408 study are serious or severe.

107. It has already been held that the second paragraph of Column 2 of Section 8.7.3. of Annex IX does not state that the (developmental) neurotoxicity effects observed in the available studies must be especially serious or severe. On the contrary, it is sufficient that the available information gives reasonable grounds for considering that a substance may cause (developmental) neurotoxicity effects.[40]

108. The OECD TG 408 study, the robust study summary and the full study report of which were both submitted to the Board of Appeal in these proceedings, shows histopathological changes in the thyroid (diffuse follicular thyroid hypertrophy at all dose levels – 15, 50 and 150 mg/kg bw/day – in both male and female rats).

109. Contrary to the Appellants' argument, the fact that the effects observed in the OECD TG 408 study were not clearly dose-related and also seen in only one animal in the control group does not invalidate that assessment. Even if observed effects cannot be demonstrated to be dose-related in the context of a study such as the OECD TG 408 study, they can still constitute reasonable grounds for considering

[39] See paragraph 77 above.

[40] See paragraphs 77 and 83 above.

that a substance may cause (developmental) neurotoxicity effects. Similarly, the fact that some effects were observed in a single animal in the control group does not mean that similar effects observed in all other groups can be disregarded. Even in the presence of effects in a single animal in the control group, the OECD TG 408 study shows a greater incidence of minimal or diffuse hypertrophy of the follicular epithelium at all dose levels in the groups of treated animals compared to the control group.

110. Similarly, it is irrelevant whether – as the Appellants argue with reference to the ESTP report – '*[f]ollicular cell hypertrophy and/or hyperplasia in adult rats without other morphological changes such as focal hyperplasia or neoplasia should not be considered intrinsically adverse at the level of an isolated animal toxicity study*'.[41] The question at issue in the present case is not whether the effects observed in the OECD TG 408 study should be considered intrinsically adverse on their own. The issue is only whether those results give reasonable grounds for considering that a substance may cause developmental neurotoxicity effects.

111. In the second place, the Agency's assessment of the OECD TG 408 study is not erroneous as regards the human relevance of the thyroid effects observed.

112. Thyroid effects in rats are presumed to be relevant to humans unless it can be shown that they are not.[42]

113. In the present case, the Appellants generically refer to xenobiotics and to a scientific publication by Chandra *et al.* (2013) as evidence of their assertion that the rat thyroid is markedly more sensitive than the human thyroid. The Appellants do not explain, however, why and how those elements are relevant to the Substance and how exactly they relate to the effects at issue.

114. The Appellants have therefore not shown that the Agency's assessment of the OECD TG 408 study is erroneous as regards the human relevance of the thyroid effects observed.

115. The Appellants' third argument, according to which the Agency committed an error in considering in the Contested Decision that the findings in the JECDB study support the findings in the OECD TG 408 study, because the JECDB study is of unknown reliability (Klimisch score 4) and its results should therefore be disregarded, must be rejected for the following reasons.

116. The findings in the OECD TG 408 study are sufficient on their own to give reasonable grounds for considering that the Substance may cause (developmental) neurotoxicity effects. The Appellants' argument, which is to the effect that the JECDB study should be disregarded, is consequently inoperative.

117. In addition, and in any event, it is true that, in order to satisfy directly the information requirements for registration set out in Annexes VII to X, a study must be conducted in accordance with the relevant test method and comply with the requirements of good laboratory practice (if applicable).[43]

118. However, in the context of assessments which involve an examination of all available information – including the assessment of the conditions set out in Column 2 of Section 8.7.3. of Annex IX – a study cannot be simply disregarded if

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[41] Huisinga M. *et al*., *Adversity Considerations for Thyroid Follicular Cell Hypertrophy and Hyperplasia in Nonclinical Toxicity Studies: Results From the 6th ESTP International Expert Workshop*, Toxicologic Pathology 2020 48(8) 920-938, at p. 8.

[42] See, to that effect, decisions of the Board of Appeal of 19 December 2016, *BASF Grenzach*, A-018-2014, paragraphs 157 and 165, and of 12 January 2021, *Chemours Netherlands*, A-007-2019, paragraphs 54, 58 to 64, and 70.

[43] Article 13(3) and (4); see also decision of the Board of Appeal of 6 June 2023, *Cytec Engineered Materials*, A-001-2022, paragraphs 46 and 56 to 58; and, to that effect, decision of 11 December 2018, *Climax Molybdenum*, A-006-2017, paragraphs 43 and 44 to 52.

it has shortcomings. In particular, the results of a study of limited or unknown reliability (Klimisch score 2/4) can still be informative, provided that its results and limitations are carefully assessed and that the conclusions drawn from it are adequately weighed and justified.[44]

119. The JECDB study – of which a study summary, the study report in Japanese, and a translation of that study report into English were submitted to the Board of Appeal – shows both significantly increased absolute and relative thyroid weights and follicular thyroid cell hyperplasia in males and females at the high dose (1 000 mg/kg bw/day). Some absolute and relative thyroid weight increase and some follicular thyroid cell hyperplasia persisted after a recovery period of two weeks.

120. Contrary to the Appellants' argument, the fact that the JECDB study used a highest dose of 1 000 mg/kg bw/day does not invalidate its results per se.[45] However, it is true that the linguistic quality of the body of the study report, which was translated into English from the Japanese using a machine translation system, could be questioned. It is also true that it is unclear whether the study was conducted according to OECD rules on good laboratory practice or a Japanese equivalent. The time at which the study was conducted (after 2007) is also unclear.

121. As the Agency explained at the hearing, even taking those shortcomings into account there is no reason to believe that the JECDB study is unreliable insofar as it shows the effects referred to above.[46] Furthermore, as the Agency explained at the hearing, the difference in findings between the JECDB study on the one hand, and the OECD TG 408 and 407 studies on the other hand, can be explained by the fact that the dose-levels used in the latter two studies were substantially lower than the ones used in the former study, and by the different duration of the studies. The Agency therefore committed no error in considering that the findings in the JECDB study support the findings in the OECD TG 408 study.

122. The Appellants' fourth argument, according to which the Agency committed an error by requiring cohorts 2A and 2B in order to investigate the potential thyroid mode of action of the Substance, instead of requiring a study in accordance with OECD TG 421 as part of a tiered approach, must be rejected for the following reasons.

123. The Agency did not include cohorts 2A and 2B in the EOGRTS in order to investigate the thyroid mode of action of the Substance as such, but because it considered that one of the conditions set out in the second paragraph of Column 2 of Section 8.7.3. of Annex IX is met. Furthermore, it has already been held above that the Agency committed no error in considering that the OECD TG 408 study, supported by the JECDB study, gives reasonable grounds for considering that the Substance may have (developmental) neurotoxicity effects in accordance with the second paragraph of Column 2 of Section 8.7.3.[47] In those circumstances, the Agency was not required to pursue the tiered approach proposed by the Appellants.

124. The Appellants' fifth argument, according to which the Agency failed to take into account the results of the OECD TG 407 study, which do not show that the substance may affect the functioning of the thyroid, must be rejected for the following reasons.

125. It is true that thyroid effects were observed in the OECD TG 408 study – and, in

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[44] See, to that effect, decisions of the Board of Appeal of 17 December 2019, *BASF and Others*, A-003-2018, A-004-2018 and A-005-2018, paragraph 108.

[45] See paragraphs 18 and 19 of OECD test guideline 407; see also, by analogy, decision of the Board of Appeal of 11 December 2018, *Climax Molybdenum*, A-006-2017, paragraph 84.

[46] See paragraph 119 above.

[47] See paragraphs 105 to 114 above.

addition, also in the JECDB study – whilst only minimal thyroid effects were observed in the OECD TG 407 study. However, as stated by the Agency, the difference between the OECD TG 408 study and the OECD TG 407 study can be explained by the longer duration of the former (90 days) compared to the latter (28 days). Similarly, the difference between the JECDB study and the OECD TG 407 study can be explained by the higher doses used in the former (1 000 mg/kg bw/day) compared to the latter (200 mg/kg bw/day). In the light of those differences, the fact that only minimal thyroid effects were observed in the OECD TG 407 study does not resolve the concern raised by the other two studies.

126. The Appellants' sixth argument, according to which the Agency failed to take into account the fact that no findings were noted on the thyroid of the pups in the OECD TG 414 study, must be rejected for the following reasons.

127. It is true that the Contested Decision does not refer to the OECD TG 414 study in the context of cohorts 2A and 2B. However, the OECD TG 414 study –the robust study summary and the full study report of which were both submitted to the Board of Appeal in these proceedings – did not evaluate thyroid weight, histopathology or thyroid hormones in the foetuses or in the dams. Therefore, the results of the OECD TG 414 study do not contradict the effects observed in the OECD TG 408 study and in the JECDB study.

128. In conclusion, the Agency did not commit errors in its scientific assessment, fail to take relevant information into account or breached the principles of legal certainty and of the protection of legitimate expectations in requiring the EOGRTS to include cohorts 2A and 2B under the second paragraph of Column 2 of Section 8.7.3. of Annex IX.

(c) Conclusion on the requirement for the EOGRTS to include cohorts 2A and 2B (second paragraph of Column 2 of Section 8.7.3. of Annex IX)

129. It follows from the reasons set out above that the Appellants' arguments concerning the requirement for the EOGRTS to include cohorts 2A and 2B under the second paragraph of Column 2 of Section 8.7.3. of Annex IX must be rejected.

5.2.3. The requirement for the EOGRTS to include investigations on learning and memory function (paragraph 37 of EU test method B.53)

Arguments of the Parties

130. The Appellants raise two lines of argument against the finding in the Contested Decision that the EOGRTS on which they must provide information must include investigations on learning and memory function in accordance with paragraph 37 of EU test method B.53.[48]

131. First, the Appellants argue that such investigations are not an information requirement for their registration of the Substance. According to the Appellants, the Agency therefore exceeded its powers by requiring those investigations in the Contested Decision.[49]

[48] See paragraphs 7 and 10 above.

[49] Third part of the second plea.

132. Second, the Appellants argue that in requiring the investigations on learning and memory function the Agency committed errors in its scientific assessment, failed to take relevant information into account and breached the principles of legal certainty and of the protection of legitimate expectations.[50]

133. The Agency disputes the Appellants' arguments.

134. First, the Agency argues that, if there are indications that a substance may affect learning and memory function, additional investigations of those functions can be required under Article 41(3) in conjunction with the second paragraph of Column 2 of Section 8.7.3. of Annex IX, Article 13(3) and paragraph 50 of EU test method B.56.

135. Second, the Agency argues that it did not commit any errors in finding in the Contested Decision that there is information showing that the Substance may affect learning and memory function as part of its potential developmental neurotoxicity effects.

136. At the hearing, the Board of Appeal drew the attention of the Parties to its decision of 25 April 2023 in *BASF Lampertheim and Metall-Chemie*, A-002-2022 and A-003-2022. In the light of that decision, the Appellants requested the Board of Appeal to rule not only on whether the Agency had the competence to require investigations on learning and memory function, but also on whether its scientific assessment was flawed. The Agency did not withdraw its arguments but requested the Board of Appeal, in the event that it should conclude that the Agency exceeded its competence, to limit the annulment of the Contested Decision to the requirement for investigations on learning and memory function.

Findings of the Board of Appeal

137. Investigations on learning and memory function are not an information requirement for the Appellants' registration of the Substance under the second paragraph of Column 2 of Section 8.7.3. of Annex IX in conjunction with Article 13(3) and paragraph 50 of EU test method B.56.[51]

138. The Appellants' argument to that effect must therefore be upheld. There is no need to examine the Appellants' remaining arguments concerning the investigations of learning and memory function.

5.3. Result

139. The present appeal is unfounded insofar as it concerns the requirement to provide information on an EOGRTS under Column 1 of Section 8.7.3. of Annex IX, including cohorts 2A and 2B under second paragraph of Column 2 of Section 8.7.3. of Annex IX.

140. By contrast, the present appeal is well-founded insofar as it concerns the requirement for the EOGRTS to include investigations of learning and memory function (paragraph 50 of EU test method B.56).

141. The Appellants and the Agency confirmed at the hearing that the annulment of the investigations on learning and memory function would not affect the remainder of the request.

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[50] Third part of the first plea.

[51] Decision of the Board of Appeal of 25 April 2023, *BASF Lampertheim and Metall-Chemie*, A-002-2022 and A-003-2022, paragraphs 30 to 52, and 62.

142. The Contested Decision can and must therefore be annulled only insofar as it requires investigations on learning and memory function, and the appeal rejected for the remainder.

6. Effects of the Contested Decision

143. Under Article 91(2), an appeal has suspensive effect. As the contested part of the Contested Decision is only partly annulled, the Appellants are still required to submit information on an EOGRTS, including cohorts 2A and 2B, under Columns 1 and 2 of Section 8.7.3. of Annex IX.

144. The deadline set in the Contested Decision was 15 September 2025, which is three years, three months, and seven days from the date of notification of that decision. The Appellants must therefore provide information on an EOGRTS, as required by the Contested Decision with the specifications described in the previous paragraph, by 26 December 2026.

7. Refund of the appeal fee

145. Under Article 10(4) of the Fee Regulation[52] the appeal fee must be refunded if the appeal is decided in favour of an appellant. As the appeal is partially upheld, the appeal fee is refunded.

[52] 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).

On those grounds,

THE BOARD OF APPEAL

hereby:

1. **Dismisses the appeal as inadmissible insofar as the Appellants request the Board of Appeal to take such other or further measures as justice may require.**
2. **Annuls the Contested Decision insofar as it requires the Appellants to conduct investigations on learning and memory function.**
3. **Dismisses the appeal as unfounded for the remainder.**
4. **Decides that information on an EOGRTS, including cohort 1A, cohort 1B without extension to mate the animals to produce the F2 generation, and cohorts 2A and 2B, must be provided by 26 December 2026.**
5. **Decides that the appeal fee is refunded.**

Antoine BUCHET
Chairman of the Board of Appeal

Alen MOČILNIKAR
Registrar of the Board of Appeal