EUROPEAN CHEMICALS AGENCY
BOARD OF APPEAL

DECISION OF THE BOARD OF APPEAL OF THE EUROPEAN CHEMICALS AGENCY

21 October 2020

(Follow-up to dossier evaluation – Article 42(1) of the REACH Regulation – Weight-of-evidence – Error of assessment)

Case number	A-001-2019
Language of the case	English
Appellant	Solvay Fluor GmbH, Germany
Representatives	Ruxandra Cana, Eléonore Mullier and Filippo Mattioli, Steptoe & Johnson LLP, Belgium
Intervener	PETA International Science Consortium Ltd. ('PISC'), United Kingdom
Contested Decision	CCH-D-2114450985-37-01/F of 15 November 2018 adopted by the European Chemicals Agency (the 'Agency') pursuant to Article 42(1) of Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (OJ L 396, 30.12.2006, p. 1; the 'REACH Regulation')

THE BOARD OF APPEAL

composed of Antoine Buchet (Chairman and Rapporteur), Andrew Fasey (Technically Qualified Member) and Ángel M. Moreno (Legally Qualified Member)

Registrar: Alen Močilnikar

gives the following

Decision

Background to the dispute

1. The Appellant is the lead registrant of sulphur hexafluoride (EC No 219-854-2, CAS No 2551-62-4; the 'Substance'). The Appellant submitted its registration for the Substance on 9 August 2010.

2. On 19 November 2013, the Agency sent a draft compliance check decision to the Appellant under Articles 41 and 50(1) of the REACH Regulation (all references to Articles and Annexes hereinafter concern the REACH Regulation unless stated otherwise).

3. In the draft compliance check decision, the Agency noted that the Appellant had sought to adapt the information requirement in Section 8.7.2. of Annex IX for a pre-natal developmental toxicity study ('PNDT study') as follows: '*In accordance with section 1 of REACH Annex XI, waiving of developmental toxicity studies is considered justified as no adverse effects were observed in acute toxicity studies and in the combined repeated dose/reproduction inhalation toxicity study and based on the substance chemical inertness and its rapid excretion*'. The Agency rejected this adaptation in the draft compliance check decision on the ground that the Appellant had inadequately documented the basis of its adaptation and therefore failed to specify which of the general rules laid down in Section 1 of Annex XI the adaptation followed.

4. The Agency also noted that the Appellant had provided a study record for a '*combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test*' (the 'TNO 422 Study'). However, in the draft compliance check decision, the Agency concluded that the TNO 422 Study does not provide the information required by Section 8.7.2. of Annex IX as it does not cover the key parameters of a PNDT study. Consequently, the Appellant was requested to '*submit the following information using the indicated test methods and the [Substance]:*

   […]

   2. [PNDT] study (Annex IX, 8.7.2.; test method: EU.B.31/OECD [TG] 414) in rats or rabbits, inhalation route;

   […]'.

5. On 18 December 2013, the Appellant submitted comments on the draft compliance check decision. The comments included a statement that, in relation to the PNDT study, '*it would be appropriate to adapt the information requirements based on exposure considerations according to Annex XI, section 3 in order to avoid unnecessary animal testing*'.

6. On 19 March 2014, the Appellant updated its registration dossier with an exposure-based adaptation under Section 3.2(a) of Annex XI.

7. On 5 February 2015, the Agency adopted a compliance check decision under Article 41(3) (the 'initial compliance check decision'). In that decision, the Agency requested the Appellant to '*submit the following information using the indicated test methods and the [Substance]:*

   […]

   2. [PNDT] study (Annex IX, 8.7.2.; test method: EU.B.31/OECD [TG] 414) in rats or rabbits, inhalation route'.

8. In the initial compliance check decision, the Agency rejected the proposed adaptation for the PNDT endpoint for the reasons already set out in the draft compliance check decision (see paragraphs 3 and 4 above). In addition, the Agency rejected the exposure-based adaptation according to Section 3.2(a) of Annex XI which the Appellant had included in its dossier after receipt of the draft compliance check decision (see paragraph 6 above).

9. On 9 August 2016, in response to the requirement in the initial compliance check decision to provide information on a PNDT study, the Appellant updated its registration dossier with a weight-of-evidence adaptation under Section 1.2. of Annex XI. In its weight-of-evidence adaptation, the Appellant referred to the following:

   (a) The TNO 422 Study;
   (b) A study of effects on fertility and embryo-fetal toxicity in CD rats by intravenous (bolus) administration of SonoVue™ according to ICH (International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use) Test Guidelines (Bracco, 1997) (the 'ICH Rat Study');
   (c) A study of effects on the embryo-fetal toxicity in the rabbit by intravenous (bolus) administration of SonoVue™ according to ICH Test Guidelines (Bracco, 1997) – ('the ICH Rabbit Study') (the 'ICH Rat Study' and the 'ICH Rabbit Study' are referred to below as 'the ICH Studies');
   (d) A sub-chronic 90-Day inhalation toxicity study in rats according to OECD TG 413 (Van Acker and Muijser, 2016) (the '2016 90-day study');
   (e) A study of blood kinetics and elimination of total SF6 after single intravenous administration to the rabbit (Pélaprat, 1994) with SonoVue™ (the 'Pélaprat 1994 study') and a toxikokinetic study (Pashin, 1987) after inhalation administration of SF6 in rats (the 'Pashin 1987 study');
   (f) A study of human pharmacokinetics and safety evaluation of SonoVue™ (the 'Morel *et al*. (2000) study'); and
   (g) Information on various properties of the Substance, such as chemical and biological reactivity.

10. According to the Appellant's weight-of-evidence adaptation:

    '[a] significant amount of guideline study data is available for [the Substance] allowing the assessment of potential developmental toxicity [...] [t]he absence of any effects on prenatal development in the available studies, lack of chemical reactivity/biotransformation and the rapid elimination of unmetabolised sulphur hexafluoride, and the absence of any adverse effect in sub-chronic limit study, allows to conclude that [the Substance] does not raise a concern for developmental toxicity.'

11. Under Articles 42(1), the Agency examined the information submitted by the Appellant in consequence of the initial compliance check decision. On 23 November 2017, the Agency notified a draft decision to the Appellant under Article 50(1) (the 'draft follow-up decision'). In the draft follow-up decision, the Agency stated that '*this decision is necessary after the follow-up evaluation according to Article 42(1) […], because in your updated registration you have provided new experimental information, which was not available to you or [the Agency] at the time when your registration was examined for the original decision*'.

12. In the draft follow-up decision, the Agency rejected the Appellant's weight-of-evidence adaptation referred to in paragraphs 9 and 10 above and concluded that the Appellant's registration dossier '*still does not comply*' with Section 8.7.2. of Annex IX.

13. On 11 January 2018, the Appellant submitted its comments on the draft decision. The Appellant argued that:

    (i) The complete weight-of-evidence adaptation, not only the individual results of single studies, as well as the quality and reliability of the available data, should be taken into account by the Agency;
    (ii) The Substance has no tendency to bio-accumulate or metabolise and is considered to be biologically inert;
    (iii) The Substance is highly regulated and therefore continuous worker exposure is unrealistic; and
    (iv) When inhaled, only a very small portion of the Substance is absorbed and systemically available.

14. On 15 November 2018, the Agency adopted the Contested Decision. In the Contested Decision, the Agency rejected the Appellant's weight-of-evidence adaptation. The Agency concluded that the Appellant's registration dossier '*still does not comply*' with Section 8.7.2. of Annex IX.

15. According to the Contested Decision, the Appellant is '*…still required to provide a [PNDT] study according to test guideline EU B.31/OECD [TG] 414'* and the '*respective Member State competent authority (MSCA) and national enforcement authority (NEA) will be informed of [the Agency's] decision […]. They may consider enforcement actions to secure the implementation of [the initial compliance check decision]*'.

Procedure before the Board of Appeal

16. On 12 February 2019, the Appellant lodged this appeal.

17. On 15 April 2019, the Agency lodged its Defence.

18. On 17 June 2019, the Appellant lodged its observations on the Defence.

19. On 5 September 2019, the Agency lodged its observations on the Appellant's observations on the Defence.

20. On 24 September 2019, PISC and ECEAE were both granted leave to intervene in support of the Appellant.

21. On 26 November 2019, ECEAE informed the Board of Appeal that it no longer wished to intervene in the case.

22. On 28 November 2019, PISC lodged its statement in intervention.

23. On 18 December 2019 and 15 January 2020, the Appellant and the Agency lodged their respective observations on the statement in intervention.

24. On 8 May 2020, Ángel M. Moreno, alternate member of the Board of Appeal, was designated to replace Sari Haukka in this case, in accordance with the first subparagraph of Article 3(2) of Commission Regulation (EC) No 771/2008 laying down the rules of organisation and procedure of the Board of Appeal of the European Chemicals Agency (OJ L 206, 2.8.2008, p. 5; the 'Rules of Procedure').

25. On 16 June 2020, a hearing took place at the Appellant's request. The hearing was held by video-conference in accordance with Article 13(7) of the Rules of Procedure. At the hearing, the Parties and the Intervener made oral submissions and answered questions from the Board of Appeal.

Form of order sought

26. The Appellant requests the Board of Appeal to annul the Contested Decision, order the Agency to refund the appeal fee, and take such other or further measures as justice may require.

27. The Intervener supports the request to annul the Contested Decision.

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

Reasons

29. The Appellant raises the following pleas in law:

    1. The Agency breached Articles 41 and 42(1) and exceeded its competence because:
        1.1. Article 42(1) is not the correct legal basis for the Contested Decision, and
        1.2. The Contested Decision does not contain a request for information with an adequate time limit to provide that information;
    2. The Agency breached the principles of legal certainty and the protection of legitimate expectations;
    3. The Agency breached the Appellant's right to be heard and its rights of defence;

4. The Agency committed an error of assessment, failed to take all relevant information into account and breached Annex XI;
5. The Agency breached Article 25; and
6. The Agency breached the principle of proportionality.

1. The Agency breached Articles 41 and 42(1) and exceeded its competence

Relevant legislation

30. Article 41 ('*Compliance check of registrations*') provides:

'1. The Agency may examine any registration in order to verify any of the following:

(a) that the information in the technical dossier(s) submitted pursuant to Article 10 complies with the requirements of Articles 10, 12 and 13 and with Annexes III and VI to X;

(b) that the adaptations of the standard information requirements and the related justifications submitted in the technical dossier(s) comply with the rules governing such adaptations set out in Annexes VII to X and with the general rules set out in Annex XI;

(c) that any required chemical safety assessment and chemical safety report comply with the requirements of Annex I and that the proposed risk management measures are adequate;

(d) that any explanation(s) submitted in accordance with Article 11(3) or Article 19(2) have an objective basis.

2. The list of dossiers being checked for compliance by the Agency shall be made available to Member States competent authorities.

3. On the basis of an examination made pursuant to paragraph 1, the Agency may, within 12 months of the start of the compliance check, prepare a draft decision requiring the registrant(s) to submit any information needed to bring the registration(s) into compliance with the relevant information requirements and specifying adequate time limits for the submission of further information. Such a decision shall be taken in accordance with the procedure laid down in Articles 50 and 51.

4. The registrant shall submit the information required to the Agency by the deadline set.

5. To ensure that registration dossiers comply with this Regulation, the Agency shall select a percentage of those dossiers, no lower than 5 % of the total received by the Agency for each tonnage band, for compliance checking. The Agency shall give priority, but not exclusively, to dossiers meeting at least one of the following criteria:

(a) the dossier contains information in Article 10(a)(iv), (vi) and/or (vii) submitted separately as per Article 11(3); or

(b) the dossier is for a substance manufactured or imported in quantities of one tonne or more per year and does not meet the requirements of Annex VII applying under either Article 12(1)(a) or (b), as the case may be; or

(c) the dossier is for a substance listed in the Community rolling action plan referred to in Article 44(2).

6. Any third party may electronically submit information to the Agency relating to substances that appear on the list referred to in Article 28(4). The Agency shall consider this information together with the information submitted according to Article 124 when checking and selecting dossiers.

7. The Commission may, after consulting with the Agency, take a decision to vary the percentage of dossiers selected and amend or include further criteria in paragraph 5 in accordance with the procedure referred to in Article 133(4).'

31. Article 42 (‘*Check of information submitted and follow-up to dossier evaluation*’) provides:

‘*1. The Agency shall examine any information submitted in consequence of a decision taken under Articles 40 or 41 and draft any appropriate decisions in accordance with these Articles, if necessary*.

2. Once the dossier evaluation is completed, the Agency shall notify the Commission and the competent authorities of the Member States of the information obtained and any conclusions made. The competent authorities shall use the information obtained from this evaluation for the purposes of Article 45(5), Article 59(3) and Article 69(4). The Agency shall use the information obtained from this evaluation for the purposes of Article 44.’

1.1. Article 42(1) is not the correct legal basis for the Contested Decision

Arguments of the Parties and Intervener

32. The Appellant, supported by the Intervener, argues that Article 42(1) is not a self-standing legal basis for a decision taken following the Agency’s examination of information submitted by a registrant in consequence of a decision taken under Article 41. When applying Article 42(1) in the follow-up to a compliance check decision, the Agency may only adopt a decision under Article 41. By failing to adopt the Contested Decision in accordance with the requirements of Article 41, the Agency breached Articles 41 and 42 and exceeded its competence.

33. The Agency disputes the Appellant’s and the Intervener’s arguments.

Findings of the Board of Appeal

34. The title of the Contested Decision is the following: ‘*Decision taken under Article 42(1) […]*’. According to Appendix 2 to the Contested Decision (‘*Procedural history*’), that Decision was *‘necessary after the follow-up evaluation according to Article 42(1) […]’* and *‘the decision making followed the procedure of Articles 50 and 51 […]’*. It is clear therefore that the legal basis used by the Agency for adopting the Contested Decision was Article 42(1).

35. An agency of the European Union has conferred powers only and the measures it adopts must refer to the legal basis enabling it to act in the field in question (see, by analogy, judgment of 13 May 2014, *McBride and Others* v *Commission*, joined cases T-458/10 to T-467/10 and T-471/10, EU:T:2014:249, paragraph 25).

36. The legal basis of a measure is therefore the provision which confers on the agency of the European Union concerned the competence to adopt that measure. That provision should be distinguished from the provisions that set out the purpose, conditions and substantive aspects of the measure to be taken. In this respect, the provisions that establish the procedure to be followed to adopt a measure do not constitute the legal basis for that measure.

37. In the present case, the measure taken by the Agency consists of an examination of the information submitted by a registrant in consequence of a decision taken under Article 41 and the drafting of an appropriate decision. The competence to adopt such a measure is conferred on the Agency by Article 42(1). Contrary to the Appellant’s arguments, Article 41 does not confer that competence on the Agency.

38. This conclusion is supported by the case-law of the Court of Justice of the European Union. In its judgment of 8 May 2018 in case T-283/15, *Esso Raffinage* v *ECHA* (EU:T:2018:263, paragraph 62), the General Court held that the evaluation of the information submitted by a registrant in consequence of an initial compliance check decision requiring that registrant to bring its registration dossier into compliance *‘is to be made pursuant to Article 42(1) […], which refers to Article 41 […] as regards the decision-making procedure*’.

39. Therefore, Article 42(1) was the correct legal basis for the Contested Decision. Consequently, the Appellant’s plea must be rejected.

1.2. The Contested Decision does not contain a request for information with an adequate time limit to provide that information

Arguments of the Parties and the Intervener

40. The Appellant, supported by the Intervener, argues that, under Article 42(1), the Agency is required to examine the information submitted by the Appellant in consequence of the initial compliance check decision. Following that evaluation, if necessary, the Agency is required to draft a new decision in accordance with Article 41.

41. The Appellant argues that, contrary to the requirements of Article 41(3), the Contested Decision does not require the Appellant to submit information to bring its registration dossier into compliance within an adequate time limit.

42. The Agency disputes the Appellant's and the Intervener's arguments.

Findings of the Board of Appeal

43. The Appellant argues that the Contested Decision must be annulled because it does not require the Appellant '*to submit any information needed to bring the registration(s) into compliance with the relevant information requirements'* and does not specify *'adequate time limits for the submission of further information'* within the meaning of Article 41(3).

44. Article 42(1), which is the correct legal basis for the Contested Decision (see Section 1.1. above), provides that follow-up compliance check decisions taken under that provision must be drafted in accordance with Article 41. This reference to Article 41 is made in generic terms and does not specify which parts of Article 41 are relevant to follow-up compliance check decisions under Article 42(1), such as the Contested Decision.

45. However, for the reasons set out below, only some of the provisions of Article 41 are relevant to follow-up compliance check decisions under Article 42(1).

Article 41(1)

46. Article 41(1) sets out the elements of a registration dossier that the Agency may verify under the procedure for the adoption of an initial compliance check decision. In order to adopt a follow-up compliance check decision under Article 42(1), the Agency verifies whether the information submitted by the registrant complies with the information requirement(s) identified in the initial compliance check decision. The elements of this verification are not included in the list set out in Article 41(1).

47. Article 41(1) is therefore not relevant to a follow-up compliance check decision adopted under Article 42(1).

Article 41(2)

48. Article 41(2) requires the Agency to make available to the Member States competent authorities a list of registration dossiers being checked for compliance by the Agency. As this action is linked to initial compliance checks, it is not necessary for the Agency to take any further action in this respect when performing a follow-up compliance check.

49. Article 41(2) is therefore not relevant to a follow-up compliance check decision adopted under Article 42(1).

Article 41(3)

50. Article 41(3) consists of two sentences.

First sentence

51. The first sentence of Article 41(3) can be broken down into two parts:

- '*on the basis of an examination made pursuant to paragraph 1, the Agency may, within 12 months of the start of the compliance check',* and

- *'prepare a draft decision requiring the registrant(s) to submit any information needed to bring the registration(s) into compliance with the relevant information requirements and specifying adequate time limits for the submission of further information'.*

52. With regards to the first part of the first sentence, as shown in paragraphs 46 and 47 above, Article 41(1) is not relevant to follow-up compliance check decisions taken under Article 42(1). In addition, it would not be possible for the Agency to prepare a draft follow-up compliance check decision under Article 42(1) '*within 12 months of the start of the compliance check*' as this time limit begins with the start of the procedure for the adoption of an initial compliance check decision.

53. Therefore, the first part of the first sentence of Article 41(3) is not relevant to the adoption of a follow-up compliance check decision under Article 42(1).

54. The second part of the first sentence of Article 41(3) contains (i) a requirement to specify the information needed to bring the registration into compliance, and (ii) a requirement to specify adequate time limits.

55. In relation to the first requirement, an initial compliance check decision identifies one or more data-gaps in the registration dossier concerned, that is to say the information missing from the registration dossier in question, and requires the registrant to submit information to fill those data-gaps. When the Agency prepares a follow-up compliance check decision under Article 42(1), it does not have to identify data-gaps because the relevant data-gaps have already been identified. The Agency therefore does not have to identify again '*further information*' within the meaning of Article 41(3) in a follow-up compliance check decision under Article 42(1).

56. The data-gaps identified in the initial compliance check decision remain the same, as does the information required to fill those data-gaps. When preparing a follow-up compliance check decision under Article 42(1), the Agency verifies whether the data-gaps identified in the initial compliance check decision have been filled by the information submitted by the registrant.

57. Therefore, the requirement to specify the *'information needed to bring the registration(s) into compliance'* in the second part of the first sentence of Article 41(3) is not relevant to the adoption of a follow-up compliance check decision under Article 42(1).

58. This conclusion is supported by the judgment in *Esso Raffinage* v *ECHA* (cited in paragraph 38 above) in which the General Court held that *'the check carried out by ECHA following a first decision requiring the registrant to bring the dossier into compliance, is merely the continuation of the same, single procedure'* (paragraph 62 of the judgment).

59. In the present case, the initial compliance check decision identified a data-gap in the Appellant's registration dossier regarding the requirement to provide information on a PNDT study under Section 8.7.2. of Annex IX. The Contested Decision, which is a follow-up compliance check decision under Article 42(1), does not identify a new data-gap but concludes that the data-gap identified in the initial compliance check decision has not been filled because the Appellant's weight-of-evidence adaptation did not meet the requirements of the REACH Regulation. Consequently, the obligation imposed in the initial compliance check decision remains unfulfilled and the registrant is still obliged to submit the information on a PNDT study required by that decision.

60. In relation to the second requirement set out in paragraph 54 above, the specification of adequate time limits is linked to the Agency's identification in the initial compliance check decision of a data-gap in the registration dossier. A time limit is specified for the registrant to fill the data-gap. Within the time limit specified in the initial compliance check decision, the registrant is required to submit *'further information'* to fill the data-gap identified.

61. At the stage of the adoption of a follow-up compliance check decision under Article 42(1), the Agency does not have to require the registrant to submit *'further information'* to that which was already identified as missing in the initial compliance check decision. The adoption of a follow-up compliance check decision under Article 42(1) is the result of a check carried out by the Agency that *'is merely the continuation of the same, single*

procedure' (*Esso Raffinage* v *ECHA*, cited in paragraph 38 above, paragraph 62 of the judgment) concerning the same data-gap and the same information requirement.

62. Therefore, the requirement to specify adequate time limits in the second part of the first sentence of Article 41(3) is not relevant to the adoption of a follow-up compliance check decision under Article 42(1).

63. In view of paragraphs 51 to 62 above, the first sentence of Article 41(3) is not relevant to a follow-up compliance check decision adopted under Article 42(1).

Second sentence

64. The second sentence of Article 41(3) refers to the decision-making procedure laid down in Articles 50 and 51. As confirmed by the General Court, that procedure applies equally to the adoption of an initial compliance check decision and to the adoption of a follow-up compliance check decision under Article 42(1) (see *Esso Raffinage* v *ECHA,* cited in paragraph 38 above, paragraph 62 of the judgment). It is undisputed that the Agency correctly followed the decision-making procedure in Articles 50 and 51 in the present case.

Article 41(4)

65. Since in a follow-up compliance check decision under Article 42(1) the Agency does not need to specify an additional time limit to submit the information already identified as missing in an initial compliance check decision, it is clear that Article 41(4) also is not relevant to the adoption of a follow-up compliance check decision under Article 42(1).

Article 41(5) and (7)

66. Article 41(5) and (7) concern the percentage of registration dossiers that must be checked by the Agency. Those provisions are therefore not relevant to a decision-making procedure for the adoption of any compliance check decision, including a follow-up compliance check decision under Article 42(1).

Article 41(6)

67. Article 41(6) requires the Agency to take into account certain information provided by third parties and the competent national authorities when selecting and examining registration dossiers during a compliance check procedure. To the extent that this provision applies to the examination of the information submitted by a registrant, it is relevant to any decision-making procedure for the adoption of any compliance check decision, including a follow-up compliance check decision under Article 42(1).

Conclusion on the relevance of the provisions of Article 41 to the follow-up procedure under Article 42(1)

68. As demonstrated in paragraphs 45 to 67 above, of the provisions of Article 41, only the second sentence of Article 41(3) and Article 41(6) are relevant to the follow-up compliance check procedure under Article 42(1).

69. Consequently, contrary to the Appellant's arguments, in adopting the follow-up compliance check decision under Article 42(1) in the present case, the Agency was not required to '*prepare a draft decision requiring the registrant(s) to submit any information needed to bring the registration(s) into compliance with the relevant information requirements and specifying adequate time limits for the submission of further information*' within the meaning of Article 41(3).

70. This conclusion is consistent with the main objective of the REACH Regulation which is to ensure a high level of protection of human health and the environment (see, to this effect, judgment of 7 July 2009, *S.P.C.M. and Others*, C-558/07, EU:C:2009:430, paragraph 45).

71. To achieve this objective, it is necessary to obtain information on substances as quickly as possible so that that information can be used for the purposes of Articles 44, 45(5), 59(3), and 69(4). With this objective in mind, registrants are obliged to submit a registration dossier containing the information set out in the REACH Regulation within the deadlines set out in that Regulation. If new and relevant information comes to light, there is an obligation to update the dossier in question with that new information without undue delay.

The compliance check procedure is the tool by which the Agency can check whether a registration dossier is compliant and, if it is not, to require the submission of the information needed to bring it into compliance.

72. Prior to a compliance check, a registrant may consider that it has satisfied the information requirements for registration purposes, for example through an adaptation, (see, to this effect, Case A-001-2018, *BrüggemannChemical, L. Brüggemann*, Decision of the Board of Appeal of 9 April 2019, paragraph 77). However, once the Agency has adopted an initial compliance check decision, the registrant is aware that its registration dossier is non-compliant with regard to the information requirements in question.

73. In an initial compliance check decision, the Agency identifies one or more data-gaps and the registrant is given the opportunity to bring its dossier into compliance within a specified time limit. If a new time limit were granted to a registrant in a follow-up compliance check decision under Article 42(1), the registrant would have a further opportunity to complete its dossier in a situation where no new data-gap or no new information requirement has been identified. This would frustrate the achievement of the objective of obtaining relevant information on a substance as quickly as possible.

74. In addition, if a registrant were granted an additional time limit in the follow-up compliance check procedure under Article 42(1), this could have an adverse effect on enforcement by the Member States. For example, the Appellant argued during these proceedings that, if the Agency were to adopt a follow-up compliance check decision under Article 42(1) with a time limit to provide the missing information, it would not be possible for the competent authorities of the Member States to take enforcement action before the expiry of that time limit. If this is the case, a new time limit specified in a follow-up compliance check decision under Article 42(1) could delay the adoption of enforcement measures by the national authorities of the Member States pursuant to Article 126.

75. In view of the above, the Appellant's plea that the Agency breached Articles 41 and 42(1) and exceeded its competence because the Contested Decision does not contain a request for information with an adequate time limit to provide that information must be rejected.

2. Breach of the principles of legal certainty and the protection of legitimate expectations

Arguments of the Parties and Intervener

76. The Appellant, supported by the Intervener, argues that the Agency breached the principle of legal certainty and the principle of the protection of legitimate expectations.

77. The Appellant argues that it is in a position of unacceptable legal uncertainty regarding its rights and obligations because the Contested Decision does not require the Appellant to submit a PNDT study within a time limit. The Appellant argues that it does not know whether it can now perform the PNDT study, which involves testing on vertebrate animals, and if so, whether the Agency will review the Appellant's dossier as updated with information on that study. The Appellant argues that, if the Agency does review its dossier update, it is uncertain when this will take place and what procedure will be followed. The Appellant argues that it is also unclear whether it can update its dossier with an improved adaptation instead of a PNDT study.

78. The Appellant argues that the wording in the Contested Decision, that the Appellant's dossier '*still does not comply*', also creates uncertainty as the initial compliance check decision did not establish that the Appellant's dossier was non-compliant. The Appellant claims that it is unclear whether it needs to comply with the initial compliance check decision or with the Contested Decision. The Appellant argues that the statement in the Contested Decision that the Agency will not inform the Member States and the competent authorities of the Member States about the completion of the dossier evaluation under Article 42(2) (the 'Article 42(2) notification') until all information requested in that decision has been received creates uncertainty. The Appellant argues that it is not clear whether the Article 42(2) notification remains on hold until such point as the Appellant provides information on an OECD TG 414 study.

79. The Appellant argues that it had a legitimate expectation that the Agency would specify a new time limit for the Appellant to provide the information on the PNDT study if the adaptation in its registration dossier was rejected. Its registration dossier would therefore not be held to be non-compliant until the new time limit had passed and its dossier reassessed. The Appellant argues that this legitimate expectation was based on the Agency's guidance, the Board of Appeal's decision in Case A-019-2013, *Solutia Europe*, and the General Court's judgment in case T-283/15, *Esso Raffinage* v *ECHA*.

80. The Agency disputes the Appellant's and the Intervener's arguments.

Findings of the Board of Appeal

2.1. Legal certainty

81. In the context of the present case, the principle of legal certainty requires that every measure of the European Union which produces legal effects should be clear and precise so that the persons concerned are able to know without ambiguity what their rights and obligations are and to take steps accordingly (judgment of 1 October 1998, *Langnese-Iglo* v *Commission*, C-279/95 P, EU:C:1998:447, paragraph 78, and judgment of 30 November 2009, *France and France Télécom* v *Commission*, T-427/04 and T-17/05, EU:T:2009:474, paragraph 300; see also Case A-008-2015, *Evonik Degussa*, Decision of the Board of Appeal of 12 October 2016, paragraph 36).

82. It is clear from the Contested Decision what information the Appellant is required to provide to bring its dossier into compliance with the REACH Regulation. For example, Appendix 1 to the Contested Decision states that '*you are still required to provide a [PNDT] study according to test guideline EU B.31 /OECD [TG] 414*'. The Appellant's argument that it is uncertain whether it is required to provide information on a PNDT study must therefore be rejected.

83. The possibility for the Appellant to propose an adaptation stems directly from the REACH Regulation, in particular Article 13 and Annex XI. The possibility to propose such an adaptation, instead of providing information on one of the studies set out in the Annexes to the REACH Regulation, is always available to a registrant, irrespective of whether this possibility is specifically mentioned in an Agency decision. The Appellant's arguments that it is unclear whether it can propose a separate adaptation or further strengthen its weight-of-evidence adaptation must therefore be rejected.

84. The Appellant argues that the wording in the Contested Decision, that the Appellant's dossier '*still does not comply*', creates uncertainty. In this respect, the Contested Decision states that '*your registration still does not comply with the following information requirement: [PNDT] study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in rats or rabbits, inhalation route*' and '*you are still required to provide a [PNDT] study according to test guideline EU B.31/OECD [TG] 414*'. There is therefore no uncertainty as regards the fact that the Appellant's registration dossier is non-compliant and that the Appellant is required to comply with the requirements of Section 8.7.2. of Annex IX. The Appellant's argument in this respect must therefore be rejected.

85. It is clear from both the Contested Decision and the initial compliance check decision that the Agency evaluated the Appellant's registration dossier and found it to be non-compliant with regards to Section 8.7.2. of Annex IX. The national authorities of the Member States will have to decide, consequent to the Contested Decision, whether to take enforcement action pursuant to Article 126 (see *Esso Raffinage* v *ECHA*, cited in paragraph 38 above, paragraphs 54 to 61 of the judgment).

86. Any enforcement actions taken by the national authorities of the Member States must be based on the Agency's findings set out in the Contested Decision, *'unless there was a particular reason based on new elements, namely elements which had not been taken into consideration by ECHA during the follow-up provided for in Article 42(1)'* (see *Esso Raffinage* v *ECHA*, cited in paragraph 38 above, paragraph 70 of the judgment). The Appellant's argument that it is uncertain what will happen next with regard to its

registration dossier for the Substance, in particular regarding the PNDT endpoint, must therefore be rejected.

87. Contrary to the Appellant's arguments, the statement in the Contested Decision that '*the Article 42(2) notification for [the initial compliance check decision] is on hold until all information requested in [that decision] has been received*' does not create legal uncertainty. It is clear from that statement, as well as from the wording of Article 42(2) itself, that the compliance check process for the endpoint in question (Section 8.7.2. of Annex IX) has not been completed until the Appellant provides information on a PNDT study or, alternatively, an adaptation which is subsequently approved by the Agency.

88. In view of paragraphs 81 to 87 above, the Appellant's plea that the Agency breached the principle of legal certainty must be rejected.

2.2. Legitimate expectations

89. The right to rely on the principle of the protection of legitimate expectations presupposes that precise, unconditional and consistent assurances originating from authorised, reliable sources have been given to the person concerned by the competent authorities of the European Union. In accordance with the Court of Justice's settled case-law, that right applies to any individual in a situation in which a European Union institution, body or agency, by giving that person precise assurances, has led that individual to entertain well-founded expectations. Precise, unconditional and consistent information, in whatever form it is given, constitutes such an assurance (see judgment of 13 June 2013, *HGA and Others* v *Commission*, joined cases C-630/11 P to C-633/11 P, EU:C:2013:387, paragraph 132; see also Case A-005-2016, *Cheminova A/S*, Decision of the Board of Appeal of 30 January 2018, paragraph 179).

90. The Appellant argues that it legitimately expected that the Agency, in examining the information submitted by the Appellant following the initial compliance check decision, would apply Article 41. The Appellant would then, if necessary, be given the opportunity to submit any information still required within a specified time limit and would not be held to be non-compliant.

91. The Appellant's arguments must be rejected for the following reasons.

92. First, the initial compliance check decision makes it clear that '*failure to comply with the request(s) in this decision, or to fulfil otherwise the information requirement(s) with a valid and documented adaptation, will result in a notification to the Enforcement Authorities of the Member States.*' The Appellant was therefore explicitly made aware that enforcement action might follow if the Appellant failed to provide the information necessary to comply with the initial compliance check decision.

93. This conclusion is supported by the case-law of the General Court, according to which '*as is clear from Article 41(4) […], if a decision is adopted, under Article 42(1) […], finding that the registration dossier is non-compliant, that lack of compliance relates, at the least, to the end of the time limit granted under the first decision requesting the dossier be brought into compliance, adopted on the basis of Article 41(3) […]. Consequently, […], on such a hypothesis, it would be for the Member State concerned to exercise the power reserved to it under Article 126 […] for the period during which the registration dossier was not compliant*' (*Esso Raffinage* v *ECHA*, cited in paragraph 38 above, paragraph 114 of the judgment).

94. Therefore, the Appellant could not legitimately expect that its registration dossier would not be held to be non-compliant until a new time limit had passed and its dossier reassessed.

95. Second, it cannot be inferred from the Agency documents referred to by the Appellant in its appeal that the Agency would specify an additional time limit to provide the missing information in adopting a follow-up compliance check decision under Article 42(1).

96. The Appellant refers to a section of the Agency's website on requests for further information which reads as follows:

'*Follow-up*

[…]

In compliance check and testing proposal cases, [the Agency] will examine information provided by the registrant in the dossier update and consider whether the information complies with the REACH requirements and whether it is sufficient for the purposes of classification and labelling and risk assessment. If the information is deemed non-compliant or the new information causes further standard information needs, [the Agency] may prepare another draft decision to request for appropriate information.'

97. That section of the Agency's website states only that the Agency '*may prepare another draft decision to request for appropriate information*'. It does not specify the procedure to be followed, and in particular does not indicate that an additional time limit to submit the information will be granted to the registrant.

98. The Appellant also refers to the following sections of a document on '*Dossier evaluation*' available on the Agency's website (PRO-0017.08, 4 September 2018):

'*4. Follow-up*

The decision specified by when the registrant must deliver the required information in an updated registration dossier. Once this deadline has passed, [the Agency] checks whether the information requested has been provided or not. This can lead to different actions:

- *Information has not been submitted or is inadequate: [the Agency] informs the relevant Member State and the registrant about non-compliance;*
- *Information complies with the request in the decision but the respective information requirement is nevertheless not fulfilled: [the Agency] drafts a new decision according to Stage 2 […]*.'

99. According to '*Stage 2*', referred to in the second indent in the previous paragraph, following the evaluation of a dossier the Agency may prepare '*a draft decision requesting to provide information*'.

100. The sections of PRO-0017.08 referred to by the Appellant suggest that a new decision may be drafted following the submission of information in response to an initial compliance check decision. However, they do not give precise and unconditional assurances that an additional time limit will be specified to provide the information missing from the registration dossier.

101. The second indent of Section 4 of PRO-0017.08 cited in paragraph 98 above refers to a situation where the registrant '*complies with the request*'. In the present case, the Agency found in the Contested Decision that the Appellant had not complied with the request to provide information on a PNDT study. That provision of PRO-0017.08 does not therefore apply to the circumstances of the present case.

102. The first indent of Section 4 of PRO-0017.08 cited in paragraph 98 above refers to a situation where, as in the present case, the information provided was considered by the Agency to be *'inadequate'*, that is to say that the registrant's dossier remains non-compliant. That provision states that the '*relevant Member State*' will be informed about the non-compliance but does not provide further information on the procedure to be followed.

103. The Appellant cannot, therefore, legitimately expect that an additional time limit would be specified in a follow-up compliance check decision under Article 42(1), based on PRO-0017.08 and the sections of the Agency's website referred to in paragraphs 96 and 98 above.

104. Third, the judgment of the General Court in case T-283/15, *Esso Raffinage* v *ECHA* was given on 8 May 2018. This was after the Appellant submitted information in consequence of the initial compliance check decision (9 August 2016) and after the Appellant submitted its comments on the draft follow-up compliance check decision (11 January 2018). It is therefore not possible for that judgment to have created legitimate expectations for the Appellant at a time where the findings of that judgment were unknown.

105. In any event, neither the General Court in its judgement in case T-283/15, *Esso Raffinage* v *ECHA,* nor the Board of Appeal in its decision in Case A-019-2013, *Solutia Europe,* state, or imply, that the Agency must specify an additional time limit for the Appellant to provide the missing information in a follow-up compliance check decision under Article 42(1).

106. In addition, there are clear factual and procedural differences between the General Court and the Board of Appeal cases referred to in the previous paragraph on the one hand and the present appeal case on the other. The questions at stake are not identical. In particular, the General Court and the Board of Appeal were not called upon to decide whether a follow-up compliance check decision adopted under Article 42(1) should include an additional time limit to provide information. In the cases before them, the General Court and the Board of Appeal were rather required to decide whether the Agency should have followed the decision-making process set out in Articles 50 and 51 in adopting a follow-up compliance check decision under Article 42(1).

107. Consequently, neither the judgment of the General Court in case T-283/15, *Esso Raffinage* v *ECHA,* nor the decision of the Board of Appeal in Case A-019-2013, *Solutia Europe*, could support a legitimate expectation that the Agency would specify an additional time limit to provide the missing information in adopting a follow-up compliance check decision under Article 42(1).

108. In view of paragraphs 89 to 107, the Appellant's plea that the Agency breached the principle of the protection of legitimate expectations must be rejected.

3. Breach of the Appellant's right to be heard and its rights of defence

Arguments of the Parties and the Intervener

109. The Appellant argues that, in adopting the Contested Decision, the Agency breached the Appellant's right to be heard and its rights of defence. This is because the Agency inserted substantial new information in the Contested Decision on which the Appellant did not have an opportunity to make its views known.

110. The Appellant argues that it commented on the statement in the draft decision that '*inhalation exposure is not covered because administration via i.v. bolus with immediate rapid elimination is not comparable to inhalation exposure lasting several hours*'. However, in the Contested Decision, this statement was changed to read '*inhalation exposure is not covered because administration in the form of i.v. bolus of stabilized sulphur hexafluoride microspheres is not comparable to inhalation exposure lasting several hours*'. The Appellant argues that it was not given the opportunity to comment on this change, in particular the implications linked to the administration of '*i.v. bolus of stabilized sulphur hexafluoride microspheres*' and the relevance of the microspheric form. The Appellant argues that it should have been given the opportunity to comment on how the form of the bolus – i.e. '*of stabilized sulphur hexafluoride microspheres*' - is relevant to the bioavailability of the Substance.

111. The Agency argues that the changes introduced into the Contested Decision only respond to the Appellant's comments on the draft decision and did not introduce new elements '*except for specifying the Agency's understanding, on the basis of the information provided by the registrant, that the form of the test item should be described as microsphere rather than microbubbles*'. The Agency argues that microspheres are in fact a subcategory of microbubbles. The Agency argues that it had already explained in the draft decision why using microbubbles as a route of administration meant that it had to reject the relevance of the ICH Studies for the weight-of-evidence adaptation.

Findings of the Board of Appeal

112. In adopting the Contested Decision, the Agency followed the procedure laid down in Articles 50 and 51. In these circumstances, a registrant is presumed to have been given all the necessary opportunities to present its position on the decision with which it will eventually be required to comply (see, to that effect and by analogy, judgment of 6 July 1993, *CT Control (Rotterdam) and JCT Benelux* v *Commission*, joined cases C-121/91 and C-122/91,

EU:C:1993:285, paragraph 49, judgment of 9 January 2003, *Italy* v *Commission*, C-177/00, EU:C:2003:6, paragraphs 23 to 25, and judgment of 26 September 2012, *Italy* v *Commission*, T-84/09, EU:T:2012:471, paragraphs 24 to 30).

113. In addition, Article 50(1) does not oblige the Agency to request comments from the concerned registrants on all amended drafts following the first draft of a compliance check decision. The words '*any draft decision*' in Article 50(1) refer to the draft of a decision concerning the examination of testing proposals, the compliance check of registrations and requests for further information during the course of substance evaluation. There is nothing in Article 50(1) to suggest that the Agency is required, under those procedural provisions, to invite registrants to comment on subsequent revised versions of an initial draft decision (see, to that effect, Case A-004-2015, *Polynt*, Decision of the Board of Appeal of 19 October 2016, paragraph 59).

114. However, in certain circumstances, the addressees of an Agency decision must be given the opportunity to comment beyond the opportunities foreseen in the REACH Regulation. For example, if relevant information comes to light during the decision-making process, the Agency may, depending for example on the relevance and importance of the new information, be required to re-start, or repeat certain steps of, the decision-making process laid down in Articles 50 and 51. This might be necessary in some cases to ensure that all the relevant actors are given the opportunity to comment on that information (see, to that effect, Case A-001-2014, *CINIC Chemicals Europe*, Decision of the Board of Appeal of 10 June 2015, paragraph 90).

115. In the draft of the follow-up compliance check decision on which the Appellant commented the Agency stated:

'*Regarding the two ICH studies, ECHA considers that the ICH test guideline is in some ways comparable to OECD 414 although gravid uterus weight and placental weight are not addressed in the ICH guideline. However, the designs of the provided studies according to the ICH guidelines have the following additional deficiencies: […] (b) inhalation exposure is not covered because administration via i.v. bolus with immediate rapid elimination is not comparable to inhalation exposure lasting several hours, and […]*' (emphasis added).

116. In the Contested Decision, the Agency states:

'*Regarding the two ICH studies, ECHA considers that the ICH test guideline is in some ways comparable to OECD 414 although gravid uterus weight and placental weight are not addressed in the ICH guideline. However, the designs of the provided studies according to the ICH guidelines have the following two major additional deficiencies: […] (b) inhalation exposure is not covered because administration in the form of i.v. bolus of stabilized sulphur hexafluoride microspheres is not comparable to inhalation exposure lasting several hours*' (emphasis added).

117. The change of wording in the Contested Decision was intended by the Agency to clarify that the form of the test item in the ICH studies should be described as '*microspheres*' rather than '*microbubbles*'.

118. For the following reason, the Agency's use of '*microspheres*' instead of '*microbubbles*' to describe the form of the test item in the ICH studies does not materially affect the findings in the Contested Decision.

119. One of the major differences between the intravenous administration applied in the ICH studies and an OECD TG 414 inhalation study would be the duration of exposure.

120. In an OECD TG 414 study in rats, using inhalation administration and applying the principles of OECD Guidance Document No. 39 on inhalation toxicity studies (second edition, 6 July 2018), it is expected that exposure lasts at least six hours per day, for at least 5 days per week.

121. In the ICH studies, the Substance was administered intravenously. The duration of exposure would have been for a few minutes after administration of a single, bolus dose. This duration of exposure would be short in comparison to the duration of the exposure in

an OECD TG 414 inhalation study irrespective of whether the Substance was contained in '*microspheres*' or '*microbubbles*'.

122. In view of the above, whether the administered substance in the ICH studies was enclosed in '*microspheres*' or '*microbubbles'* is not decisive to the findings in the Contested Decision. Therefore, there was no need for the Appellant to be given an opportunity to comment on the implications of administration of '*i.v. bolus of stabilized sulphur hexafluoride microspheres*' and the relevance of the microspheric form.

123. Therefore, the Appellant's plea that the Agency breached its right to be heard and its rights of defence must be rejected.

4. Error of assessment, failure to take all relevant information into account and breach of Annex XI

Relevant legislation

124. Section 1.2. of Annex XI provides:

'*There may be sufficient weight of evidence from several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous property, while the information from each single source alone is regarded insufficient to support this notion.*

[…]

Where sufficient weight of evidence for the presence or absence of a particular dangerous property is available:

- *further testing on vertebrate animals for that property shall be omitted,*
- *further testing not involving vertebrate animals may be omitted.*

In all cases adequate and reliable documentation shall be provided.'

125. Column 1 ('*Standard information required*') of Section 8.7.2. of Annex IX reads:

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

Arguments of the Parties and Intervener

126. The Appellant, supported by the Intervener, argues that the Agency committed an error of assessment, failed to take all relevant information into account and breached Annex XI in rejecting the Appellant's weight-of-evidence adaptation, and therefore concluding that the Appellant's registration dossier '*still does not comply with the following information requirement: [PNDT] study (Annex IX, Section 8.7.2.; test method: EU B.31./OECD TG 414) in rats or rabbits, inhalation route*'.

127. The Appellant argues that the weight-of-evidence adaptation it submitted as a follow-up to the initial compliance check decision meets the requirements of Section 1.2. of Annex XI. The Appellant argues that it relied on a '*solid dataset*' including a significant number of reliable, high quality studies performed on the Substance according to Good Laboratory Practice ('GLP'), OECD and/or the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use ('ICH') Guidelines and standards. The Appellant argues that nothing in the '*dataset*' submitted shows adverse effects which might suggest developmental toxicity related to the Substance. The Appellant argues that this information is sufficient to '*assume/conclude*', within the meaning of Section 1.2. of Annex XI, that the Substance is not a developmental toxicant.

128. The Appellant argues that the Agency committed an error of assessment and breached Annex XI by examining the TNO study and the ICH studies individually rather than together. The Appellant argues that the information submitted by the Appellant, taken together, provides an equivalent level of information to that which would be provided by an OECD TG 414 study. In particular, all of the parameters investigated in an OECD TG

414 study are addressed by the studies included in the weight-of evidence adaptation, when taken together.

129. The Appellant argues that the Agency failed to consider all the information supporting the weight-of-evidence justification. In particular, the Agency failed to take into consideration the 2016 90-day study (see paragraph 9 above), which had been prepared in response to the initial compliance check decision, and the physico-chemical information on the properties of the Substance which shows that the Substance is stable and chemically inert. The Appellant also argues that the Agency failed to take into account its comments on the draft follow-up compliance check decision regarding the relevance of the ICH studies and information on placental weights and placental abnormalities. The Appellant argues that the information it submitted on realistic worker exposure was also not taken into account by the Agency.

130. The Appellant argues that the Agency erred in concluding that the ICH studies are not adequate to support the weight-of-evidence adaptation. In these two studies, one in rats and one in rabbits, no maternal toxicity was observed and there was no evidence of embryotoxicity, teratogenicity or foetotoxicity at any exposure level.

131. The Appellant argues that the Agency erred in concluding that the dose levels in the ICH studies were too low. The Agency also committed an error in concluding that the ICH studies could not be used to assess the developmental toxicity of the Substance because of the route of administration used. In particular, the Agency failed to properly assess and justify why the toxicokinetics and systemic availability of the Substance differ when administered by inhalation or intravenously and why the doses used in the ICH studies cannot be used for hazard and risk assessment.

132. The Agency disputes the Appellant's and Intervener's arguments.

Findings of the Board of Appeal

133. Articles 6 and 7 provide a general obligation for manufacturers or importers of substances on their own, in mixtures or in articles in quantities of one tonne or more per year to register their substances with the Agency.

134. Registrants must submit a registration dossier containing all the information required by the REACH Regulation. In accordance with Article 10(a)(vi) and (vii), this includes information on the intrinsic properties of a substance in accordance with the requirements of Annexes VII to X (the 'testing Annexes').

135. A registrant meets those requirements by submitting information on the relevant study (Column 1 of the relevant section of the testing Annexes). Alternatively, a registrant may submit a specific adaptation (under Column 2 of the relevant section of the testing Annexes, where applicable) or a general adaptation (under Annex XI).

136. In the present case, the Appellant did not submit information on a PNDT study under Column 1 of Section 8.7.2. of Annex IX, as required in the initial compliance check decision. Instead, the Appellant submitted a weight-of-evidence adaptation in accordance with Section 1.2. of Annex XI (see paragraphs 9 and 10 above for an overview of the Appellant's adaptation).

137. In the Contested Decision, the Agency rejected the Appellant's weight-of-evidence adaptation. The Appellant argues that in rejecting the adaptation the Agency committed an error of assessment:

    (i) in concluding that the weight-of-evidence adaptation fails to meet the requirements of Section 1.2. of Annex XI, and
    (ii) by failing to take into consideration the 2016 90-day study and the physico-chemical information on the properties of the Substance.

138. It is therefore necessary to examine whether the arguments put forward by the Appellant are capable of demonstrating that the Agency made an error of assessment in rejecting the weight-of-evidence adaptation contained in the Appellant's registration dossier (see, by analogy, judgment of 20 September 2019, *BASF Grenzach* v *ECHA*, T-125/17,

EU:T:2019:638, paragraph 89). In this respect, it is necessary to examine whether the Agency has examined carefully and impartially all the relevant facts of the individual case, and whether those facts support the conclusions that the Agency drew from them (see, by analogy, judgment of 19 January 2012, *Xeda International and Pace International* v *Commission*, T-71/10, EU:T:2012:18, paragraph 71; see Case A-006-2017, *Climax Molybdenum*, Decision of 11 December 2018, paragraph 38).

(i) Error of assessment in concluding that the weight-of-evidence adaptation failed to meet the requirements of Section 1.2. of Annex XI

139. The Agency rejected the weight-of-evidence adaptation on several grounds. One of those grounds was that the duration of the daily exposure to the Substance in the ICH studies, included as part of the weight-of-evidence adaptation, was too short to adequately assess the pre-natal developmental toxicity of the Substance. According to the Contested Decision, the ICH studies '*are not adequate for hazard and risk assessment in the context of dossier evaluation'.* One of the reasons for this conclusion is that *'administration in the form of i.v. bolus of stabilized sulphur hexafluoride microspheres is not comparable to inhalation exposure lasting several hours*'.

140. The requirements for a general adaptation under Section 1.2. of Annex XI must be read in conjunction with the specific information requirement in the testing Annexes which the adaptation seeks to fulfil (see Case A-011-2018, *Clariant Plastics & Coatings (Deutschland)*, Decision of the Board of Appeal of 4 May 2020, paragraphs 39, 76, and 85). In order to successfully rely on an adaptation under Section 1.2. of Annex XI to fill Section 8.7.2. of Annex IX, a registrant must demonstrate that the available information adequately identifies and characterises the pre-natal developmental toxicity of the substance at issue.

141. In order to adequately identify and characterise the pre-natal developmental toxicity of a substance there must be a sufficiently long duration of exposure to that substance in the studies relied on by the registrant. As stated in the Agency's Guidance on Information Requirements and Chemical Safety Assessment (version 6.0, July 2017, Chapter R.7.6.2.2.2), '*the [PNDT] study provides a focused evaluation of potential effects following prenatal exposure, although only effects that are manifested before birth can be detected. More specifically, this study is designed to provide information on substance-induced effects on growth and survival of the foetuses, and increased incidences in external, skeletal and soft tissue malformations and variations in foetuses.'* The studies used to fill the information requirement in Column 1 of Section 8.7.2. of Annexes IX must therefore provide information on the effects of a substance on the developing organism *in utero*. The *in utero* development of the embryo and foetus is a continuous process. A sufficiently long duration of exposure of pregnant animals to the substance at issue allows an assessment of whether that substance has the potential to damage the developing embryo/foetus, in other words whether the substance can cause skeletal and visceral abnormalities of the foetuses. If the duration of exposure is too short, hazards related to exposure to the substance at issue may remain undetected.

142. The standard information requirement in Column 1 of Section 8.7.2. of Annex IX is for a '*[PNDT] study, one species, most appropriate route of administration, having regard to the likely route of human exposure' (B.31 of the Commission Regulation on test methods as specified in Article 13(3) or OECD [TG] 414)*'. On this basis, it must be assumed that the duration of exposure in the OECD TG 414 study is at the level required to identify and characterise the pre-natal developmental toxicity of a substance.

143. In an OECD TG 414 study, applying the principles of OECD Guidance Document, No. 39, the duration of exposure to the test substance is for at least 6 hours per day, for at least 5 days per week, during the study. In the ICH studies, the duration of exposure, via bolus intravenous administration (see paragraphs 119 to 121 above), was, in comparison, very short. There is a crucial difference in the duration of the internal exposure, which in the ICH Studies lasted only minutes after intravenous administration of the bolus dose, whereas it would persist for at least six hours during and after inhalation administration in an OECD 414 study.

144. The Appellant argues that the short duration of exposure in the ICH studies is irrelevant in assessing whether the Substance is a developmental toxicant because the Substance will be rapidly eliminated from the body. The Appellant argues that a longer exposure through inhalation will not provide more information about developmental toxicity. This argument must be rejected for the following reason.

145. The Appellant submitted a [CONFIDENTIAL] study with its Notice of Appeal which makes it clear that the duration of exposure is relevant. [CONFIDENTIAL].

146. In view of paragraphs 139 to 145 above, the Agency did not make an error of assessment in finding that, due to the short duration of exposure to the Substance in the ICH studies, those studies cannot answer the critical question of whether the Substance has any effects on the embryo/foetal development, and more specifically whether the Substance can cause skeletal and/or visceral abnormalities following continuous exposure.

147. The Agency also did not make an error of assessment in finding that the deficiency in the ICH studies regarding the duration of exposure cannot be compensated by any other information in the weight-of-evidence adaptation proposed by the Appellant, including the OECD TG 422 study. In particular, the OECD TG 422 study has the correct route of administration, duration and level of exposure, and investigates some, but not all, relevant parameters in relation to developmental toxicity and maternal toxicity/fertility. The OECD TG 422 study does not examine foetuses for skeletal and visceral abnormalities, in other words whether the Substance can cause skeletal and visceral abnormalities of the foetuses which is one of the aims of the PNDT study.

148. Therefore, from the weight-of-evidence adaptation submitted by the Appellant, even when the evidence is taken together, it is not possible to identify and characterise the pre-natal developmental toxicity of the Substance. The Appellant's weight-of-evidence adaptation did not contain sufficient evidence leading to the '*assumption/conclusion*', within the meaning of Section 1.2. of Annex XI, that the Substance is not a pre-natal developmental toxicant.

149. The deficiency related to the limited duration of exposure in the ICH studies, and the fact that this deficiency could not be compensated by the other information submitted by the Appellant, was sufficient on its own to reject the Appellant's weight-of-evidence adaptation. It is therefore not necessary to examine the Appellant's arguments related to the Agency's other reasons for rejecting the weight-of-evidence adaptation.

150. The Appellant's claim that the Agency committed an error of assessment in concluding that the weight-of-evidence adaptation fails to meet the requirements of Section 1.2. of Annex XI must therefore be rejected.

(ii) Failure to take into account the 2016 90-day study and the physico-chemical information on the properties of the Substance

151. The Appellant argues that, in rejecting the weight-of-evidence adaptation, the Agency failed to take into account the 2016 90-day study, which it presented in its comments on the draft decision, and the physico-chemical information on the properties of the Substance.

152. The 2016 90-day study is not referred to in the Contested Decision. However, that study is a 90-day sub-chronic toxicity study designed to assess and evaluate the toxicity of a substance in adult animals which are not pregnant. Developmental toxicity parameters - that is to say pregnant animals, placentas, skeletal and visceral abnormalities of the foetuses - are not examined in such a study. Consequently, the results of the 2016 90-day study do not provide any relevant information which would contribute to the evaluation on the pre-natal developmental toxicity of the Substance and could not have altered the Agency's conclusion to reject the weight-of-evidence adaptation.

153. Similarly, the information on the physico-chemical properties of the Substance provided by the Appellant is not sufficient to support an '*assumption/conclusion*' that the Substance cannot cause pre-natal developmental toxicity. In particular, as stated in the Contested Decision, no data has been provided by the Appellant to substantiate the claim that the

chemical inertness of the Substance also renders the Substance toxicologically inert. Consequently, the information submitted by the Appellant on physico-chemical properties could not have altered the Agency's conclusion to reject the weight-of-evidence adaptation.

154. The Appellant's plea that the Agency committed an error of assessment by failing to take into account the 2016 90-day study and the physico-chemical information on the properties of the Substance must therefore be rejected.

5. Breach of Article 25 and of the principle of proportionality

Arguments of the Parties and Intervener

155. The Appellant, supported by the Intervener, argues that the Agency breached Article 25, as well as the principle of proportionality, by rejecting the Appellant's weight-of-evidence adaptation.

156. The Appellant argues that the Contested Decision breaches the principle of proportionality because the PNDT study requested by the Agency is not necessary to satisfy the objective pursued of obtaining sufficient information to fulfil the developmental toxicity endpoint for the Substance. The Appellant's dossier contains a valid weight-of-evidence adaptation which shows that the Substance is not a developmental toxicant.

157. The Agency disputes the Appellant's and the Intervener's arguments.

Findings of the Board of Appeal

158. In order to respect the principle of proportionality, measures adopted by the European Union institutions and agencies must not exceed the limits of what is appropriate and necessary in order to achieve the objectives legitimately pursued by the measure in question. When there is a choice between several appropriate measures recourse must be had to the least onerous, and the disadvantages caused must not be disproportionate to the aims pursued (judgment of 21 July 2011, *Etimine*, C-15/10, EU:C:2011:504, paragraph 124; Case A-005-2011, *Honeywell Belgium*, Decision of the Board of Appeal of 29 April 2013, paragraphs 115 to 117).

159. In the Contested Decision, the Agency rejected the Appellant's adaptation and concluded, without committing an error, that the Appellant's registration dossier still has a data-gap under Section 8.7.2. of Annex IX.

160. The consequences of this finding flow directly from the REACH Regulation. Pursuant to Article 10(a)(vi), read in conjunction with Section 8.7.2. of Annex IX and Annex XI, the Appellant is obliged to submit either information on a PNDT study in accordance with a relevant test method or, alternatively, an acceptable adaptation.

161. As a consequence, the Agency was neither required nor empowered to consider whether it is proportionate, or consistent with Article 25, for the Appellant to be required to submit this information (see, to this effect, Case A-017-2014, *BASF*, Decision of 7 October 2016, paragraphs 83, 88 and 89, Case A-006-2017, *Climax Molybdenum*, Decision of 11 December 2018, paragraphs 118 to 123, and *Clariant Plastics & Coatings (Deutschland)*, cited in paragraph 140 above, paragraphs 46 to 52 of the decision). In this respect, the Contested Decision clearly serves to attain the regulatory objectives of the REACH Regulation.

162. The Appellant's pleas that the Agency breached the principle of proportionality and Article 25 must therefore be rejected.

Result

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

Refund of the appeal fee

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

On those grounds,

THE BOARD OF APPEAL

hereby:

1. Dismisses the appeal.

2. Decides that the appeal fee is not refunded.

Antoine Buchet
Chairman of the Board of Appeal

Alen Močilnikar
Registrar of the Board of Appeal