EUROPEAN CHEMICALS AGENCY
BOARD OF APPEAL

DECISION OF THE BOARD OF APPEAL OF THE EUROPEAN CHEMICALS AGENCY

23 April 2024

(Substance evaluation – DPHP – Amphibian metamorphosis assay with non-standard specifications – Proportionality – Necessity – Appropriateness to achieve the objective pursued – Burden of proof)

Case number	A-010-2022
Language of the case	English
Appellant	BASF SE, Germany Represented by Jean-Philippe Montfort and Thomas Delille Mayer Brown Europe-Brussels LLP, Belgium
Intervener	Bundesanstalt für Arbeitsschutz und Arbeitsmedizin, Germany
Contested Decision	Decision of 8 August 2022 on the substance evaluation of the substance bis(2-propylheptyl) phthalate, adopted by the European Chemicals Agency pursuant to Article 46 of the REACH Regulation

THE BOARD OF APPEAL

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

Registrar: Alen Močilnikar

gives the following

Decision

1. Background to the dispute

1. This appeal concerns the substance evaluation for the substance bis(2-propylheptyl) phthalate (**DPHP**).[1]

2. The Appellant is the lead registrant for DPHP. That substance is manufactured in and/or imported to the European Economic Area in quantities of 100 000 to 500 000 tonnes per year. It is used for the production of a variety of materials or articles including polymers, PVC, rubbers, plastic films and formulations used by consumers and professional workers in formulation, re-packing and at industrial sites.

3. The Agency included DPHP in the Community rolling action plan for substance evaluation due to initial concerns relating to endocrine disruption.

4. The competent authority of Germany, the Bundesanstalt für Arbeitsschutz und Arbeitsmedizin (**BAuA**), was appointed to carry out the substance evaluation. BAuA prepared a draft decision in accordance with Article 46(1) of the REACH Regulation[2], requiring further information in order to clarify whether DPHP has endocrine disrupting properties in the environment.

5. On 6 April 2021, the draft decision was notified to the registrants of DPHP in accordance with Article 50(1).

6. On 12 May 2021, the registrants submitted comments on the draft decision in accordance with Article 50(1). BAuA took those comments into account and revised the draft decision.

7. On 3 March 2022, BAuA submitted the revised draft of the decision to the competent authorities of the other Member States and to the Agency in accordance with Article 52(1).

8. By 4 April 2022, the competent authority of Belgium and the Agency submitted proposals for amendment in accordance with Articles 52(2) and 51(2).

9. On 4 May 2022, the registrants of DPHP submitted comments on those proposals for amendment in accordance with Articles 52(2) and 51(5). The registrants' comments were submitted, together with a further revised draft of the decision, to the Member State Committee.

10. On 8 August 2022, following the unanimous agreement of the Member State Committee, the Agency adopted the Contested Decision in accordance with Articles 52(2) and 51(6).

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[1] EC No 258-469-4; CAS No 53306-54-0.

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

2. Contested Decision

11. The Contested Decision requires the Appellant to submit, by 13 February 2025, an amphibian metamorphosis assay (**AMA**) with DPHP pursuant to test guideline No 231 of the Organisation for Economic Cooperation and Development (**OECD TG 231**), including the following specifications:

a) The test material must be representative for DPHP, in particular with respect to the concentrations of isomers, constituents and impurities.

b) Because of the low water solubility (2 ng/L) of DPHP, the AMA must be conducted with dietary exposure, including the following non-standard specifications to OECD TG 231:

- DPHP must be dissolved in acetone, afterwards mixed with the dry Sera Micron feed and evaporated with filtered air to dryness again. Caution should be taken to ensure that DPHP does not crystallise as the solvent is removed.
- A negative control with Sera Micron feed similarly treated with acetone without DPHP must be prepared.
- The test must be conducted under flow-through conditions to ensure an acceptable water quality.
- The spiked Sera Micron feed must be fed as a suspension prepared with dilution water. This solution must be prepared shortly before the beginning of the test and divided into individual aliquots, e.g. in scintillation vials, so each aliquot holds enough food for an entire treatment for a single day.
- Before the beginning of the test, the intended concentration of DPHP in the spiked diet must be verified by analytical measurements. To check the concentration, triplicate samples of the dosed Sera Micron feed must be extracted with a suitable extraction method and DPHP concentration in the extracts must be measured by an appropriate analytical method.
- A dose range-finding test must be performed in order to reduce technical challenges and increase the robustness and quality of the data obtained in the main study.
- At least five concentration levels with four replicates must be tested in the main study to obtain a full dose-response relationship to derive a sound LOEC/NOEC.
- In addition, the concentration of DPHP and the two metabolites mono-(2-propylheptyl) phthalate (**MPHP**) and mono-(2-propyl-6-hydroxyheptyl) phthalate (**OH-MPHP**) in the animals, must be analytically measured. Analytical measurement of the total body burden of DPHP, MPHP and OH-MPHP must be performed in full body homogenate at the end of the test. From each treatment group at least three animals must be pooled and analysed using an adequate sample preparation and analytical set up.
- Liver histopathology and assessment of the hepatosomatic index must be performed.

12. In addition, the Contested Decision recommends that when performing the test the registrants should consider including a second control group using untreated Sera Micron feed. This is recommended in addition to the control group using acetone-treated Sera Micron feed, in order to determine whether treatment of the feed with acetone impacts the quality and consistency of the food.

3. Procedure before the Board of Appeal

13. On 7 November 2022, the Appellant filed its appeal.

14. On 30 January 2023, the Agency submitted its Defence.

15. On 8 February 2023, BAuA was granted leave to intervene in these proceedings in support of the Agency.

16. On 28 February 2023, the Appellant submitted its observations on the Defence.

17. On 3 April 2023, the Agency submitted its observations on the Appellant's observations on the Defence.

18. On 5 April 2023, BAuA submitted its statement in intervention.

19. On 10 and 11 May 2023, the Agency and the Appellant submitted their respective observations on the statement in intervention.

20. On 6 July 2023, the Appellant submitted further documents following a measure of organisation of the procedure taken by the Board of Appeal under Article 15(1) and 3(d) of the Rules of Procedure[3].

21. On 10 October 2023, a hearing was held on the Appellant's request. The hearing was held at the Agency's premises. At the hearing, the Appellant, the Agency and BAuA made oral submissions and responded to questions from the Board of Appeal.

4. Form of order sought

22. The Appellant requests the Board of Appeal to annul the Contested Decision and order the refund of the appeal fee.

23. The Agency, supported by BAuA, requests the Board of Appeal to dismiss the appeal as unfounded.

5. Assessment of the case

24. The Appellant raises four pleas in law in support of its appeal, alleging that the Agency:

- breached Article 46(1) and the principle of proportionality (first plea), in particular because the AMA study (i) is not necessary, (ii) is not appropriate to achieve its objective, and (iii) is not the least onerous measure;
- breached Article 13(3) (second plea);
- breached the principle of legal certainty (third plea); and
- breached the Appellant's right to be heard (fourth plea).

[3] 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).

5.1. First part of the first plea: Breach of Article 46(1) and of the principle of proportionality because the AMA study is not necessary

Arguments of the Parties and the Intervener

25. The Appellant argues that the Agency breached Article 46(1) and the principle of proportionality because the AMA study required in this case is not necessary.

26. First, according to the Appellant, the Agency has failed to demonstrate that DPHP poses a potential risk to the environment as there is neither evidence of a potential hazard concerning environmental endocrine disruption, nor of potential environmental exposure to DPHP.

27. As regards the existence of a potential hazard, the Appellant argues that the Agency based its assessment essentially on two studies: a 90-day repeated-dose toxicity study in accordance with OECD TG 408 (the **BASF (1995) study**), and a two-generation reproductive toxicity study according to OECD TG 416 (the **BASF (2009) study**). According to the Appellant, these studies are not sufficient to demonstrate that DPHP poses a potential hazard concerning environmental endocrine disruption for the following reasons:

- The thyroid effects observed in those two studies are not mediated by an endocrine disruptive mode of action but are a secondary result of hepatotoxicity. The results of those two studies do not, therefore, establish a potential hazard concerning environmental endocrine disruption. This is borne out by two publications (the **Bhat et al. (2014) publication**[4] and the **UBA (2015) position paper**[5]) which were submitted during the present proceedings. Moreover, this could be confirmed by carrying out a liver enzyme induction study in rats with DPHP.
- The Contested Decision refers to the fact that other possible modes of action than effects on the hypothalamo-pituitary-thyroid (**HPT**) axis have been observed for certain other phthalates than DPHP. However, the Agency has not adequately substantiated this finding.
- The Contested Decision states that it cannot be excluded that DPHP may pose a hazard concerning environmental endocrine disruption, whilst, according to the Appellant, it is for the Agency to establish that such a potential risk exists and is not purely hypothetical.

28. As regards the existence of potential environmental exposure, the Appellant argues that the Contested Decision is too imprecise and partially based on unverified information. Furthermore, the Appellant argues that the Agency failed to assess the real level of environmental exposure to DPHP. According to the Appellant, DPHP is poorly soluble in water and readily biodegradable, so that there is no realistic possibility that organisms in the environment may be exposed to sufficient concentrations of DPHP to cause the alleged endocrine disrupting effects. The Appellant relies, in that regard, on paragraph 65 of the decision of the Board of Appeal of 23 September 2015, *Akzo Nobel Industrial Chemicals and Others*, A-005-2014.

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[4] V.S. Bhat *et al*.: *Derivation of an oral reference dose (RfD) for the plasticizer, di-(2-propyl-heptyl)phthalate (Palatinol® 10-P)*, Regulatory Toxicology and Pharmacology 70 (2014) 65.

[5] Umweltbundesamt/Human Biomonitoring Committee: *Stoffmonografie für Di-2-propylheptyl-phthalat (DPHP) – Human Biomonitoring (HBM)-Werte für die Summe der Metaboliten Oxo-Monopropylheptylphthalat (oxo-MPHP) und Hydroxy-Monopropylheptylphthalat (OH-MPHP) im Urin von Erwachsenen und Kindern*, B.Ges.Bl. (2015) DOI 10.1007/S00103-015-2172-Z.

29. Second, according to the Appellant, the Agency has failed to demonstrate that there is a need to clarify the alleged potential risk. In the first place, it is clear from the available information that DPHP does not pose a potential risk concerning environmental endocrine disruption. In the second place, the Agency appears to have already concluded – incorrectly – that DPHP has endocrine disrupting properties, so that there is no real need for further information.

30. Third, according to the Appellant, the Agency has failed to demonstrate that the information required by the Contested Decision has a realistic possibility of leading to improved risk management measures. According to the Appellant, the AMA study is 'only' a screening study and may not produce a definitive conclusion as to the endocrine disrupting properties of DPHP.

31. The Agency, supported by BAuA, disputes the Appellant's arguments.

Findings of the Board of Appeal

32. In order to demonstrate that a request for further information is necessary, the Agency must establish that (i) there are grounds for considering that, based on a combination of information on potential hazard and potential exposure, a substance constitutes a potential risk to human health or the environment; (ii) the potential risk needs to be clarified; and (iii) the requested information, needed to clarify the concern, has a realistic possibility of leading to improved risk management measures.[6]

33. To request information under substance evaluation, it is not necessary for the Agency to demonstrate an actual risk, only a potential risk. The aim of requesting additional information under substance evaluation is to clarify the risk.[7]

34. This is consistent with the different types of risk that must be taken into account at different stages of the processes established by the REACH Regulation.

35. This is also consistent with the European Union Courts' interpretation of the precautionary principle according to which a preventive measure may be taken only if the risk, although the reality and extent thereof have not been 'fully' demonstrated by conclusive scientific evidence, appears nevertheless to be adequately backed up by the scientific data available at the time the measure was taken.[8]

36. A request for further information under substance evaluation cannot be triggered by a purely hypothetical risk or by a failure to prove the lack of any risk.[9]

37. It is the Agency's responsibility to justify a request for further information under substance evaluation by demonstrating that the three conditions of the necessity test referred to above are met.

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6 Judgments of 16 December 2020, *3v Sigma* v *ECHA*, T-176/19, EU:T:2020:621, paragraph 44, and of 20 September 2019, *BASF Grenzach* v *ECHA*, T-125/17, EU:T:2019:638, paragraph 276; decision of the Board of Appeal of 17 January 2023, *SCAS Europe*, A-009-2021, paragraph 75.

7 Judgment of 20 September 2019, *BASF Grenzach* v *ECHA*, T-125/17, EU:T:2019:638, paragraphs 269 to 273; decision of the Board of Appeal of 17 January 2023, *SCAS Europe*, A-009-2021, paragraph 76.

8 Judgment of 11 September 2002, *Pfizer Animal Health* v *Council*, T-13/99, EU:T:2002:209, paragraph 144; decision of the Board of Appeal of 17 January 2023, *SCAS Europe*, A-009-2021, paragraph 78.

9 Decision of the Board of Appeal of 17 January 2023, *SCAS Europe*, A-009-2021, paragraph 79.

38. When an appellant challenges such information request it must show that the Agency erred in its conclusions on one or more of those three conditions.

39. In assessing the Appellant's pleas that the Agency committed errors of assessment, it must therefore be examined whether the arguments put forward by the Appellant demonstrate that the Agency made errors and failed to take all relevant information into account in concluding that those three conditions are met in the present case.[10]

5.1.1. Potential risk to the environment

40. Potential risk is a combination of potential hazard and potential exposure.[11]

- *Potential hazard*

41. The Contested Decision states that DPHP poses a potential hazard potential hazard concerning environmental endocrine disruption. That conclusion is based on two studies, namely the BASF (1995) study and the BASF (2009) study.

42. The BASF (1995) study shows thyroid follicular hypertrophy in both sexes with a dose-dependent increased incidence. In addition, the BASF (2009) study shows a dose-dependent increase of thyroid weight and of the incidence of thyroid follicular hyperplasia in the F1 generation. The fact that these effects were observed in the two studies at issue is common ground between the parties. The parties disagree, however, on the interpretation of these effects.

43. First, the parties disagree as to whether the effects observed in the two studies are indicative of a potential endocrine disrupting mode of action or whether they are secondary effects due to hepatotoxicity. The Appellant argues that the thyroid effects observed in the two studies are secondary effects resulting from peroxisome proliferation and liver enzyme induction. In support of that argument, the Appellant argues that in the two studies, significant thyroid hypertrophy was observed only at dose-levels at which liver cell hypertrophy was also observed.

44. As the Agency and BAuA point out, in both the BASF (1995) study and the BASF (2009) study, thyroid hypertrophy/hyperplasia occurred not only at the same, but also at lower dose levels than the ones at which liver hepatocyte hypertrophy effects were observed. Furthermore, in the BASF (2009) study thyroid weight was statistically significantly increased in F1 males from the low-dose level whereas liver weight was statistically significantly increased from the mid-dose level in F1 males. Overall, thyroid effects also occurred at lower dose levels than the doses at which liver effects were observed.

45. This suggests that the effects observed in the two studies are not secondary due to hepatotoxicity but primary effects and potentially mediated by an endocrine disruptive mode of action. In those circumstances, it must be held that the results of the BASF (1995) study and of the BASF (2009) study establish that DPHP may disrupt the thyroidal endocrine system. This is sufficient to consider that DPHP poses a potential hazard potential hazard concerning endocrine disruption.

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[10] Decision of the Board of Appeal of 17 January 2023, *SCAS Europe*, A-009-2021, paragraph 82.

[11] Decision of the Board of Appeal of 17 January 2023, *SCAS Europe*, A-009-2021, paragraph 84.

46. That conclusion is not called into question by the Bhat et al. (2014) publication and the UBA (2015) position paper, which the Appellant submitted with its observations on the defence. Neither of those documents determines conclusively whether the thyroid effects at issue are mediated by an endocrine disruptive mode of action or secondary effects due to hepatotoxicity.

47. Furthermore, the potential hazard of endocrine disruption identified from the BASF (1995) study and the BASF (2009) study, which were carried out in rats, is relevant also to other vertebrate species in the environment. As the Agency and BAuA argue without being contradicted on that point by the Appellant, the thyroid system is highly conserved across vertebrates.

48. Second, it is true that a request for further information under substance evaluation cannot be triggered by a purely hypothetical hazard or by a failure to prove the lack of any hazard.[12] However, the Contested Decision is not based merely on the assumption that a potential hazard exists because it cannot be excluded that DPHP might be an endocrine disruptor. It is clear from the reasoning of the Contested Decision, read as a whole, that the Agency correctly and adequately explained why it considers that DPHP may have endocrine disrupting properties.

49. Third, the generic reference in the Contested Decision to the endocrine disruptive mode of action of other phthalates than DPHP is not an essential element of the reasoning of the Contested Decision. The relevant part of the Contested Decision confines itself to stating that although it is possible that the thyroid effects observed in the two studies may be secondary effects due to hepatotoxicity, it is also possible that those effects may be due to endocrine disruptive effects and there is no conclusive information either way.[13] Therefore, even assuming that the Agency's reference to other phthalates than DPHP had to be disregarded for being too generic, this would not alter the fact that the available information on DPHP shows that this substance poses a potential hazard concerning endocrine disruption.

50. The Appellant's arguments contesting the existence of a potential hazard must consequently be rejected.

- *Potential exposure*

51. The Appellant argues that the Contested Decision is vitiated by error insofar as it finds that there is potential environmental exposure to DPHP. The Appellant's argument consists, in essence, of two lines.

52. First, the Appellant argues that the Agency has failed to establish that DPHP may be released into the environment. According to the Appellant, the Contested Decision is not sufficiently precise in that regard and relies on unverified information.

53. As the Agency stated in the Contested Decision and explained in these proceedings, DPHP is manufactured or imported in high quantities (100 000 to 500 000 tonnes per year). It is not disputed that DPHP is used by consumers, in articles, by professional workers (widespread uses), in formulation or re-packing, at industrial sites and in manufacturing for the production of a variety of materials and articles used in the European Economic Area.

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[12] Decision of the Board of Appeal of 17 January 2023, *SCAS Europe*, A-009-2021, paragraph 79.

[13] Contested Decision, p. 4.

54. This gives sufficient reason to believe that under the current set of operational and occupational measures the environment may be exposed to DPHP as a potential endocrine disruptor in the course of the manufacture, use and disposal of those products. Besides, DPHP has even been empirically detected in the environment within the European Union.[14]

55. The Appellant's first line of argument must therefore be rejected.

56. Second, the Appellant argues that the Agency failed to assess the real level of environmental exposure to DPHP based on the properties of the substance. According to the Appellant, DPHP is poorly soluble in water and readily biodegradable. As a consequence, the Appellant argues that there is no realistic possibility that organisms in the environment may be exposed to sufficient concentrations of DPHP to cause the alleged endocrine disrupting effects.

57. However, the Agency is not required to establish real or realistic exposure levels in order to demonstrate potential exposure. Such a requirement would be inconsistent with the objectives of the substance evaluation process and the precautionary principle referred to in Article 1(3).

58. The Appellant's reference to paragraph 65 of the decision of the Board of Appeal in *Akzo Nobel Industrial Chemicals and Others*[15] is immaterial in that regard. In that case, the Board of Appeal examined whether further information was necessary for a substance which was already highly regulated. At paragraph 65 of its decision it held, in essence, that the Agency had failed to explain why it considered that further information was necessary in light of the stringent measures already in place. That case consequently concerned a different issue than the present case.

59. Finally, the Appellant's argument is not sufficiently substantiated. As the Contested Decision explains, the environment may be exposed to DPHP. The Appellant argues DPHP is poorly soluble in water and readily biodegradable. However, the Appellant has not established that the Agency committed an error as it has not provided any evidence to show that there is a concentration threshold, generally or in any specific environmental compartment, below which DPHP could not exert its potential endocrine disrupting properties.

60. The Appellant's second line of argument must therefore also be rejected.

- *Conclusion on the potential risk*

61. The Agency committed no error in finding, in the Contested Decision, that DPHP poses a potential hazard concerning environmental endocrine disruption, and that there is potential environmental exposure to DPHP. The Agency did not commit an error in concluding that DPHP poses a potential risk to the environment.

5.1.2. Need to clarify the potential risk

62. A potential risk needs to be clarified if the available information shows that a substance may have a certain hazardous property, but is not sufficient to conclude that the substance in fact has that property.

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[14] M. Lampi *et al*., *Environmental Monitoring of high molecular weight phthalate esters in the Netherlands*, 2012.

[15] Decision of the Board of Appeal of 23 September 2015, *Akzo Nobel Industrial Chemicals and Others*, A-005-2014.

63. It has already been concluded above that, contrary to the Appellant's arguments, DPHP poses a potential risk concerning environmental endocrine disruption. As the Contested Decision correctly states, the available information does not allow to conclude whether this is in fact the case.

64. It follows that the potential risk posed by DPHP needs to be clarified.

5.1.3. Realistic possibility of improved risk management measures

65. Clarifying the potential hazard identified for DPHP may lead to that substance being, for example, identified as a substance of very high concern in accordance with Article 57(f), and subsequently subjected to authorisation or restriction requirements. There is consequently a realistic possibility of improved risk management measures.

5.1.4. Conclusion on the first part of the first plea

66. It follows from the reasons set out above that the Agency did not commit an error in finding that it is necessary to require further information on DPHP in this case.

67. The first part of the first plea must consequently be rejected as unfounded.

5.2. Second part of the first plea: Breach of the principle of proportionality because the AMA study is not appropriate to achieve its objective

Arguments of the Parties and the Intervener

68. Under the second part of the first plea, the Appellant argues that the required AMA study is not appropriate to achieve the objective of clarifying the potential risk to the environment identified by the Agency.

69. First, according to the Appellant, the required AMA study is only a screening study and will not therefore allow to draw a definitive conclusion as to the potential endocrine disrupting properties of DPHP.

70. Second, according to the Appellant, the required AMA study will not produce meaningful results in the present case because DPHP is not sufficiently soluble in water, and the method for dietary administration prescribed in the Contested Decision is not feasible. The Appellant relies, in support of that argument, on a feasibility study which was finalised during the appeal proceedings (the **new feasibility study**).[16]

71. The Agency, supported by BAuA, disputes the Appellant's arguments.

72. First, the Agency argues that, due to the specifications of the test method set out in the Contested Decision, the AMA study is the appropriate study to clarify the potential risk at issue and is very likely to provide sufficient information to conclude on the endocrine disruption concern.

73. Second, the Agency argues that the Contested Decision takes into account and addresses the Appellant's concerns regarding the feasibility of the method for dietary administration prescribed in the Contested Decision.

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[16] BASF, *Feasibility Evaluation of Diet Preparation and Efficacy for Dietary Exposure of African Clawed Frog, Xenopus laevis to DPHP in the 21-d Amphibian Metamorphosis Assay (AMA)*, 2023.

74. In the first place, according to the Agency, the Contested Decision provides for the use of control groups, which will detect any problems concerning the quality and consistency of the feed. At the time of adoption of the Contested Decision, there was no information demonstrating that the method of preparation and administration of the feed is not feasible.

75. In the second place, according to the Agency, the new feasibility study submitted by the Appellant is not sufficient to show that the required AMA study with the method for dietary administration as prescribed in the Contested Decision is not feasible.

Findings of the Board of Appeal

76. The principle of proportionality requires that the requested information must be capable of achieving its objective. Therefore, in order to demonstrate the appropriateness of an information request in the context of substance evaluation, the Agency must be able to establish that the potential risk posed by the substance can be clarified by the requested information.[17]

77. The Appellant argues that the required AMA study does not satisfy this requirement for two reasons.

78. First, the Appellant argues that the required AMA study is only a screening study and will not therefore allow to draw a definitive conclusion as to the potential endocrine disrupting properties of DPHP.

79. Contrary to the Appellant's argument, the principle of proportionality does not require the Agency to establish *ex ante* that a study will certainly produce a definitive conclusion as to whether or not a substance has a certain property. It is sufficient that the study is capable of contributing to the objective of clarifying the property at issue.[18]

80. As stated in paragraph 2 of OECD TG 231, the AMA study is an appropriate study to investigate the thyroidal endocrine disrupting properties of a substance. Indeed, apical endpoints in some of the 'level 3 assays' (specifically, metamorphosis in the AMA) can provide evidence of adverse effects which may, in combination with mechanistic evidence, contribute to a conclusion that the test substance is an endocrine disruptor.[19] In principle, therefore, the AMA study is an appropriate study in the present case.

81. The Appellant's first argument must therefore be rejected.

82. Second, the Appellant argues that the required AMA study will not produce meaningful results in the present case because DPHP is not sufficiently soluble in water, and the method for dietary administration prescribed in the Contested Decision is not feasible.

83. The principle of proportionality requires the Agency to establish that the requested study can produce meaningful results.

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[17] Decision of the Board of Appeal of 17 January 2023, *SCAS Europe*, A-009-2021, paragraph 83.

[18] See, to that effect and by analogy, judgments of 21 March 2024, *Landeshauptstadt Wiesbaden*, C-61/22, EU:C:2024:251, paragraphs 86, 94 and 119; and of 13 July 2018, *Chrysostomides and Others* v *Council and Others*, T-680/13, EU:T:2018:486, paragraphs 293 and 330.

[19] See OECD, *Revised Guidance Document 150 on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption*, OECD 2018, paragraph 64.

84. As regards the distribution of the burden of proof on that point, it falls first of all to the Agency to establish, in its decision under Article 46(1), that the study which it requires is capable of producing meaningful results. At the stage of the appeal proceedings, it then falls to an appellant to establish that the study is not capable of doing so. If the appellant provides admissible, credible, and convincing evidence to that effect, the burden of proof shifts to the Agency, which must then rebut the point.[20]

5.2.1. The Contested Decision

85. The Contested Decision sets out and explains a specific method for ensuring that the required AMA study will produce meaningful results despite the fact that DPHP is poorly soluble in water. The AMA study should be carried out – in essence – by dissolving DPHP in acetone, drenching the Sera Micron feed with the solution, and evaporating the acetone so as to produce feed coated in DPHP. The treated feed should then be suspended in water and fed to the test animals.[21] In addition, control groups may be used to verify whether treating the feed in this way affects its quality and consistency.[22]

86. The Agency therefore explained, in the Contested Decision, why it considered that the required AMA study in this case is capable of achieving its objective. It fell to the Appellant, in the course of the appeal proceedings, to establish that the considerations set out in the Contested Decision are incorrect.

5.2.2. Assessment of the Appellant's arguments

87. During the appeal proceedings, the Appellant argued that the AMA study is not capable of achieving its objective in the present case as treating the feed with acetone will alter its quality, consistency, and nutritional properties. This will cause the study to deliver results which will not be meaningful. In support of that argument, the Appellant submitted the results of a feasibility study which was finalised during the appeal proceedings.

88. As regards the admissibility of the new feasibility study, it must be noted that that study was submitted with the Appellant's observations on the defence. The delay is justified under Article 12(1) of the Rules of Procedure as the study was not yet finalised at the time of the submission of the notice of appeal.

89. Furthermore, the administrative review by the Board of Appeal is different in nature than the judicial review by the European Union Courts. Evidence may therefore be taken into account by the Board of Appeal even if it was not available to the Agency at the time of the adoption of the contested decision, provided that it is intended to support facts already alleged at the time of the initial decision-making procedure.[23] That requirement is fulfilled in this case.

90. The new feasibility study is consequently admissible.

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[20] See, to that effect, judgment of 20 September 2019, *BASF Grenzach* v *ECHA*, T-125/17, EU:T:2019:638, paragraphs 431 and 432; decision of the Board of Appeal of 4 May 2020, *Clariant Plastics & Coatings (Deutschland)*, A-011-2018, paragraph 119.

[21] Contested Decision, pp. 9-10.

[22] Contested Decision, p. 12.

[23] See, to that effect, decisions of the Board of Appeal of 19 June 2013, *Dow Benelux*, A-001-2012, paragraph 46; of 19 October 2016, *Polynt*, A-004-2015, paragraph 133; and of 6 June 2023, *Cytec Engineered Materials*, A-001-2022, paragraph 123.

91. As regards the findings of the new feasibility study, the Appellant followed in essence the method which is prescribed by the Contested Decision. Sunflower oil – in one concentration, as a substitute for DPHP – was dissolved in acetone, the Sera Micron feed drenched with the solution, and the acetone evaporated. The resulting feed was suspended in water and then fed to tadpoles. The study included a control group applying Sera Micron feed treated with acetone only, and another control group applying untreated Sera Micron feed.

92. The new feasibility study showed:

- a mortality rate of 30% (the acceptable mortality rate in an AMA study is 10%[24]) in the tadpoles fed with Sera Micron feed treated with acetone alone or with acetone and sunflower oil, but not in the tadpoles fed with untreated feed; and
- adverse developmental effects (e.g. malformation) and clinical signs of toxicity in the tadpoles fed with acetone-treated feed, but not in the tadpoles fed with untreated feed.

93. The Appellant has therefore produced admissible, credible, and convincing evidence in support of its argument. It consequently falls to the Agency, supported by BAuA, to rebut the Appellant's arguments and evidence in that regard.

5.2.3. Assessment of the Agency's and BAuA's arguments

94. During the present appeal proceedings the Agency, supported by BAuA, disputed the arguments and evidence submitted by the Appellant.

- *Mortality effects observed in the new feasibility study*

95. The Agency and BAuA deny the relevance of the mortality effects observed in the new feasibility study. They raise four arguments in that regard.

96. First, according to the Agency, it is not scientifically justified to relate the mortality observed in the new feasibility study with the acetone. The Agency argues that the mortality observed in the new feasibility study cannot be due to residual acetone in the Sera Micron feed because the acetone is supposed to be evaporated before the feed is given to the tadpoles and in any event residual acetone would not have such an effect. Furthermore, the mortality occurred on a single day (study day 12) and there was no dose or time-related trend in this effect. Food intake appears to increase over time, and study day 12 is not a critical phase in the development of the tadpoles. The Agency therefore considers that the mortality was not related to the acetone treatment but to some other cause – possibly an oxygenation problem in the tanks.

97. Although it is clear from the study report that the acetone was evaporated before the feed was given to the tadpoles, the Agency offers no explanation as to why mortality was observed only in the tanks with the acetone-treated feed, and not in the tanks with the untreated feed. Moreover, abnormal swimming was observed in the groups with the acetone-treated feed on study days 10 and 11. Furthermore, the concentration of dissolved oxygen in the test tanks was measured three times per week and the study report does not contain any indications of a possible problem with oxygenation.

[24] See paragraphs 17, 40 and 44 of OECD TG 231.

98. Second, the Agency argues that the Appellant should have terminated the new feasibility study as soon as the mortality was observed, that the test is invalid because mortality was higher than 10%,[25] and that no conclusions can be drawn from it. However, the point of the study was precisely to determine whether the method prescribed in the Contested Decision is feasible, so that its results cannot be disregarded due to the observed mortality.

99. Third, the Agency referred to certain studies which allegedly show the innocuity of acetone when used to incorporate a substance in the feed. However, the Agency has not submitted these studies to the Board of Appeal, which is therefore not in a position to examine their content.

- *Malformation (tail flexure) observed in the new feasibility study*

100. As regards the reported malformation (i.e. tail flexure) observed in the new feasibility study, the Agency argues that this effect can occur spontaneously in the test species (*X. laevis*). Furthermore, according to the Agency, the study suggests that the acetone-treated feed is more accessible to the animals, which therefore develop more tail flexure, and in any event tail flexure does not invalidate an AMA study.

101. This argument, even if accepted, does not explain the mortality rate of 30% observed in the new feasibility study in the tadpoles fed with acetone-treated Sera Micron feed. Furthermore, it is apparent from the study that tail flexure was observed only in the tanks with the acetone-treated feed. This undermines the argument that the problem is genetic or due to an interaction of genetic and dietary factors, and not due to the acetone treatment of the feed.

- *General clinical signs observed in the tadpoles in the new feasibility study*

102. As regards the general clinical signs observed in the tadpoles in the new feasibility study, the Agency denies those effects on two grounds.

103. First, the Agency argues that the tadpoles receiving acetone-treated feed did not show any negative effects on weight and length. This observation indeed supports the Agency's position. However, it also appears that the development of the same animals was delayed. The study report states that *'the trend in stage distribution at SD 21 in the SMN + acetone (removed) and SMN + 0.1 mg/L sunflower oil (SFO) (acetone removed) treatments was significantly decreasing relative to the SMN control'* and that *'the median developmental stages attained at SD 21 in the SMN + acetone (removed) and SMN + 0.1 mg/L sunflower oil (SFO) (acetone removed) treatments was significantly decreasing relative to the SMN control'.*

104. Second, the Agency argues that the requested AMA study will include two control groups – one with the acetone-treated feed, and one with untreated feed. According to the Agency, this will allow to determine, once the study is finalised, whether and which effects were due to the acetone treatment of the feed, and which were due to DPHP. This is correct, but it cannot be expected to add any value in the context of the present decision. The new feasibility study did essentially the same as the control groups would do in the AMA study.

[25] See paragraphs 17, 40 and 44 of OECD TG 231.

- *Conclusion on the Agency's and BauA's arguments*

105. The Agency, supported by BAuA, has not been able, in the present appeal proceedings, to rebut the arguments and evidence put forward by the Appellant.

5.2.4. Conclusion on the second part of the first plea

106. The Appellant argues that the AMA study with the specifications prescribed in the Contested Decision is not feasible and supports that argument with admissible, credible, and convincing evidence, namely the new feasibility study. The Agency, supported by BAuA, has not been able to rebut that argument. The Appellant has therefore established, for the purposes of the present case, that the AMA study with the specifications prescribed in the Contested Decision is not appropriate to achieve its objective.

107. The second part of the first plea must consequently be upheld.

108. This conclusion does not put in question the general feasibility of AMA studies using acetone-treated feed and is based solely on the distribution and discharge of the parties' respective burden of proof in the context of the present appeal proceedings.

5.3. Result

109. The available information shows that DPHP poses a potential risk to the environment due to its potential endocrine disrupting properties and potential environmental exposure. That potential risk needs to be clarified, and doing so has a realistic possibility of leading to improved risk management measures.

110. However, the Appellant has established, for the purposes of the present appeal proceedings, that the AMA study with the specifications prescribed in the Contested Decision is not appropriate to achieve its objective.

111. The Contested Decision must consequently be annulled, and the case remitted to the competent body of the Agency for further action in accordance with Article 93(3). There is no need to examine the remainder of the Appellant's pleas or arguments.

6. Refund of the appeal fee

112. Under Article 10(4) of the Fee Regulation[26] the appeal fee must be refunded if the appeal is decided in favour of an appellant. As the appeal is upheld, the appeal fee is refunded.

[26] 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. **Annuls the Contested Decision.**
2. **Remits the case to the competent body of the Agency for further action.**
3. **Orders the refund of the appeal fee.**

Antoine BUCHET
Chairman of the Board of Appeal

Alen MOČILNIKAR
Registrar of the Board of Appeal