EUROPEAN CHEMICALS AGENCY
BOARD OF APPEAL

DECISION OF THE BOARD OF APPEAL OF THE EUROPEAN CHEMICALS AGENCY

29 April 2013

(Compliance check of a registration – Testing involving vertebrate animals – Principle of last resort - Section 8.6.4 of Annex X– Discretion of the Agency - Principle of proportionality)

Case number	A-005-2011
Language of the case	English
Appellant	Honeywell Belgium N.V. Belgium
Representative	Messrs Herbert Estreicher and Marcus Navin-Jones Keller and Heckman LLP Brussels Belgium
Intervener (I)	DuPont de Nemours (Nederland) B.V. The Netherlands Represented by: Mr Terrence A. Vandeveld and Ms Teny Nicoghossian Du Pont de Nemours International Sàrl Geneva Switzerland
Intervener (II)	European Coalition to End Animal Experiments (ECEAE) United Kingdom Represented by: Dr Katy Taylor London United Kingdom
Contested decision	CCH-D-0000001396-72-03/F of 22 March 2011 adopted by the European Chemicals Agency (hereinafter the 'Agency') pursuant to Article 41 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; corrected by OJ L 136, 29.5.2007, p. 3; hereinafter the 'REACH Regulation')

THE BOARD OF APPEAL

composed of Mercedes ORTUÑO (Chairman), Andrew FASEY (Technically Qualified Member and Rapporteur) and Barry DOHERTY (Legally Qualified Member)

Registrar: Sari HAUKKA

gives the following

Decision

RELEVANT LEGISLATION

The REACH Regulation

1. Article 1(1) of the REACH Regulation provides:

   '*The purpose of this Regulation is to ensure a high level of protection of human health and the environment, including the promotion of alternative methods for assessment of hazards of substances, as well as the free circulation of substances on the internal market while enhancing competitiveness and innovation.*'

2. Article 13(2) and (3) of the REACH Regulation provides:

   '*2. […] The Commission, following consultation with relevant stakeholders, shall, as soon as possible, make a proposal, if appropriate, to amend the Commission Regulation on test methods adopted in accordance with the procedure referred to in Article 133(4), and the Annexes of this Regulation, if relevant, so as to replace, reduce and refine animal testing. […]*

   3. Where tests on substances are required to generate information on intrinsic properties of substances, they shall be conducted in accordance with the test methods laid down in a Commission Regulation or in accordance with other international test methods recognised by the Commission or the Agency as being appropriate. […]'

3. Article 25(1) of the REACH Regulation provides:

   '*In order to avoid animal testing, testing on vertebrate animals for the purposes of this Regulation shall be undertaken only as a last resort. It is also necessary to take measures limiting duplication of other tests.*'

4. Article 41(1)(a) and (3) of the REACH Regulation 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;

   […]

   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.'

5. Article 51(1) to (7) of the REACH Regulation provides:

'*1. The Agency shall notify its draft decision in accordance with Articles 40 or 41, together with the comments of the registrant, to the competent authorities of the Member States.*

2. Within 30 days of circulation, the Member States may propose amendments to the draft decision to the Agency.

3. If the Agency does not receive any proposals, it shall take the decision in the version notified under paragraph 1.

4. If the Agency receives a proposal for amendment, it may modify the draft decision. The Agency shall refer a draft decision, together with any amendments proposed, to the Member State Committee within 15 days of the end of the 30-day period referred to in paragraph 2.

5. The Agency shall forthwith communicate any proposal for amendment to any registrants or downstream users concerned and allow them to comment within 30 days. The Member State Committee shall take any comments received into account.

6. If, within 60 days of the referral, the Member State Committee reaches a unanimous agreement on the draft decision, the Agency shall take the decision accordingly.

7. If the Member State Committee fails to reach unanimous agreement, the Commission shall prepare a draft decision to be taken in accordance with the procedure referred to in Article 133(3).'

6. Section 8.6.4 of Annex X to the REACH Regulation provides:

'*Further studies shall be proposed by the registrant or may be required by the Agency in accordance with Articles 40 or 41 in case of:*

- *toxicity of particular concern (e.g. serious/severe effects), or*
- *indications of an effect for which the available evidence is inadequate for toxicological evaluation and/or risk characterisation. In such cases it may also be more appropriate to perform specific toxicological studies that are designed to investigate these effects (e.g. immunotoxicity, neurotoxicity), or*
- *particular concern regarding exposure (e.g. use in consumer products leading to exposure levels which are close to the dose levels at which toxicity is observed).*'

Commission Regulation (EC) No 440/2008

7. Section 1.6.2.1 of test protocol B.29 on sub-chronic inhalation toxicity study 90-day repeated inhalation dose study using rodent species which is set out in Commission Regulation (EC) No 440/2008 of 30 May 2008 laying down test methods pursuant to the REACH Regulation (OJ L 142, 31.5.2008, p. 1) provides:

'*Experimental animals*

Unless there are contra-indications, the rat is the preferred species. Commonly used laboratory strains of young healthy animals should be employed. […] Where a subchronic inhalation study is conducted as a preliminary to a long-term study, the same species and strain should be used in both studies.'

OECD Guideline 413 Subchronic Inhalation Toxicity: 90-Day Study

8. OECD (2009), *Test No. 413: Subchronic Inhalation Toxicity: 90-day Study* (OECD Guidelines for the Testing of Chemicals, Section 4, OECD Publishing) addresses at point 6 the selection of animal species and provides:

   'Healthy young adult rodents of commonly used laboratory strains should be employed. The preferred species is the rat. Justification should be provided if other species are used'.

Directive 2010/63/EU of the European Parliament and of the Council

9. Article 13(1) and (2) of Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes (OJ L 276, 20.10.2010, p. 33) provides:

   'Choice of methods

   1. Without prejudice to national legislation prohibiting certain types of methods, Member States shall ensure that a procedure is not carried out if another method or testing strategy for obtaining the result sought, not entailing the use of a live animal, is recognised under the legislation of the Union.

   2. In choosing between procedures, those which to the greatest extent meet the following requirements shall be selected:

   (a) use the minimum number of animals;

   (b) involve animals with the lowest capacity to experience pain, suffering, distress or lasting harm;

   (c) cause the least pain, suffering, distress or lasting harm;

   and are most likely to provide satisfactory results'.

SUMMARY OF THE FACTS

10. On 11 December 2009, the Appellant submitted a registration for the substance 2,3,3,3-tetrafluoropropene (hereinafter 'the Substance') at the tonnage level of 1,000 tonnes or more per year.

11. In the registration dossier submitted the Appellant provided three repeated dose toxicity studies in the rat (2, 4 and 13 weeks' exposure) pursuant to Sections 8.6.1 and 8.6.2 of Annexes VIII and IX to the REACH Regulation, a pre-natal developmental toxicity study and a two-generation reproductive study in the rat pursuant to Section 8.7.2 of Annex IX and Section 8.7.3 of Annex X respectively, as well as a pre-natal developmental toxicity study in the rabbit pursuant to Section 8.7.2 of Annex X.

12. The toxicological hazard assessment, prepared by the Appellant on the basis of the variety of rat studies present in the dossier (ranging from acute toxicity, through sub-chronic toxicity to pre-natal and multi-generation toxicity assays), showed that the Substance has fairly low potency in the rat. However, the results in the robust study summary of the pre-natal developmental toxicity study in the rabbit via inhalation showed a potent toxicity, with lethality at doses much lower as compared with rats.

13. On 26 April 2010, the Agency initiated a dossier compliance check of the Appellant's registration dossier for the Substance. Further to this, the Agency prepared a draft decision pursuant to Article 41(3) of the REACH Regulation by which its intention was to require the Appellant to submit, pursuant to Articles 10(a)(vi) and (vii), 12(1)(e), 13(3), 41(1)(a) and 41(3), as well as Section 8.6.4

of Annex X to the REACH Regulation, inter alia a 90-day repeated dose toxicity study in the rabbit by inhalation (Test Method ('TM') B.29 of Regulation (EC) No 440/2008 or OECD Test Guideline ('TG') 413). The Agency draft decision further requested that the study protocol should be modified with additional clinical pathology and histopathological evaluations to examine effects on reproductive organs, specifically as described in OECD TG 416 and in particular paragraphs 29 to 32, 39 and 41 to 45 thereof. The modified repeated dose toxicity study in the rabbit by inhalation as described in this paragraph is hereinafter referred to as 'the Study'.

14. The draft decision gave the following reasons for requiring the Study:

    (i) The death of pregnant rabbits in the Appellant's prenatal developmental toxicity testing on rabbits satisfies the criterion 'toxicity of particular concern' as set out in Section 8.6.4 of Annex X;

    (ii) The available evidence is inadequate for toxicological evaluation and/or risk characterisation because the data submitted shows that the rabbit is more sensitive to toxicity from the Substance as compared with the rat; and

    (iii) The available information on the toxicity of the Substance on the rabbit is inadequate for toxicological evaluation and/or risk characterisation.

15. On 19 August 2010, the Agency notified the draft decision to the Appellant and invited it, pursuant to Article 50(1) of the REACH Regulation, to submit comments on the draft decision by 20 September 2010. At the same time, the Agency offered the Appellant an opportunity to discuss the scientific background to the draft decision with the Agency.

16. On 2 September 2010, the Agency and the Appellant held a teleconference to discuss the draft decision.

17. On 17 September 2010, the Appellant submitted comments on the draft decision, and subsequently on 30 September 2010, submitted a revised IUCLID file to the Agency with certain additional information.

18. On 29 October 2010, the Agency, pursuant to Article 51(1) of the REACH Regulation, notified the draft decision to the Member States Competent Authorities (hereinafter the 'MSCAs' or 'MSCA' if singular) and invited them to propose amendments.

19. By 28 November 2010, the Agency received comments and proposals for amendments from five MSCAs.

20. On 1 December 2010, the Agency notified the MSCAs' comments to the Appellant in accordance with Article 51(5) of the REACH Regulation, and invited the Appellant to comment on the proposed amendments. On 21 December 2010, the Appellant submitted further comments to the Agency.

21. The Agency considered the MSCAs' proposals for amendments, and amended the draft decision. These amendments did not however relate to the Study.

22. On 13 December 2010, the Agency referred the draft decision (as amended) to the Member State Committee (hereinafter 'MSC'), in accordance with Article 51(4) of the REACH Regulation.

23. On 1, 2 and 3 February 2011, a meeting of the MSC (MSC-16) took place at which the Agency's draft decision was discussed. The Appellant participated at the meeting as the case owner and was present at the initial discussions of the MSC on the Agency's draft decision. Following certain amendments to the draft decision, which pertained only to the time limit accorded to the Appellant to submit the results of the Study, the MSC reached a unanimous agreement on the Agency's draft decision.

24. On 22 March 2011, the Agency adopted the Contested Decision and notified it to the Appellant. Hereinafter, 'Contested Decision' refers to that part of the Contested Decision which is the subject of the appeal, namely section II part 2) of Decision CCH-D-0000001396-72-03/F of 22 March 2011 adopted by the European Chemicals Agency, to the extent that the Agency required the Appellant to conduct a 90-day repeated dose toxicity study in the rabbit by inhalation (Test Method B.29 of Regulation (EC) No 440/2008 or OECD Test Guideline 413) as modified by the additional clinical pathology and histopathalogical evaluations specified in the Contested Decision with reference to OECD Test Guideline 416.

PROCEDURE BEFORE THE BOARD OF APPEAL

25. On 21 June 2011, the Appellant lodged a notice of appeal at the Registry of the Board of Appeal seeking the annulment of the Contested Decision to the extent that the Agency required the Appellant to conduct the Study. The Appellant also requested the refund of the appeal fee.

26. The notice of appeal also contained a request to treat certain information as confidential. More specifically, the Appellant requested that the identity of the Substance (including the IUPAC name, the chemical and trade names, the EC and CAS numbers, as well as the REACH registration and dossier submission numbers) be treated as confidential, as well as information on the uses of the Substance, the precise tonnage data, the identity of and comment by a MSCA, the names of three contract research organisations that provided expert statements on the Appellant's behalf, and details of certain studies submitted to the Agency.

27. On 29 July 2011, and further to two requests by the Registry of the Board of Appeal for clarifications, the Chairman adopted a decision on the Appellant's request for confidential treatment. By that decision, the Chairman rejected the Appellant's request insofar as it pertained to the identity of the Substance and its uses, and the names of the contract research organisations (hereinafter 'CROs'). The Chairman also rejected the Appellant's request with respect to information on the precise tonnage data and information on certain studies that had been submitted to the Agency. Finally, the Chairman granted the Appellant's request to treat as confidential certain personal data.

28. On 22 September 2011, and further to a request of 29 July 2011 for an extension of the time limit, which was accepted by the Board of Appeal, the Agency submitted the defence. The Agency's defence also contained a request to treat certain personal data as confidential which was granted by the Chairman.

29. By letters received on 28 September 2011, DuPont de Nemours (Nederland) B.V. (hereinafter 'DuPont') and the European Coalition to End Animal Experiments (hereinafter 'ECEAE') applied to intervene in the proceedings before the Board of Appeal. On 14 October 2011, the Agency submitted observations on the applications to intervene in which it supported the intervention by DuPont but contested the application lodged by ECEAE. On 20 October 2011, the Appellant submitted its observations on the applications to intervene in which it expressed its support for both applications. By separate decisions of 8 November 2011, the Board of Appeal granted both applications to intervene.

30. On 23 November 2011, the Agency lodged a request for rectification of the Decision of the Board of Appeal granting ECEAE's application to intervene. By Decision of 15 December 2011, the Board of Appeal rejected the Agency's request for rectification.

31. On 22 December 2011, the Appellant lodged observations on the defence. The Appellant's observations contained a request for confidential treatment with respect to DuPont and ECEAE (hereinafter 'the interveners').

32. On 31 January 2012, and further to correspondence between the Appellant, the Agency and the Registry aimed at clarifying the parties' requests for confidential treatment vis-à-vis the interveners, the non-confidential versions of the notice of appeal, the defence, the Appellant's observations on the defence, and the parties' observations on the applications to intervene were notified to the interveners.

33. On 9 February 2012, the Agency lodged observations on the Appellant's observations on the defence.

34. On 16 March 2012, the Appellant submitted further observations on the Agency's observations of 9 February 2012.

35. On 21 March 2012 and 22 March 2012, respectively, DuPont and ECEAE lodged observations on the procedural documents submitted in the case.

36. On 20 April 2012, the Agency submitted observations on the Appellant's further observations.

37. On 25 April 2012 and 11 May 2012, respectively, the Appellant and the Agency submitted observations on the interveners' observations.

38. In response to the Board of Appeal's request for further information and documents, on 11 and 12 June 2013 respectively, the Appellant and the Agency submitted copies of correspondence between them, as well as certain documents related to the decision-making process, in particular where it concerned the MSC and the MSCAs.

39. The Agency's reply contained a request for confidential treatment with respect to the Appellant and the interveners. By Decision of 26 June 2012, the Chairman rejected the Agency's request for confidential treatment with respect to the Appellant.

40. On 18 July 2012 and 2 August 2012, respectively, the Agency and the Appellant lodged observations on each other's replies to the request of the Board of Appeal for further information.

41. On 22 August 2012, the parties and interveners were notified of the Board of Appeal's decision to close the written procedure.

42. On 17 October 2012, since a member of the Board of Appeal was precluded from participating in the proceedings, the Chairman designated an alternate member, Mr Barry Doherty, to act in the present case as the legally qualified member of the Board of Appeal.

43. In accordance with Article 13 of Commission Regulation (EC) No 771/2008 of 1 August 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; hereinafter the 'Rules of Procedure'), following the request of both parties for a hearing to be held, the parties were summoned to an oral hearing which was held on 12 December 2012. The interveners were also invited to participate in the hearing. Oral presentations were made by the parties and both interveners. The members of the Board of Appeal also posed questions to the parties and interveners.

ARGUMENTS OF THE PARTIES

Appellant's arguments

44. In the notice of appeal, the Appellant requests the Board of Appeal to annul the portion of the Contested Decision that requires the Appellant to submit the Study. The Appellant supports its request with the following pleas of law and fact:

    (i) First plea: the Contested Decision breaches Article 41 of the REACH Regulation, read together with Section 8.6.4 of Annex X, insofar as the

Agency can require additional information as part of a compliance check only to the extent necessary to answer specific questions concerning toxicity or risk. In the present case, the scientific questions regarding the Substance could be answered by a 28-day inhalation study on rabbits and therefore the Agency should have selected the shorter study.

(ii) Second plea: the Contested Decision is inconsistent with Article 13(3) of the REACH Regulation as the test methods identified by the Agency in the Contested Decision (EU TM B.29 or OECD TG 413) apply to rodents but not to rabbits. Accordingly there is no established test method for the Study. Moreover, the Study is virtually unprecedented in the history of toxicology.

(iii) Third plea: the Contested Decision is inconsistent with Article 13(2) of the REACH Regulation. As there is no standard test protocol for the Study, Regulation (EC) No 440/2008 should have been amended, as part of which stakeholders should have been consulted on any amendment.

(iv) Fourth plea: the Contested Decision breaches and is inconsistent with Article 25(1) of the REACH Regulation which requires that testing on vertebrate animals is undertaken only as a last resort. Given the absence of historical control data, and the rabbit's susceptibility to stress, the Study is likely to lead to false positives. Also, the Study is disproportionate as it imposes substantial testing burdens on the Appellant without a sufficient likelihood that it will provide scientifically meaningful results. Additionally, testing on vertebrate animals must be consistent with the relevant requirements for the protection of laboratory animals as set out in Directive 2010/63/EU including the use of the minimum number of animals.

45. Subsequently, in its observations to the Agency's reply to the request of the Board of Appeal for further information submitted on 2 August 2012, the Appellant introduced a fifth plea, on the basis of a document contained in the Agency's reply dated 12 June 2012, claiming that the Contested Decision was adopted in breach of Article 51(6) and (7) of the REACH Regulation insofar as unanimous agreement was not reached in the MSC on the Agency's draft decision.

Agency's defence

46. On 22 September 2009, the Agency submitted its defence. The Agency's arguments can be summarised as follows:

(i) Section 8.6.4 of Annex X to the REACH Regulation provides the Agency with wide discretion to decide on what is an appropriate test for a registrant to perform to allay any concerns identified by the Agency.

(ii) Following the evaluation of the Appellant's registration dossier, the Agency concluded that there was an inter-species difference in toxicity between rats and rabbits and therefore the information requirements were to be satisfied on the most sensitive species, that is, the rabbit. According to the Agency, the Appellant contests neither the Agency's finding of the most sensitive species nor the Agency's authority to require further studies pursuant to Section 8.6.4 of Annex X.

(iii) A 90-day repeated dose toxicity study is a standard requirement for substances registered in the 100 tonnes or higher tonnage band. The Study will provide the Agency with much more reliable information than a 28-day study as: it carries greater statistical power to detect an effect; it provides for histopathological examination of a wider range of organs; it allows for an easier, better and wider investigation of some reproductive effects; and detects on average an approximately three-fold more potent effect of chemicals than a 28-day toxicity study. Additionally, given several

structurally-related compounds that are carcinogenic, the interpretation of hyperplastic and metaplastic lesions in the 90-day study is potentially of importance as such a response in a 28-day study could be transient. Further, during the decision-making process, the Appellant never proposed to carry out a 28-day inhalation study on rabbits.

(iv) The EU TM B.29 and OECD TG 413 cover both rodent and non-rodent species. More specifically, while OECD TG 413 recommends the use of rodents and preferably rats, it also accepts the use of other species, if justified. Such justification exists in the present case given that the rabbit is more sensitive to the Substance than the rat. As regards EU TM B.29, it is based on OECD TG 413 and its scope should be interpreted by reference to the latter. Consequently, established test methods exist for the conduct of a 90-day repeated dose toxicity study in the rabbit, by inhalation. Furthermore, the Study is technically feasible. The Appellant's arguments on consultation with relevant parties should be dismissed.

(v) As the Study is to be conducted in accordance with a standard test method (EU TM B.29 or OECD TG 413), Article 13(2) of the REACH Regulation does not apply. Thus, there was no need to review or amend Regulation (EC) No 440/2008, and no need to follow the procedure set out in Article 13(2) of the REACH Regulation.

(vi) The Appellant has failed to indicate how Article 25(1) of the REACH Regulation has been breached. The animal welfare perspective was carefully considered during evaluation of the dossier and the decision-making procedure. Specifically, the Agency and the MSC considered the need, inter alia, for a study to provide a better chance to avoid further animal testing. In addition, the Contested Decision is proportionate.

Interveners' arguments

47. On 28 September 2011, DuPont submitted its application to intervene in support of the Appellant and, on 21 March 2012, it submitted further observations on the appeal. The arguments presented by DuPont can be summarised as follows:

(i) When requiring 'further studies' pursuant to Section 8.6.4 of Annex X to the REACH Regulation, the Agency should take into account Articles 13(1) and 25(1) of the REACH Regulation. The Study was not selected in accordance with these two provisions, as otherwise the Agency would have required a 28-day rather than a 90-day repeated dose toxicity study by inhalation.

(ii) A 28-day study is more appropriate and sufficient, inter alia, as it is compliant with OECD TG 412, it can provide data relevant for a detailed assessment of the Substance's toxicity and it can be used to evaluate repeated exposure effects on the same or additional organs, tissues and processes as those normally evaluated in the 90-day study. As the Appellant had satisfied the REACH requirements, the Agency's request for additional information can only be about the shortest possible test.

(iii) While historical control data is not required to carry out the Study, it is necessary to evaluate the results. However, irrespective of whether a 28-day or a 90-day inhalation study is performed, given the lack of historical control data, it would be necessary to increase the number of animals used to ensure the scientific validity of the study.

(iv) The evaluation process under the REACH Regulation is similar to a tiered or step-wise approach.

(v) The Contested Decision is inconsistent with Article 13(3) of the REACH Regulation given that the Study is inconsistent with OECD TG 413. The evidence provided by the two CROs on behalf of the Agency demonstrates that a 90-day rabbit inhalation study is not scientifically appropriate. One of those CROs notes the need for a dose range finding study before undertaking the 90-day study, while the test proposed by the other CRO does not comply with OECD TG 413.

(vi) The Contested Decision is inconsistent with Article 13(2) of the REACH Regulation. As the Study is not a standard test, the process prescribed in Article 13(2) of the REACH Regulation should have been followed.

(vii) Finally, as the 90-day study lacks solid scientific justification, a 28-day study should have been preferred in accordance with Article 25(1) of the REACH Regulation.

48. On 28 September 2011, ECEAE submitted its application to intervene in support of the Appellant and, on 22 March 2012, it submitted further observations on the appeal. The arguments presented by ECEAE can be summarised as follows:

(i) The Agency has discretion, and it is in principle entitled to request additional information pursuant to Section 8.6.4 of Annex X to the REACH Regulation. However, in the present case, the Agency's exercise of discretion has been unlawful and disproportionate. In particular, the Appellant has done everything required of it and therefore the Agency should have exercised its discretion with circumspection and proportionately. Further, the Agency has neither identified any information gaps in terms of standard REACH information requirements nor claimed that the information provided is not of the requisite standard. Therefore, there is no legal need to require the Study.

(ii) The Agency must have regard to the risks that a substance poses in the real world. In the present case, the risk of exposure of the population or the environment to the Substance is negligible. Moreover, the nature of exposure, even if it did occur, would bear no relationship to the Study given that any exposure to the Substance would be acute. The Agency's primary concern appears to be the potential carcinogenicity although, given the nature of possible exposure to the Substance, it is difficult to see how this would be an outcome in practice.

(iii) The Contested Decision is scientifically flawed. The Study is virtually unprecedented and it would not generate reliable information.

(iv) EU TM B.29 and OECD TG 413 do not apply to rabbits. Moreover, it does not follow that because the use of a particular animal species is allowed by a test guideline, the results of a study using that guideline must be reliable, and that it therefore eliminates concerns about unnecessary animal suffering. The conduct of the Study would cause a very high degree of suffering to rabbits. The prior studies using rabbits, as cited by the Agency, show several physical symptoms of suffering. The Agency's arguments that the previous studies do not show that rabbits were highly stressed are complacent and misplaced.

(v) The REACH Regulation pursues a number of different objectives, including a high level of protection of human health and the environment as well as the promotion of alternative methods (the replacement, reduction and refinement of animal testing, hereinafter the '3Rs'). Thus, animal welfare is a key consideration under the REACH Regulation.

(vi) A step-wise approach is built into the REACH Regulation, for example Article 25(1) of the REACH Regulation implies that other measures must be

considered before testing on vertebrate animals is required. Moreover, a step-wise approach is a well-recognised principle of toxicology.

(vii) The Agency cannot merely state that it has had regard to Article 25(1) of the REACH Regulation without demonstrating the reasoning that led to the conclusion that animal testing is unavoidable.

(viii) The Agency's decision is wholly disproportionate, and the desired information could be provided in a different way. The Agency should have required the Appellant to apply appropriate assessment factors to ensure the protection of human health while avoiding the use of animals in testing.

REASONS

I. Admissibility

49. The Board of Appeal will firstly examine the inadmissibility pleas that have been raised by the Agency during the proceedings.

1. Admissibility of the evidence submitted by the Appellant in response to the Board of Appeal's request for further information and documents

50. In its submission dated 18 July 2012, the Agency claimed that a document, which the Appellant submitted in response to the request of the Board of Appeal for further information, did not fall within the scope of that request. The document in question, an electronic communication dated 28 January 2011, contains the Appellant's internal talking points that were prepared by its representative and a toxicology expert for the MSC meeting at which the Substance was discussed.

51. According to the Agency, this document was never sent to, or shared with, the Agency or the MSC, and it therefore falls outside the scope of the request of the Board of Appeal.

52. Pursuant to Article 15 of the Rules of Procedure, the Board of Appeal invited the Appellant to provide '*[c]opies of any submissions to, or correspondence with, the Agency and the Member State Committee during the Agency's decision-making process, to the extent that such documents have not previously been submitted to the Board of Appeal. Such documents would include, for example, comments made by the Appellant pursuant to Article 51 of the REACH Regulation (if additional to, and different from, Annexes 3 and 4 to the Agency's Defence), and copies of expert evidence (or extracts of material) that was presented on the Appellant's behalf at the MSC-16 […] meeting.*'

53. The Board of Appeal observes, first, that the wording of its request for further information and documents should not be read restrictively. The request was aimed at uncovering all relevant information and documents that relate to the Agency's evaluation of the Appellant's dossier for the Substance. Having regard to this, it is clear that the Appellant's internal talking points relate, from the Appellant's side, to the Agency's evaluation of the Substance, and thus are relevant for the purposes of the present proceedings.

54. Second, the Board of Appeal observes that only limited records are available of the discussions that took place at the MSC meeting in question. Thus, the Appellant's internal talking points are the closest proxy to a record of statements made, or intended to be made, on the Appellant's behalf at the MSC meeting. The talking points are prima facie evidence of the Appellant's submissions to the Agency and so come within the scope of the Board of Appeal's letter.

55. Furthermore, and by way of a more general observation, the Board of Appeal notes that the Agency manages the process of recording discussions at the MSC

meetings. Whilst the MSC Secretariat prepares draft minutes, and the case owners are invited to provide comments thereto, the Agency ultimately decides on the final content and wording of the MSC meeting minutes. The Board of Appeal therefore considers that any limitations in MSC meeting minutes should not act to the detriment of a party to appeal proceedings.

56. Therefore, for the above reasons, the Board of Appeal finds that the Appellant's internal talking points, which were submitted in response to a request of the Board of Appeal pursuant to Article 15 of the Rules of Procedure, are within the scope of that request, and are therefore admissible in the present proceedings.

57. Consequently, the Board of Appeal dismisses the Agency's claim of inadmissibility.

2. Admissibility of the Appellant's arguments contesting the rabbit as the most sensitive and appropriate species

58. In its submission dated 22 December 2011, the Appellant argued that, on the facts currently available, it was possible that the rabbit is the most sensitive species. The Appellant also stated that it was not clear at that stage which species, the rat or the rabbit, was more relevant or appropriate for human risk assessment.

59. In its submissions dated 9 February 2012 and 20 April 2012, the Agency claimed that the Appellant had introduced a new plea in law by contesting, in the submissions lodged on 22 December 2011 and 16 March 2012, respectively, the Agency's finding that the rabbit is the most sensitive species. The Agency considers that the Appellant's argumentation contesting the rabbit as the most sensitive and appropriate species and the resulting need of further data to be generated on that species should not be accepted by the Board of Appeal.

60. In accordance with Article 12(2) of the Rules of Procedure, a new plea may be introduced after the first exchange of written pleadings only if the Board of Appeal decides that it is based on new matters of law or fact that came to light in the course of the proceedings. It falls therefore on the Board of Appeal to examine whether the Appellant's argumentation on the most appropriate test species constitutes an inadmissible new plea in law, as claimed by the Agency.

61. The Board of Appeal recalls that, in accordance with settled case-law a plea which may be regarded as amplifying or developing a plea made previously, whether directly or by implication, must be considered admissible (see, by analogy, Case C-66/02 *Italy* v *Commission* [2005] ECR I-10901, paragraph 86).

62. In light of the above considerations, the Board of Appeal finds that the Appellant's arguments on the appropriateness of the rabbit do not alter the subject-matter of the dispute between the parties. It suffices to note that by the pleas raised in the notice of appeal, the Appellant has contested the legality of the Contested Decision in light of Article 41 of the REACH Regulation. As part of this plea, the Appellant has contested, inter alia, the imposition of the Study and the appropriateness of the rabbit as a test animal for conducting the Study. As such, the Appellant's observations amplify and develop the plea that was raised in the notice of appeal, and they do not therefore constitute an inadmissible new plea in law.

63. Consequently, the Agency's plea of inadmissibility must be rejected as unfounded.

II. Claims under investigation

1. The Agency's margin of discretion under Section 8.6.4 of Annex X to the REACH Regulation

64. As a preliminary step, the Board of Appeal will discuss the Agency's margin of discretion under Section 8.6.4 of Annex X to the REACH Regulation. In its first plea the Appellant raises questions regarding the extent of the Agency's discretion to decide on the appropriate study for a registrant to perform to allay concerns identified by the Agency.

65. The Board of Appeal observes that it is uncontested in the present proceedings that Section 8.6.4 of Annex X confers discretion on the Agency to require the conduct of further studies with regard to the repeated dose toxicity end-point.

66. Indeed the Agency's discretionary powers in general have already been recognised by the European Union Courts which have held that '*[…] the Agency has a broad discretion in a sphere which entails political, economic and social choices on its part, and in which it is called upon to undertake complex assessments*' (see Case T-96/10 *Rütgers Germany GmbH and Others v ECHA*, judgment of 7 March 2013, not yet reported, paragraph 134). The Board of Appeal notes further that Article 41 of the REACH Regulation, read together with Section 8.6.4 of Annex X thereto, confers a wide margin of discretion on the Agency in the context of a dossier compliance check. In this respect, Section 8.6.4 of Annex X differs from those sections of Annexes VII to X to the REACH Regulation for which standard information requirements are set out as there is no standard information requirement and the Agency therefore has considerable discretion.

67. This follows, in particular, from the use of the word 'may' in the relevant provisions of the legislation. Thus, Article 41(3) of the REACH Regulation provides that '*[...] the Agency may [...] 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'*.

68. Similarly, as regards the provision on the repeated dose toxicity end-point, Section 8.6.4 of Annex X stipulates that *'[f]urther studies [...] may be required by the Agency in accordance with Articles 40 and 41 [of the REACH Regulation] in case of toxicity of particular concern (e.g., serious/severe effects), or indications of an effect for which the available evidence is inadequate for toxicological evaluation and/or risk characterisation [...]'.*

69. Furthermore, Section 8.6.4 of Annex X does not define the scope of the 'further studies' that the Agency may require a registrant to provide for the repeated dose toxicity end-point. By implication, the choice of study has been left within the Agency's discretion.

70. The Board of Appeal observes that the Agency's margin of discretion under Section 8.6.4 of Annex X applies first to the assessment of the need for further information and second to the determination of what further studies are appropriate to address the concerns identified.

71. The assessment of the need for further information involves a finding by the Agency that a substance gives rise to one or several of the concerns specified in Section 8.6.4 of Annex X. It is incumbent on the Agency to establish in each individual case and reflecting the available scientific evidence submitted in a registration dossier that one or several of the criteria in Section 8.6.4 of Annex X is met.

72. As regards the present case, the Appellant accepts that the results of the rabbit pre-natal developmental toxicity (hereinafter 'PNDT') study were unusual and unexpected. The Appellant however questions whether the Study is the most appropriate to explore these results or whether other tests should first have been

conducted to further understand and explore the reasons for that result and in particular to explore whether that result is not a scientific anomaly.

73. The Board of Appeal observes that in the present case the Agency has provided reasons in the Contested Decision for its finding that the criteria in Section 8.6.4 of Annex X were met. The Agency concluded, on the basis of the results of the rabbit PNDT study, that the Substance raised concerns of toxicity of particular concern and an effect for which the available evidence is inadequate for toxicological evaluation and risk characterisation.

74. In light of the evidence submitted during the proceedings, the Board of Appeal finds that the results of the rabbit PNDT study on the Substance raises concerns about the hazards posed by the Substance that need to be subject to further investigation and that the criteria set out in Section 8.6.4 of Annex X for requiring further studies were therefore met.

75. Whilst the Appellant has not contested the Agency's decision that further information is necessary it disputes the Agency's choice of Study to generate that information. The Agency's use of its discretion with regard to the choice of Study to meet the concern identified in this case will be addressed as part of the analysis of the proportionality of the Contested Decision below.

76. The Board of Appeal also underlines, however, that the fact that the Agency has a wide margin of discretion does not prevent the Board of Appeal from assessing whether that discretion was correctly used. In particular, as part of its evaluation of the Appellant's pleas, the Board of Appeal will seek to establish, among other things, whether the evidence upon which the Agency relied to reach its decision is factually accurate, reliable and consistent and also whether that evidence contains all the information which must be taken into account in order to assess a complex situation and whether the evidence is capable of substantiating the conclusions drawn from it (see, by analogy, Case C-386/10 P *Chalkor v Commission* judgment of 8 December 2011, not yet reported, paragraph 54, and the case-law cited there). The Agency is also under a duty to examine carefully and impartially all the relevant elements of the individual case (see, by analogy, Case C–269/90 *Technische Universität München* [1991] ECR I–5469, paragraph 14). The EU Courts have also held that even where an EU institution has a discretion, it must still be established '[…] *whether the evidence relied on is factually accurate, reliable and consistent but also whether that evidence contains all the information which must be taken into account in order to assess a complex situation and whether it is capable of substantiating the conclusions drawn from it*' (Case C-12/03 P *Tetra Laval* [2005] ECR I-987, paragraph 39).

77. In conclusion, the Board of Appeal finds that the Agency's broad discretion applies not only to the nature and scope of the measures to be taken but also, to some extent, to the finding of the basic facts. However, this discretion requires that the Agency must be able to show that in adopting the act it actually exercised its discretion, which presupposes the taking into consideration of all the relevant factors and circumstances of the situation the act was intended to regulate (see by analogy Case T-96/10 *Rütgers Germany GmbH and Others v ECHA*, judgment of 7 March 2013, not yet reported, paragraph 100).

78. When considering the relevant pleas, the Board of Appeal will examine whether all the relevant factors and circumstances were considered by the Agency in the preparation of the Contested Decision. The fourth plea, which is broadest in scope, will be examined first.

2. First part of the fourth plea alleging the infringement of Article 25(1) of the REACH Regulation

79. The Appellant claims in the first part of its fourth plea that the Contested Decision breaches and is inconsistent with Article 25(1) of the REACH Regulation, which requires that testing on vertebrate animals is undertaken only as a last resort.

80. The Appellant argues that Article 25(1) and Recitals 37 and 47 of the REACH Regulation establish the principle that vertebrate animal testing must be performed as a last resort and in any event be performed in accordance with the provisions of Council Directive 86/609/EEC of 24 November 1986 on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes (OJ L 358, 18.12.1986, p. 1). Recitals 37 and 47 of the REACH Regulation refer to Directive 86/609/EEC which was subsequently repealed by Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes (OJ L 279, 20.10.2010, p. 33). In accordance with Article 62(2) of the latter Directive, any references to Directive 86/609/EEC must be construed as references to Directive 2010/63/EU.

81. ECEAE argues that the REACH Regulation pursues a number of different objectives, including a high level of protection of human health and the environment, as well as the promotion of alternative methods as part of the 3Rs. Thus, ECEAE contends that animal welfare is a key consideration under the REACH Regulation but that in the Contested Decision the Agency has focused almost exclusively on seeking to achieve a high level of protection of human health to the detriment of other objectives and animal welfare in particular.

82. The Agency argues, however, that the Appellant has failed to indicate how Article 25(1) of the REACH Regulation has been breached. The Agency also claims that Article 25 of the REACH Regulation is limited to the part of the REACH Regulation entitled '*data sharing and avoidance of unnecessary testing*' and is therefore not applicable to the case at hand.

83. The Agency adds further that the animal welfare perspective was carefully considered during the evaluation of the dossier and the decision-making procedure. The Agency states specifically that the Agency and the MSC considered, inter alia, that the Study would help avoid further animal testing. The Agency refers to the Final Minutes of the MSC (MSC/M/016/2011; hereinafter the 'MSC Minutes') in support of its claim that the animal welfare perspective was carefully considered during evaluation of the dossier and the decision-making process.

84. The Agency claims that the Appellant's reference to Recital 47 merely echoes the objective set out in Article 1 of the REACH Regulation to promote alternative methods for assessing the specific hazards of substances. However, the Agency states that there are currently no alternative methods for assessing the specific hazards of the Substance addressed in the Contested Decision.

85. The Agency also argues that there are doubts as to whether the 28-day study would be able to provide sufficient certainty on the toxicological issues of concern. Specifically, the Agency states that it is possible that some hyperplastic and/or metaplastic lesions would not be evident in a 28-day study. The Agency argues that in such a situation the 28-day study would be followed by a request to obtain results from a 90-day study and therefore that the selection of the 90-day study at this stage provides a better chance of avoiding further animal testing.

86. The Appellant submits that, as it does not currently know what the results of the 28-day study would be, the Agency cannot argue that a 90-day study would be necessary in the future. The Appellant goes further and submits that conducting a

90-day study at this stage is in fact less likely to provide reliable and meaningful results than if it was conducted later, presuming a 90-day was needed at all. The Appellant considers that if a 90-day study is conducted now it will only require a further 90-day, or other studies, to be conducted in the future and therefore, the selection of the 90-day study at this stage is in fact more likely to cause greater suffering to animals.

2.1 Obligation to ensure that testing on vertebrate animals is undertaken only as a last resort

87. The Board of Appeal considers that the Appellant effectively makes two separate arguments on this point. Firstly, the Appellant, and the interveners, claim that under Article 25(1) of the REACH Regulation the Agency is under an obligation to ensure that testing on vertebrate animals is undertaken only as a last resort. Secondly, the Appellant, and the interveners, claim that where the Agency has decided that testing on vertebrate animals is the only option to meet the information requirements identified, the number of animals used in those tests should be kept to a minimum. These two arguments will be addressed in turn.

88. The Board of Appeal will firstly examine the Appellant's claim that the Contested Decision breached the requirement in Article 25(1) of the REACH Regulation that testing on vertebrate animals must be undertaken only as a last resort.

89. The Agency states that Article 25 of the REACH Regulation is contained under Title III of the REACH Regulation entitled '*Data sharing and avoidance of unnecessary testing*'. As a result, the Agency considers that the scope of Article 25 is limited to that Title which sets out the conditions under which registrants should avoid animal testing and how the Agency can assist registrants in sharing data in order to avoid duplication of animal testing.

90. It should be noted however that whilst data sharing is one of the methods employed to avoid unnecessary testing it cannot be assumed to be the only one. The Board of Appeal finds that it cannot be stated that the two parts of the heading of Title III, namely '*data sharing*' and '*avoidance of unnecessary testing*', are inseparably linked. This conclusion is supported by the wording of the first sentence of Article 25(1) of the REACH Regulation which states that '*[i]n order to avoid animal testing, testing on vertebrate animals for the purposes of this Regulation shall be undertaken only as a last resort*'. The Board of Appeal considers that the reference to '*this Regulation*' in Article 25(1) shows that the requirement to avoid unnecessary testing goes beyond the requirement for data sharing only.

91. The Board of Appeal emphasises that the present proceedings concern the Agency's decision to require a study to be performed under Section 8.6.4 of Annex X for which there is no standard information requirement. A requirement for information has in this case been identified by the Agency and the test required to meet that information requirement was likewise prescribed by the Agency. In this respect, other sections of Annexes VII to X differ from Section 8.6.4 of Annex X in that specific information requirements are set out and the performance of a study is not necessarily a prerequisite to meeting the information requirement.

92. During the present proceedings the Agency stated that it is not its task under the compliance check procedure to balance animal welfare considerations with the actual need to fulfil information gaps. The Agency claims that its role is limited to evaluating if the information in registration dossiers meets the information requirements set out in the annexes to the REACH Regulation.

93. Without concluding on the Agency's role generally under the compliance check procedure, the Board of Appeal will assess the Agency's role in relation to Section

8.6.4 of Annex X where a specific information requirement is not set out. The Board of Appeal considers that when the Agency has identified an information gap pursuant to Section 8.6.4 of Annex X and when considering how that gap should be addressed, the Agency must ensure that all reasonable and relevant options have been examined before requiring tests on vertebrate animals.

94. In this respect the Board of Appeal considers that where the Agency requires a test to meet an information requirement it has itself identified under Section 8.6.4 of Annex X, it in effect assumes the responsibility, which in most cases belongs primarily to the registrant, to ensure that testing on vertebrate animals was required as a last resort.

95. If this were not the case, testing on vertebrate animals prescribed under Section 8.6.4 of Annex X could be required by an Agency decision without it being ensured that testing was indeed undertaken only as a last resort. Furthermore, in these circumstances, the Appellant cannot be expected to verify the Agency's decision to ensure that animal testing had been prescribed only as a last resort.

96. The Board of Appeal notes that if a registrant were to make a testing proposal for the provision of the information in Annexes IX or X, the procedure under Article 40 of the REACH Regulation regarding the examination of testing proposals, and in particular the third party consultation, would have been triggered. One of the objectives of that procedure is to avoid unnecessary testing on vertebrate animals. When the test is prescribed by the Agency in a decision, for example under Section 8.6.4 of Annex X, no such procedure takes place and the Agency must therefore pay particular attention to the obligation to undertake testing only as a last resort.

97. The Board of Appeal considers that the Agency's argument that the last resort principle contained in Article 25 of the REACH Regulation does not apply to the present case must therefore be rejected. The Board of Appeal therefore finds that, when considering whether to require a test under Section 8.6.4 of Annex X, the obligation to ensure that vertebrate animal testing is only undertaken as a last resort applies also to the Agency. In this particular case, whilst the Agency points in its submissions to discussions at the MSC regarding the choice of a 90-day study over a 28-day study, there is no evidence that alternative methods, not requiring the use of vertebrate animals, were considered by the Agency to generate the required information.

98. In the case at hand, without concluding on whether any alternative methods would be appropriate in this case, and noting the Agency's observation that no suitable alternative method exists, the Board of Appeal nonetheless finds that the Agency has not demonstrated that in the decision-making process or in the Contested Decision that it attempted to ensure that testing on vertebrate animals was undertaken only as a last resort, in other words that the required information could not have been obtained by other means. Thus, the Agency failed to assess '*all the information which must be taken into account in order to assess a complex situation*' as required by the case-law cited in paragraph 76 above and consequently exceeded its margin of discretion.

99. Consequently, the Board of Appeal finds that there are grounds to annul the Contested Decision as it was taken in breach of the requirement in Article 25(1) of the REACH Regulation for testing on vertebrate animals to be undertaken only as a last resort.

100. Whilst the Board of Appeal could annul the Contested Decision on the grounds given above it will nonetheless consider certain of the Appellant's other claims to assist the Agency in its preparation of a new decision.

2.2 Use of the minimum number of animals

101. In the first part of its fourth plea the Appellant also argues that the Agency's decision to require a 90-day study is not consistent with Article 13 of Directive 2010/63/EU inter alia because it requires the use of more animals than a 28-day study. In particular, the Appellant refers to Article 13(2)(a) of Directive 2010/63/EU which provides that '*[i]n choosing between procedures, those which to the greatest extent meet the following requirements shall be selected: (a) use the minimum number of animals […].*' The Appellant also refers to Recitals 37 and 47 of the REACH Regulation in support of its claim.

102. Recital 37 of the REACH Regulation states that '*if tests are performed, they should comply with the relevant requirements of protection of laboratory animals, set out in [Directive 2010/63/EU]*'. Similarly, Recital 47 of the REACH Regulation states that '*in* accordance *with Directive [2010/63/EU] it is necessary to replace, reduce or refine testing on vertebrate animals […]*' and '*[…] the Commission and the Agency should ensure the reduction of animal testing is a key consideration in the development and maintenance of guidance for stakeholders and in the Agency's own procedures*'.

103. As mentioned in paragraph 80 of this Decision the Board of Appeal observes that Recitals 37 and 47 of the REACH Regulation refer to Directive 86/609/EEC which must now be construed as a reference to Directive 2010/63/EU. Article 13(2) of Directive 2010/63/EU reflects Article 7(3) of Directive 86/609/EEC.

104. The Board of Appeal considers it to be clear that the REACH Regulation reflects the principles of the 3Rs as set out in Directive 2010/63/EU with regard to testing on vertebrate animals.

105. This position is also supported by the Agency's own REACH Practical Guidance on how to avoid unnecessary testing on animals which states that '*[f]urthermore, when new animal testing is necessary, where possible, scientifically sound approaches to the implementation of the 3Rs (reduction, refinement or replacement of animal use) which are already stipulated under the REACH Regulation* should *be used*' (ECHA Practical Guide 10: How to avoid unnecessary testing on animals, Section 4, page 15).

106. The Board of Appeal also notes that Recital 11 of Directive 2010/63/EU states that '*[w]here* no *alternative method is recognised by the legislation of the Union, the numbers of* animals *used may be reduced by resorting to other methods and by implementing testing strategies, such as the use of in vitro and other methods that would reduce and refine the use of animals*'.

107. In view of the above, the Board of Appeal considers that when requiring tests under Section 8.6.4 of Annex X to the REACH Regulation, the Agency should consequently have examined how the fewest number of animals possible could be used to satisfy the objective pursued.

108. It should also be added that although Directive 2010/63/EU cannot be treated as directly imposing any obligations on the Agency, the latter's actions should not run counter to the principles laid down therein. This is necessary for example to avoid a potential conflict at the Member State level as MSCAs could be required to enforce an Agency decision which they may consider to be in conflict with Directive 2010/63/EU or the national laws implementing it. When requiring a test under Section 8.6.4 of Annex X to the REACH Regulation the Agency should therefore consider carefully whether the test in question might face regulatory obstacles and is consistent with the fundamental principles in Directive 2010/63/EU. This is particularly important where the test is unusual and/or it is hard to define the results being sought.

109. The Board of Appeal also considers that the Agency argument that animal lives would de facto be saved by conducting a 90-day study has not been substantiated as the results of a 90-day study are uncertain and may or may not satisfy the objective pursued. The Board of Appeal also rejects as unsubstantiated the Agency's argument that the uncertain results of a 28-day study justify the conduct of a 90-day study, which uses a greater number of animals, the results of which are also uncertain.

110. Furthermore, in the context of decisions made pursuant to Section 8.6.4 of Annex X, the Board of Appeal considers that the Agency cannot merely state that it has had regard to the need to reduce the number of animals used in tests without demonstrating that this had in fact been the case. The Board of Appeal considers that the MSC Minutes do not demonstrate that the need to minimise the number of animals used in the tests was actually considered.

111. The Board of Appeal therefore considers that in the present case, even in the event that the Agency could demonstrate that testing on vertebrate animals was unavoidable, it has nonetheless failed to fulfil its obligation, when proposing tests under Section 8.6.4 of Annex X to the REACH Regulation, to ensure that the test using the fewest animals is employed. The lack of evidence to support the Agency's claim that animal welfare was considered during the decision-making process leads the Board of Appeal to find, in addition, that the Agency failed to assess '*all the information which must be taken into account in order to assess a complex situation*' as required by the case-law cited in paragraph 76 above and in this way exceeded its margin of discretion.

112. Consequently, the Board of Appeal finds that there are grounds to annul the Contested Decision on this point, in addition to the other grounds discussed above.

113. For the sake of completeness, the Board of Appeal will next consider the claims made by the Appellant with regard to proportionality which were also made in the fourth plea.

3. Second part of the fourth plea alleging a breach of the principle of proportionality

114. The Appellant claims in the second part of its fourth plea that the Contested Decision breaches the principle of proportionality, in particular as it imposes substantial testing burdens on the Appellant without a sufficient likelihood that it will provide scientifically meaningful results.

115. As a preliminary observation on this plea, the Board of Appeal observes that the principle of proportionality is a general principle of European Union law that applies also to the Agency. Pursuant to that principle, measures adopted by the Agency must not exceed the limits of what is appropriate and necessary in order to attain the objectives legitimately pursued by the legislation 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 (see for example Case T-96/10 *Rütgers Germany GmbH and Others v ECHA*, judgment of 7 March 2013, not yet reported, paragraph 133).

116. With regards to judicial review of the conditions referred to in the previous paragraph, the EU Courts have highlighted that the Agency has a broad discretion in a sphere which entails political, economic and social choices on its part, and in which it is called upon to undertake complex assessments (see paragraph 66 of this Decision). According to the EU Courts, the legality of a measure contested before it and adopted in that sphere can be affected only if the measure is manifestly inappropriate having regard to the objective which the legislature is

seeking to pursue (see for example Case T-96/10 *Rütgers Germany GmbH and Others v ECHA*, judgment of 7 March 2013, not yet reported, paragraph 134).

117. However, in relation to the 'manifestly inappropriate' criterion set by the EU Courts when conducting a judicial review of the proportionality of a measure, the Board of Appeal underlines the clear differences between itself and the EU Courts. In particular, the latter refrain from substituting their own assessment for that of the EU institution whose decision is being reviewed (see, by analogy, Case C-525/04 P *Spain* v *Commission* [2007] ECR I-9947, paragraphs 60 and 61). However, under Article 93(3) of the REACH Regulation, the Board of Appeal '*may exercise any power which lies within the competence of the Agency […]*'. Thus, the Board of Appeal can inter alia replace a decision under appeal with a different decision. Moreover, in conducting its administrative review of Agency decisions, the Board of Appeal possesses certain technical and scientific expertise which allows it to enter further into the technical assessment made by the Agency than would be possible by the EU Courts. As a result, when examining whether a decision adopted by the Agency is proportionate, the Board of Appeal considers that it should not be limited by the need to establish that the decision is 'manifestly inappropriate' to the objective pursued. In the present proceedings, the Board of Appeal will therefore consider the Appellant's claim that the Contested Decision is disproportionate against the criteria set out in paragraph 115.

118. In the following sections, the Board of Appeal will identify the objective(s) pursued by the Agency in the Contested Decision before examining whether, in the light of those objectives, that Decision is proportionate.

3.1 Objective pursued by the requirement to conduct a 90-day study

119. As an initial part of the analysis of the Appellant's proportionality claims, the Board of Appeal considers it appropriate to examine the objective(s) pursued by the Agency's decision to require the Study.

120. The Agency stated during the proceedings that in its evaluation of a registration dossier it needs to ensure that the dossier complies with Article 1 of the REACH Regulation and, in the case at hand, that in particular the objective that a high level of protection of human health is guaranteed.

121. According to the case law of the EU Courts, it is apparent from Article 1(1) of the REACH Regulation that that Regulation seeks to ensure a high level of protection of human health and the environment including the promotion of alternative methods for assessment of hazards of substances, as well as the free circulation of substances on the internal market while enhancing competitiveness and innovation (see Case C-558/07 *S.P.C.M and Others* [2009] ECR I-5783, paragraph 35). According to the EU Courts, having regard to Recital 16 of the preamble to the REACH Regulation, the legislature established, as the main objective, the first of those three objectives, namely to ensure a high level of protection of human health and the environment (see, to that effect, Case T-96/10 *Rütgers Germany GmbH and Others v ECHA*, judgment of 7 March 2013, not yet reported, paragraph 135).

122. The Board of Appeal observes that although the protection of human health is, together with protection of the environment, the most important of the objectives of the REACH Regulation it must be weighed against the other objectives of the REACH Regulation and EU law more widely (see, by analogy, Case C-504/04 *Agrarproduktion Staebelow GmbH* [2006] ECR I-679, paragraph 37). Furthermore, it is not sufficient for the Agency to invoke the protection of human health without being able to identify the precise objectives in requiring the Study, and how these objectives can serve the protection of human health.

123. More specifically, the Board of Appeal observes that the aim of the dossier compliance check procedure under Article 41 of the REACH Regulation is to ensure that the registration being examined complies with all the relevant information requirements set out in the REACH Regulation.

124. In addition to the overarching aims of the REACH Regulation and the dossier compliance check procedure, it falls to the Board of Appeal to further analyse the precise objectives pursued by the Agency's decision to require the Study.

125. The Agency states in its defence that the 90-day study allows for further investigation of all possible effects which are covered by the standard requirement for such high-tonnage level substances, in order to provide evidence allowing for adequate (both scientifically and with reference to the tiered information requirements) toxicological evaluation and/or risk characterisation. The MSC Minutes reflect the Agency view that '*…for substances with a tonnage band above 1000 [tonnes per annum] the standard information requirement of REACH is a 90-day study*'.

126. The Board of Appeal observes that the Study cannot be considered to be a standard information requirement as the standard information requirement for repeated dose toxicity had been met in this case by a 90-day inhalation study on rats meeting the requirement in Section 8.6.2 of Annex IX to the REACH Regulation. Section 8.6.4 of Annex X requires 'further studies' if one or more of three criteria are met, which the Agency has found to be the case in this instance. Any 'further studies' required must therefore depend on the objective pursued.

127. The Board of Appeal observes that a further objective stated in the Contested Decision is the generation of information on the most sensitive species, the rabbit, in order to address the concern that there is inadequate information for toxicological evaluation and/or risk characterisation of toxicity in adult rabbits and '*that the information in rabbit does not cover the fertility endpoint for the reproductive toxicity information requirement*'.

128. The Board of Appeal finds however that whilst the statements made by the Agency may help to justify the choice of the 90-day study, the lack of clarity regarding the precise toxicological objectives pursued by the Agency's decision to require the Study, for example regarding carcinogenicity, may create uncertainties for the Appellant regarding for example how to design the Study to deliver the information required.

129. The Board of Appeal further observes that during the decision-making process, in the Contested Decision, and in other submissions made during the present proceedings a number of concerns have been mentioned that may go wider than the repeated dose toxicity end-point covered by Section 8.6.4 of Annex X. These include consumer exposure through the rupturing of air conditioning units in car crashes, evidence of damage to the reproductive system, and evidence of damage which may be a precursor of carcinogenic change. For example, the MSC Minutes state that '*[a] 90-day study gives also more reliable indications for possible carcinogenicity and reproductive toxicity […]*'. In addition, the MSC Minutes indicate that at least one MSCA and one MSC member considered carcinogenicity to be relevant to the decision. It is not completely clear to the Board of Appeal which of these issues the Contested Decision was intended to address and which were not relevant.

130. To support the concern about the carcinogenic potential of the Substance, the Agency's defence states that there are several structurally-related compounds which are carcinogenic, the interpretation of hyperplastic and/or metaplastic lesions in the 90-day study is potentially of importance while hyperplasia and/or metaplasia seen in a 28-day study could be a transient response (or may not be evident at all in such a study) and would anyway need to be confirmed (or

followed) by a longer-term (i.e. 90-day) study. However, the Board of Appeal notes that this statement was only made during the present proceedings. The Agency further stated during the proceedings that in relation to hyperplasia and/or pre-neoplastic lesions, it is the Agency's view that the interpretation of such findings (if any) in a 90-day study could be a key issue in determining whether there is a need to conduct a carcinogenicity study.

131. However, if the investigation of carcinogenicity was one of the objectives pursued by the Contested Decision, the Board of Appeal would expect this to have been made explicit in both the decision-making process and the Contested Decision itself. The Appellant has made it clear in its submissions during these proceedings that it does not believe that there is any reason to suspect the Substance of being either a carcinogen or a reproductive toxicant. For example, in its observations on the defence the Appellant stated that the Agency cannot rationally suggest that in the face of negative genotoxicity data and a complete absence of hyperplasia or metaplasia in a 90-day rat study, it would reach conclusions regarding potential carcinogenicity on the basis of hypothetical lesions in a species for which there is a complete absence of data supporting the interpretation of such lesions for human health risk. The Appellant also stated that the PNDT study, which was the trigger for the Study being required, provides no reason to believe that the Substance is likely to display any carcinogenicity or reproductive toxicity, and there is no basis in any of the other existing toxicity data to suggest that it is. The Appellant claims that to suggest otherwise is misleading and contrary to existing precedent. The Appellant was however not given the possibility to comment in this regard during the decision making process as this concern was never made explicit to it as a registrant. Likewise, the MSCAs and MSC did not have the possibility of considering such statements when commenting on the draft decision.

132. In light of the above, the Board of Appeal finds that whilst the broader objectives of the Contested Decision can be identified, the Agency's identification of the precise objectives pursued during the decision-making process, in the Contested Decision itself, and during these appeal proceedings to be confusing. The Board of Appeal finds that the Agency has not demonstrated that it gave sufficient consideration to the precise objectives pursued, in other words what information the Agency was actually seeking to discover from the Study. The lack of clear and precise objectives makes it difficult for the Appellant to design and conduct a study or otherwise provide the information required. Furthermore, the Board of Appeal finds that the precise objectives pursued were not made sufficiently clear during the decision-making process thereby making it impossible for the Appellant to comment in a meaningful manner. In addition, if the consideration of carcinogenicity was an objective pursued but not made explicit in the draft decision circulated to the MSCAs and MSC then the MSCAs and MSC members would not have been able to comment accordingly.

133. The Board of Appeal considers therefore that the aims of the Study were not clearly articulated in the Agency's decision-making process or communicated clearly to the Appellant, and that even now, following an exhaustive appeals procedure, the precise objectives of the Study are not clearly known. The Board of Appeal finds that the fundamental problem with the lack of clarity of the objectives pursued by the Contested Decision is that the Study could be performed and yet the cause of death of the pregnant rabbits in the PNDT study might remain unknown. The overarching objective of protection of human health might therefore not be met. In practice, the Board of Appeal considers therefore that an objective pursued by the Contested Decision should be the generation of information to identify the cause of death of pregnant rabbits in the PNDT study.

134. The Board of Appeal will next examine the proportionality of the Contested Decision. In light of the lack of clarity surrounding the precise objectives pursued the examination of proportionality will work on the basis that the objective

pursued is the protection of human health by identifying the cause of death of pregnant rabbits in the PNDT study. The Board of Appeal will examine the various arguments related to the appropriateness of the Study before considering whether the Contested Decision is the least onerous option to satisfy the objective(s) pursued. The Board of Appeal will also briefly conclude on the necessity for the Study.

3.2 The appropriateness of the Study to meet the objectives pursued

135. The Board of Appeal will now examine whether the Study was appropriate to achieve the objectives pursued. The Board of Appeal finds, however, that this assessment is made more difficult by the fact that, as noted above, the Agency's precise objectives were themselves not clearly identified.

136. As part of its plea that the Study is disproportionate, the Appellant claims that the test is not appropriate inter alia because the absence of historical control data and the rabbit's susceptibility to stress mean that the Study is likely to lead to false positives. In addition, in its second plea, the Appellant argues that the Study is inappropriate as it is virtually unprecedented.

137. The Agency stated during the proceedings that in choosing the Study a reasonable balance was struck between the aims pursued and the interests affected, as the concern for human health in view of the precautionary principle which underpins the provisions of REACH Regulation makes the provision of a 90-day study a necessity and there is no reason to expect that it will not provide scientifically meaningful and reliable results. The Board of Appeal observes however that the Agency did not make any arguments based on the precautionary principle beyond this passing reference.

3.2.1 The unprecedented nature of the Study and the lack of historical data

3.2.1.1 Unprecedented nature of the Study

138. As part of its second plea the Appellant claims that the Study is virtually unprecedented. In support of this claim the Appellant submitted statements from four experts. Three of these are employed in CROs and the fourth is a professor of toxicology. The latter, who also participated on behalf of the Appellant at the MSC meeting at which the Substance was discussed, stated in a written submission attached to the notice of appeal that 90-day repeated dose toxicity studies in the rabbit, by inhalation '*[...] are virtually unprecedented in the history of toxicology. To my knowledge only 3 such studies have ever been reported and the studies were conducted over 20 years ago.*'

139. This view was repeated by the three experts working at different CROs whom the Appellant contacted for the purposes of the present proceedings. Two of the experts state that the laboratories for which they work have not conducted long-term repeat dose inhalation studies in the rabbit in the past 15 years (and possibly even longer) and 25 years, respectively. They both also observe the lack of historical control data, one of them expressing the view that '[…] *there is little or no useful data to allow interpretation of any unexpected findings*'.

140. The third expert also stated that '*[r]abbit inhalation studies are rarely performed*' and that 'there *is little experience anywhere in running studies for as long as 90 days with rabbits*'.

141. Finally, one of the three experts also stated that '*[…] such studies are so unusual that our…* Licence *would not permit us to run such studies in [EU Member* State*] without amending our Project Licence which would need a very strong scientific reason.*'

142. During the proceedings, ECEAE submitted a report by a toxicologist, submitting evidence on its behalf, which supports ECEAE's and the Appellant's contention that the 90-day inhalation study in the rabbit is unprecedented.

143. The experts' statements reflect comments made by the Appellant during the decision-making process. For instance, in letters dated 17 September 2010 and 21 December 2010, by which the Appellant commented on the draft versions of the Contested Decision, the Appellant informed the Agency that it had contacted several CROs regarding the Study, and that none of them had conducted such studies on industrial chemicals with rabbits.

144. The Agency has submitted literature evidence dating from 1979 to 1989 of seven studies that, it claims, illustrate that rabbit sub-chronic studies by inhalation are possible. The Agency accepts that the experimental designs are not directly comparable to the Study but notes that the key element of exposure (inhalation) is the same.

145. The Board of Appeal notes that whilst the Agency has identified inhalation studies on rabbits in the literature provided, these studies are not the same as the Study nor have they been conducted in the last 24 years. Furthermore, the Agency has not contested the evidence presented by the CROs contacted by the Appellant nor the expert providing evidence on behalf of the Appellant. In light of the evidence provided by the Appellant and uncontested by the Agency, the Board of Appeal finds therefore that the Study is unprecedented.

3.2.1.2 Lack of historical control data

146. The Board of Appeal observes that a consequence of the unprecedented nature of the Study is the lack of historical control data. The arguments of the parties on this point will therefore now be examined.

147. The Appellant submits that historical data is used to determine if specific effects are caused by the test article or are attributable to confounding factors caused by non-specific effects associated with, for example, the method of exposure. The Appellant notes that, without historical control data, false positive and false negative results cannot be readily identified and data adapted and interpreted accordingly. As such, without historical control data, the results of a study may be misunderstood and/or over- or under-interpreted. The Appellant submits that a 90-day study such as the one required by the Agency, carried out in isolation from any relevant historical data would be scientifically redundant and of no benefit whatsoever in understanding the toxicological issues raised regarding the Substance. The Appellant states that, amongst other things, this is because it will not be possible to assess the importance of the data in a wider perspective, in particular its significance to human health risk assessment.

148. The Agency notes that there is an absence of historical control data for rabbits used in 90-day inhalation testing, such as may be used to aid the interpretation of any findings. The Agency also notes that the OECD TG 413 requires the use of historical data or concurrent data demonstrating that the 'vehicle of exposure' does not interfere with the outcome of the study, and that the provision of other historical data is merely an option. In this case, the vehicle of exposure to the substance would be air, and so concurrent control data for air-exposed animals would be provided. Thus, the Agency claims that the OECD TG 413 does not require the provision of historical control data in this case.

149. The Agency also notes that the results of the inhalation study on pregnant rabbits (the 22-day PNDT study) were analysed by the Appellant without historical control data being provided. The Agency states that the results obtained were clearly dose dependent and the Appellant was able to identify, without mentioning

historical data, adverse cardiac pathology in the histopathological examination from the organs selected in the rabbit developmental toxicity study, on the basis of dose-response relationship. Thus, according to the Agency, the Appellant itself has already proved that it is entirely possible to interpret studies without historical control data.

150. The Board of Appeal finds that, in the context of the Study, the absence of historical control data may make it more difficult to interpret the results of an unprecedented study. The Board of Appeal finds the Agency's argument that OECD TG 413 does not require historical control data could be misleading. OECD TG 413 has normally been applied to tests on rodents for which there is no shortage of historical control data. In any case, as testing on rodents is less likely to provide false positive and false negative results any absence of historical control data would be less important. As these arguments are to an extent hypothetical, and whilst not decisive in the Board of Appeal's deliberations, they nevertheless add to the Board of Appeal's concerns over the appropriateness of the Study. The Board of Appeal considers that this aspect should therefore have been more thoroughly considered by the Agency before it concluded that the Study was appropriate to achieve the objective pursued. Thus, the Agency failed to assess '*all the information which must be taken into account in order to assess a complex situation*' as required by the case-law cited in paragraph 76 above.

3.2.2 Choice of Species

3.2.2.1 Most significant for human risk assessment

151. The Contested Decision states that the Study is to be performed on the rabbit which is '*much more sensitive to toxicity from* [the Substance]*, as compared with the rat.*' To this end, the Agency relied on its Guidance on information requirements and chemical safety assessment Chapter R.7a: Endpoint specific guidance (R.7.5.4.1, page 321, May 2008). It provides that *'[s]tudies on the most sensitive animal species should be selected as the significant ones, unless toxicokinetic or toxicodynamic data show that this species is less relevant for human risk assessment.*'

152. The Appellant accepts that the rabbit may be the most sensitive species but argues further that the rabbit's sensitivity is more likely to be species-specific, and not relevant to the risk posed to human health.

153. The Appellant submits that without more specific research on the issue, it cannot be concluded that the rabbit is the most significant species. The Appellant submits that it is precisely the need to answer this question that underpins why testing should be carried out on a step-by-step basis and that requiring a 90-day study is at this stage premature.

154. The Appellant continues that without first understanding the answers to questions in relation to the toxicity of the Substance, a 90-day study is more likely to: (a) be poorly designed and executed; (b) not provide the information sought by the Agency; and (c) not answer the more nuanced and complex questions regarding sub-chronic toxicity of the Substance.

155. The Board of Appeal notes that in these proceedings the terms 'significant' and 'appropriate' have been used interchangeably by the Appellant and the Agency and are interpreted in this context as meaning the same thing. The Board of Appeal finds that, bearing in mind the importance of the most appropriate or significant species to the hazard assessment and risk characterisation of the Substance, in this case, where the Agency is proposing an unprecedented Study under Section 8.6.4 of Annex X to the REACH Regulation, it is incumbent on it to

consider which is the most appropriate species for the study identified and justify its decision accordingly.

156. On the basis of the facts and evidence presented, however, the Board of Appeal observes, and without taking a position on the Agency's findings on the issue of the most sensitive animal species, that the Agency did not sufficiently address the issue of the most appropriate (or significant) species for assessing any risks that the Substance may pose to human health during its decision-making process or in the Contested Decision. The Board of Appeal notes that effects were seen in the 22-day PNDT study on rabbits that were not seen in a 90-day sub-chronic study on rats. The Board of Appeal would therefore expect, in this particular case, attention to be given to whether there were species-specific effects.

157. In particular, the Board of Appeal finds that the Agency has not shown, in its draft decision, the Contested Decision, other documents it produced during the decision-making process, or during these proceedings, evidence of the reasons which led it to conclude that the rabbit, as the most sensitive species, was also the most appropriate (or significant) species for conducting the Study. In this respect, the Board of Appeal also finds that the Agency failed to assess '*all the information which must be taken into account in order to assess a complex situation*' as required by the case-law cited in paragraph 76 above.

3.2.2.2 The inherent nature of the rabbit and the generation of false positive results

158. As part of its fourth plea, the Appellant, supported by the interveners, argues that it is 'common knowledge' amongst toxicologists that rabbits refuse food when stressed; to support this position the Appellant also submits the professional opinions of three CROs contacted on its behalf. As a result, the Appellant claims that there is a significant risk that a 90-day rabbit study may generate false positives.

159. The Agency argues that such a concern is not supported by the experience with such studies in the relevant literature presented by the Agency. The Agency claims that in all the cases encountered during its literature search, experimental data were found to show that there were substance-specific effects on the rabbits, thus demonstrating that the 90-day inhalation study in rabbits can be used to yield interpretable results.

160. The Appellant notes that none of the literature data submitted by the Agency is directly comparable to the Study and goes on to dispute some of the conclusions that the Agency draws from them. The Appellant reiterates that rabbits are susceptible to stress and states that the concern regarding false positives cannot be discounted, particularly with a study of this extended period.

161. The Board of Appeal finds that the Agency's arguments in this regard are not convincing. The literature studies mentioned in paragraph 144 above are not recent and there has been evidence presented by the Appellant and ECEAE showing that rabbits can be stressed by sub-chronic inhalation studies and that false positives are a distinct possibility. The Board of Appeal finds the evidence presented by the Appellant and ECEAE, showing that rabbits are stressed during such tests, more convincing. Whilst substance-specific effects on rabbits were seen in previous studies this does not negate the possibility that rabbits are susceptible to stress and that false positives can occur as a result. This may be one reason why no long term inhalation tests have been conducted in rabbits in the recent past. These arguments are, however, to an extent hypothetical. Whilst not decisive in the Board of Appeal's deliberations, they nevertheless add to the Board of Appeal's concerns over the appropriateness of the Study. The Board of Appeal considers that this should therefore have been more thoroughly considered

by the Agency before it concluded that the Study was appropriate to achieve the objective pursued. Thus, the Agency failed to assess '*all the information which must be* taken *into account in order to assess a complex situation*' as required by the case-law cited in paragraph 76 above.

3.2.3 The problems related to commissioning such a study

162. The Appellant states that none of the three CROs contacted by it had conducted a 90-day inhalation study in the rabbit. The Agency states, however, that two CROs that it contacted stated that the Study would be possible and that they would be willing to conduct it.

163. The Appellant notes that the CROs referred to by the Agency are commercial entities and that their 'willingness' to carry out a study for commercial gain is no indication that the study itself is likely to bear reliable scientific results. The Appellant maintains that in theory it may be possible to carry out the Study, nonetheless significant doubts remain as to its ability to produce meaningful results.

164. ECEAE has also questioned whether the Appellant would be given permission by any competent national authority to conduct the Study given the requirements of Directive 2010/63/EU.

165. The Board of Appeal firstly notes that the Agency is not required in every case to contact CROs to check whether it is possible to carry out a specific study. In fact, the Agency is to be commended for taking this step in this case. However, the fact that this step was considered necessary may reflect the unprecedented nature of the Study. Moreover, if the Agency considered it appropriate to investigate whether the Study was feasible, this investigation should have been a thorough one.

166. The Board of Appeal also observes that one of the CROs contacted by the Agency suggested the route of administration as 'inhalation – nose only' while the other stated that due to reasons of animal welfare the route of administration would need to be 'whole body exposure'.

167. The Board of Appeal finds the fact that a CRO is willing to consider performing a test is not a sufficiently rigorous test of whether such a study should be commissioned and, furthermore, would be approved by the relevant national authorities. When the Agency considers requiring an unprecedented study under Section 8.6.4 of Annex X to the REACH Regulation, it cannot leave the problem of both its design and whether it will be approved solely to the Appellant. In this case, it would be particularly problematic for both the Appellant and the CRO conducting the test to design an appropriate testing regime as the objective pursued is not sufficiently clear in terms of the outputs required. National authorities in the country concerned may also not be able to give approval for such a test. For example, in the notice of appeal the Appellant quoted one CRO as stating that without a *'…strong scientific reason…'* for amending the CRO's licence, approval to conduct the Study would not be given.

168. The Board of Appeal is not convinced that a sufficiently strong case has been provided by the Agency in the Contested Decision for approval to conduct the Study to be given in all EU countries. When requiring testing on vertebrate animals, the Agency should therefore consider carefully whether the test in question might face regulatory obstacles. This is all the more necessary where the test is unusual and it is hard to define the results being sought. In view of the unprecedented nature of the Study, the Board of Appeal considers that this should therefore have been more thoroughly considered by the Agency before it concluded that the Study was appropriate to achieve the objective pursued. Thus,

the Board of Appeal finds that the Agency failed to assess '*all the information which must be taken into account in order to assess a complex situation*' as required by the case-law cited in paragraph 76 above.

3.2.4 Findings on the appropriateness of the test to achieve the objective(s) pursued

169. The Board of Appeal finds that whilst the broader objectives pursued by the REACH Regulation and the dossier evaluation process are clear, the precise objective(s) pursued by the Agency in requiring the Study are not (see paragraphs 119 to 134 of this Decision). This lack of clarity poses problems for the Appellant both in designing an appropriate study and in providing the information required. The Board of Appeal further concludes that the Study is unprecedented and there are credible grounds to doubt whether it would yield useful results. These grounds include, for example, the lack of information over whether the rabbit is the most appropriate species for such a study, and less decisively, uncertainty over the implications of the lack of historical control data and the inherent nature of the rabbit as a test species for such a study. The Board of Appeal observes furthermore that there may be problems in commissioning the Study.

170. More importantly, the Appellant could conduct a 90-day rabbit study and therefore be in compliance with the Contested Decision and yet the toxicity of particular concern (i.e. the death of pregnant rabbits in the PNDT study) might not have been identified nor sufficiently characterised. It is incumbent on the Agency to ensure that any study or studies it requires pursuant to Section 8.6.4 of Annex X to the REACH Regulation would have a realistic probability of satisfying the objective(s) pursued and the Board of Appeal has concerns over whether the Study would do so. For the reasons given above the Board of Appeal is not satisfied that the Study was appropriate to achieve the aim of protecting human health, which was the overall objective pursued by the Agency, or the more precise objective of identifying the cause of death of pregnant rabbits in the PNDT study.

171. The Board of Appeal therefore considers that the Agency has failed to demonstrate that it correctly exercised its discretion in evaluating whether the Study was appropriate to achieve the objectives pursued and indeed did not make it clear what precise objectives it was pursuing. In particular, with regards to its evaluation of the appropriateness of the Study, the Board of Appeal considers that the Agency failed to take into consideration all the relevant factors and circumstances surrounding the conduct of the Study to achieve the objective pursued. Specifically, the Agency failed to assess '*all the information which must be taken into account in order to assess a complex situation*' as required by the case-law cited in paragraph 76 above.

3.3 Adoption of the least onerous measure

172. The Board of Appeal has already found that the Agency failed to demonstrate that the test was appropriate, failed to ensure that testing was undertaken as a last resort and failed to ensure that the minimum number of animals were used. The appeal could be decided on those grounds alone. However, the Board of Appeal considers it necessary, to assist the Agency in preparing a new decision, to discuss certain of the Appellant's other claims related to the proportionality of the Contested Decision, and in particular whether the Study was the least onerous measure that could have been taken to satisfy the objective(s) pursued.

3.3.1. The Study as the least onerous measure

173. As part of its first plea, the Appellant argues that a 28-day study would have answered the scientific questions raised by the Agency regarding the Substance. The Appellant and the interveners also stated that a step-wise approach would have been a less onerous and more appropriate way of achieving the objectives pursued.

174. The Agency states that even for substances registered in a tonnage band of 100 tonnes or more per year, per manufacturer/importer, a sub-chronic toxicity study (90-day) is a standard requirement pursuant to section 8.6.2 of Annex IX to the REACH Regulation.

175. The Agency continues that, in principle, for a dossier registering a substance in quantities of 100 tonnes or more, the 28-day study cannot be used to replace the information requirement for a 90-day study. Only in very specific circumstances described in the second column of Section 8.6.2 of Annex IX, may a 28-day study be sufficient to waive the need for a 90-day study.

176. In addition, the Agency states that the 90-day study provides additional information which may not necessarily be obtained from the 28-day study. In the current case, the Agency states that it, together with the MSC, took the view that the 90-day study provides more sensitive detection of toxicity than a 28-day study, and that it is intrinsically more capable of detecting effects associated with longer exposure which are relevant to human health, including evidence of damage to the reproductive system and evidence of damage which may be a precursor of carcinogenic change.

177. The Agency states, in effect, that the 90-day study was the only option available to it as it was the only study that would produce the results that it is seeking. This is contested by the Appellant and the interveners.

178. The Board of Appeal observes that, in accordance with the case-law cited in paragraph 115 above, when the Agency has a choice between several appropriate measures that will meet the objectives pursued, recourse should be had to the least onerous. The Board of Appeal will therefore firstly examine whether the Agency had other, less onerous, options available to it which would have achieved the objective pursued.

179. As noted in paragraphs 66, under Section 8.6.4 of Annex X, the Agency has a broad margin of discretion as to the study or studies it requires to further examine the toxicology of particular concern identified with regard to the Substance.

180. The Board of Appeal does not accept the Agency's argument that the 90-day Study was in this case the only possible option. In particular, the Board of Appeal has already found that the Agency did not clearly identify the precise objectives of the Study. It is therefore difficult, if not impossible, to rule out the possibility that other tests would provide the information it was seeking before the results of such tests were known.

181. The Board of Appeal also considers that in this particular case there are a number of options that the Agency could have considered to examine the toxicity of particular concern before arriving at its conclusion. These options, which are not mutually exclusive, include a 90-day sub-chronic toxicity study in rabbits by inhalation, a short-term repeated dose toxicity study in rabbits by inhalation (28-day), further toxicokinetic investigations of the behaviour of the Substance, examining species-specific effects in the rabbit and pregnant rabbits, a step-wise approach, and an integrated testing strategy.

182. In this context, the Board of Appeal has also already found in paragraph 97 of the present Decision that, pursuant to Article 25(1) of the REACH Regulation, in examining the options available to it when an information gap has been identified

under Section 8.6.4 of Annex X, the Agency must ensure that testing on vertebrate animals is undertaken only as a last resort. In that sense the Board of Appeal has already found that the Agency has not demonstrated that it adequately evaluated the use of methods that do not entail testing on vertebrate animals.

183. Without itself examining whether methods which do not require testing on vertebrate animals would be suitable to achieve the objective pursued by the Agency in this specific instance, the Board of Appeal finds that it is clear that in general such alternative methods would be less onerous than a 90-day rabbit study, and therefore should have been investigated.

184. With regards to the possibility of requiring a 28-day study, the Agency states that it doubts that a study of that length would be able to provide sufficient certainty on the toxicological issues of concern and therefore could result in the need for further tests to be performed. The Board of Appeal considers however that this statement is flawed. Firstly, the Board of Appeal considers that the evidence presented to it shows that there is doubt over whether a 90-day or a 28-day study will satisfy the objective pursued. In other words, either study, both studies, or neither study may provide the information required. Given this uncertainty, the Agency is obliged to choose the least onerous option available. Secondly, the Board of Appeal believes this Agency statement is also scientifically flawed as the Agency is simply assuming that the results of the 28-day study will not meet the objectives pursued to justify the decision to immediately require the 90-day study. The Board of Appeal considers that the Agency has a duty to require the least onerous method of satisfying the objective pursued, and doubt over the effectiveness of one option is not sufficient justification for moving to a more onerous one where similar doubts also exist.

185. In view of the above, the Board of Appeal considers that the Agency has not established that the 90-day study was the least onerous way to achieve the objectives pursued. Furthermore, the Agency has not demonstrated that it fully considered whether less onerous options of achieving the aim were available to it and whether they would meet the objective(s) pursued.

186. In particular, in view of the uncertainties regarding the appropriateness of the Study and the lack of clarity as to the precise objectives, the Board of Appeal considers that the Agency should have considered the use of a step-wise approach to achieve the objectives pursued. The Board of Appeal will therefore turn its attention to the possible use of a step-wise approach.

3.3.2 Step-wise approach to achieve the objective pursued

187. In the notice of appeal the Appellant proposes that the Agency should postpone the decision requiring a 90-day study to be performed until the Appellant has completed a 28-day study in order to ensure that a 90-day study is indeed necessary and likely to generate reliable results. The Appellant maintains that the 28-day study is technically feasible, scientifically justified and involves fewer animals. As all the information sought by the Agency might be provided by a 28-day study, the Appellant contends that the Contested Decision has been adopted prematurely. In its subsequent observations, the Appellant developed its argumentation and stated, inter alia, that a 28-day study would have the same aims as a 90-study, and in particular, it would reveal the toxicity of particular concern, including indications for adverse effects on reproductive organs and all major tissues.

188. Both interveners also argue for a step-wise approach. DuPont maintains that the evaluation process under the REACH Regulation is similar to a tiered approach while ECEAE considers that such an approach is built into the REACH Regulation

and notes that a step-wise approach is a well-recognised principle of toxicology. Furthermore, ECEAE refers to the integrated testing strategy, as described in the Agency's Guidance on information requirements and chemical safety assessment.

189. The Agency argues however that it is not possible to employ a step-wise approach in this case. More specifically, the Agency maintains that such an approach is not envisaged by Section 8.6.4 of Annex X, and there is no other legal requirement for a step-wise regulatory approach. In addition, the Agency claims that such an approach would be in direct conflict with the primary objective of the REACH Regulation, which is gathering data on substances, and would paralyse the Agency's decision-making procedure.

190. The Board of Appeal notes that it is incumbent on registrants to update their registration dossiers if new information becomes available or is required, for example, following a dossier evaluation decision or when a higher tonnage is reached. It is therefore essential that the Agency is able to conduct a compliance check of registrations under the dossier evaluation procedure at any time to ensure continued compliance with the requirements placed on registrants by the REACH Regulation. Furthermore, the REACH Regulation does not limit the number of compliance checks that can be conducted on a registration dossier. In fact, the Contested Decision states '*[t]his compliance check decision does not prevent ECHA from initiating further compliance checks on the present dossier at a later stage*'.

191. The Board of Appeal also refers to the Agency's Guidance on information requirements and chemical safety assessment. This provides, inter alia, for an integrated testing strategy that foresees in the context of a repeated dose toxicity study that '*[...] the results of one study are evaluated before another study is initiated*'. According to this guidance, the strategy seeks to '*ensure that the data requirements are met in the most efficient and humane manner so that animal usage and costs are minimised*.' It also establishes a framework so that '*[...] informed decisions can be made on the need for further testing*' (Guidance on information requirements and chemical safety assessment, Chapter R.7a: Endpoint specific guidance, R.7.5.6.1, page 292, November 2012 Version 2.0).

192. In light of the foregoing, the Board of Appeal finds that the Agency's arguments that a step-wise approach is in this case not possible are inconsistent both with the REACH Regulation and its own guidance. Moreover, the Board of Appeal finds the Agency's arguments based in essence on administrative convenience to be unconvincing.

193. Accordingly, the Board of Appeal finds that in certain circumstances it falls on the Agency to consider whether an integrated and step-wise approach to testing may be appropriate. This might be the case, for example, where there is a significant degree of scientific uncertainty as to the feasibility and appropriateness of a study or where the objective(s) pursued may need to be refined in light of information received.

194. It should be borne in mind that a step-wise approach may mean that the testing strategy takes longer to complete and this could have implications for the protection of human health and the environment. The Board of Appeal notes that in the present case, however, the Appellant has addressed the toxicity of particular concern, to a certain extent, by ensuring that the relevant Derived No-Effect Level (hereinafter 'DNEL') reflects the result of the rabbit PNDT study; risk management measures should therefore limit the possible adverse effects of the Substance on human health. In deciding whether to employ a step-wise approach, with the consequent timing implications, the adequacy of risk management measures with regard to the protection of human health and the environment should also be taken into account by the Agency.

195. In the interests of clarity the Board of Appeal would like to stress that a step-wise approach is not a standard requirement that must be considered by the Agency in all evaluation decisions following a compliance check. In most cases the information requirements for registration purposes are clear and set out in Annexes VII to X to the REACH Regulation. In such cases it is up to the registrant to decide how to meet the information requirements including by taking a step-wise approach, if appropriate.

196. In the present case, in light of the uncertainties over, for example, the cause of the toxicity of particular concern as seen in the rabbit PNDT test, the most appropriate species, the suitability of the rabbit for long-term inhalation studies, and how a 90-day repeated dose toxicity test by inhalation on rabbits (an unprecedented test) should be conducted, the Board of Appeal finds that a step-wise approach might have been less onerous than a 90-day test. Furthermore, a step-wise approach would also have been more likely to generate the information needed to identify the toxicity of particular concern, less likely to result in the unnecessary use of vertebrate animals, and offer greater scientific rigour. Although the Agency should therefore have carefully considered this option, there is no evidence in this case that it in fact did.

3.4. Necessity for the Study

197. As regards the necessity for the Contested Decision, which is another part of the proportionality test cited at paragraph 115, the Board of Appeal agrees with the Agency on the need to address the concerns raised by the results of the rabbit PNDT study on the Substance. However, in light of the Board of Appeal's findings in this Decision with regard to the appropriateness of the Study and whether the least onerous option to meet the objectives pursued has been prescribed, the Board of Appeal finds that the necessity, at this point in time, for the specific Study required in the Contested Decision has not been demonstrated. The Board of Appeal observes, however, that if concerns over the appropriateness of the Contested Decision are adequately addressed and the Study is shown to be the least onerous option to satisfy the objectives pursued, for example as part of a step-wise approach, then it may be possible for the Agency to demonstrate the necessity for the Study.

3.5 Findings of the Board of Appeal on the proportionality of the Contested Decision

198. The Board of Appeal agrees with the Agency's conclusion that further information on the Substance is required following the result of the PNDT study on rabbits. However, as noted in paragraph 170, the Appellant might conduct the Study, and so comply with the Contested Decision, but the information provided as a result might not clarify the toxicity of particular concern identified in the Contested Decision. Thus, while the Board of Appeal accepts that further information is required, the Study does not have a realistic probability of providing the information required to identify the toxicity of concern and so it is not appropriate to meet the objective pursued. As a result, the Contested Decision fails to meet the first requirement of the proportionality test set out in paragraph 115 above. The Board of Appeal notes that the Appellant states that it has taken account of the uncertainty resulting from the PNDT study in the derivation of the appropriate DNEL in the chemical safety assessment.

199. Whilst further information on the Substance is required, the Board of Appeal finds that the Study may not be appropriate or the least onerous method of providing the information required. Whilst a 28-day repeated dose toxicity by inhalation study on the rabbit may satisfy some or all of the information requirements, the

Board of Appeal is not convinced that this will necessarily be the case either as some of the problems identified with the Study (over 90 days) will also apply to a test over 28 days. Any concerns over whether a 28-day test will deliver meaningful results should also therefore be addressed before such a test is prescribed by the Agency, potentially as part of a step-wise approach.

200. The Board of Appeal finds that there is enough evidence to conclude that there is considerable uncertainty over how and whether the Study can be performed with a realistic probability of useful information being generated. This is because the Study is unprecedented, and because of concerns over the lack of historical control data, uncertainty over the best way to apply the appropriate test methods, the lack of experience in CROs with sub-chronic inhalation studies on rabbits, and the linked problems associated with using rabbits in such tests (for example stress and false positives). The Board of Appeal finds that the Agency should have, as part of its decision making, placed greater emphasis on ensuring that there was a realistic prospect that the Study could be conducted (from both a practical and a regulatory perspective) and would provide useful information to address the information required. The statement in the Contested Decision that the Study was 'technically feasible' should have been supported by more rigorous analysis based on evidence.

201. The Board of Appeal finds that, bearing in mind the objectives of the REACH Regulation, it is unreasonable on the part of the Agency to require a test using vertebrate animals when considerable uncertainty remains over whether the information generated by the Study will be useful. The Agency's statement that the Study would reduce animal testing, compared to starting with a 28-day study, has not been substantiated.

202. The Board of Appeal understands that it may be difficult for the Agency to frame its decision on further information requirements when the cause of an effect is unclear. In such cases the Board of Appeal finds that the Agency should have paid greater attention to the possibility of applying a step-wise approach to both the identification of the information required and how this information should subsequently be generated. This is in accordance with sound scientific principles and also in line with the principles embedded in, and objectives of, the REACH Regulation.

203. The Board of Appeal finds that there is an apparent difference in toxicity between rat and rabbit. However, the Board of Appeal finds that in this particular case when an unprecedented study has been required, greater attention should have been given to considering whether the rabbit is both the most sensitive and the most appropriate species for testing purposes related to repeated dose toxicity and whether there may have been another reason for this apparent inter-species difference in toxicity.

204. Consequently, the Board of Appeal finds that the second part of the Appellant's fourth plea is well founded and that the Contested Decision could be annulled on the grounds given above as it breaches the principle of proportionality.

4. Other pleas raised by the Appellant

4.1. The Appellant's third plea regarding the possible inconsistency with Article 13(2) and fifth plea regarding a possible breach of Article 51(6) and (7)

205. The Board of Appeal has found in favour of the Appellant because the Agency did not correctly apply Article 25(1) of the REACH Regulation, the Agency did not ensure that a minimum number of vertebrate animals would be used, as well as on the grounds that the Contested Decision breached the principle of proportionality. On all of these matters, the Agency failed to assess '*all the*

information which must be taken into account in order to assess a complex situation' as required by the case-law cited in paragraph 76 above and consequently exceeded its margin of discretion.

206. As a result, the Board of Appeal considers that it is not necessary for the purposes of this appeal to consider those pleas of the Appellant's that are not necessary to enable the Agency to take a new decision. In particular, the Board of Appeal will not examine the fifth plea raised in the Appellant's submission of 2 August 2012 that the Contested Decision was adopted in breach of Article 51(6) and (7) of the REACH Regulation. The Board of Appeal also takes account of the fact that the Agency was not given an opportunity to comment on this argument. Likewise, the Board of Appeal does not consider it necessary to examine the Appellant's third plea in which the Appellant claims that the Contested Decision is inconsistent with Article 13(2) of the REACH Regulation.

4.2 First part of the second plea regarding possible inconsistency with Article 13(3) of the REACH Regulation

207. However, the Board of Appeal considers it appropriate to consider the first part of the Appellant's second plea as this may be relevant to the Agency when considering a new decision. In that plea, the Appellant claims that the Contested Decision is inconsistent with Article 13(3) of the REACH Regulation as the test methods identified by the Agency in the Contested Decision (EU TM B.29 or OECD TG 413) apply to rodents but not to rabbits. Accordingly there is no established test method for the Study.

208. The Appellant submits that it is clear that the underlying intention of OECD TG 413 is that the test animals to be used are rodent species and not rabbits. The Appellant quotes point 6 of OECD TG 413, which has been cited in paragraph 8. The Appellant notes that there is no provision within OECD TG 413 for the use of rabbits or anything that facilitates or allows adaptation of the test guideline for testing on rabbits.

209. The Appellant continues that to assume that OECD TG 413 can apply to any species, particularly the rabbit which is not a widely used species for the assessment of general systemic toxicity, is to ignore the explicit text of the test guideline itself and also to ignore the underlying intention of the OECD in drafting the test guideline.

210. The Agency, however, considers that OECD TG 413 covers both studies in rodents and in non-rodent species. The Agency continues that it is clear from section 6 of OECD TG 413 that although the test guideline recommends carrying out such studies on rodents, and preferably on rats, the guideline also accepts that this study can be performed in other species if justified. The Agency continues that there may be circumstances where a deviation from the preferred species would be acceptable, if justified, and that the Contested Decision is such an example.

211. The Agency continues that the Contested Decision clearly states that the Study must be carried out on the rabbit, but by referring to OECD TG 413 it indicates that otherwise the conditions of the test should adhere to the framework provided by the guideline. The Agency disputes the Appellant's claim that using OECD TG 413 would not provide useful results for risk assessment. According to the Agency it is clear that OECD TG 413 can be used as a basis for performing a 90-day sub-chronic inhalation study in rabbits.

212. The Board of Appeal considers firstly that the OECD TG 413 was clearly written with rodents in mind and does not address the use of rabbits in such a test. This is clear from the wording of Section 6 of OECD TG 413 itself, and supported by the title of test method EU B.29, which is based on the OECD document, and refers

specifically to 'rodent species'. It should be noted, however, that, as stated above in paragraphs 64 to 78, the Agency has a margin of discretion under Section 8.6.4 of Annex X to the REACH Regulation to identify 'further studies' to examine the repeated dose toxicity end-point.

213. As neither of the parties has cited any internationally recognised test methods which explicitly apply to a 90-day repeated dose toxicity study by inhalation in the rabbit, the Board of Appeal considers that, based on the evidence submitted in the present proceedings, OECD TG 413 is the most relevant internationally recognised test method for the Study. Consequently, the Board of Appeal considers that the Agency did not make an error in identifying OECD TG 413 as the appropriate test method. However, the Board of Appeal notes that OECD TG 413 would nonetheless require substantial adaptations to be made in order for it to be used on rabbits and this should be borne in mind by the Agency when requiring the test to be conducted on rabbits in the future.

214. Consequently, the Board of Appeal rejects the first part of the Appellant's second plea as unfounded.

CONCLUSIONS

215. The Board of Appeal finds that under Section 8.6.4 of Annex X to the REACH Regulation the Agency was entitled to require further information on the Substance because of concerns arising from the results of a pre-natal developmental toxicity study on rabbits. The Board of Appeal also finds that under Section 8.6.4 of Annex X the Agency had a margin of discretion to identify the most appropriate study or studies to examine these concerns. However, the Agency also had a duty to exercise that discretion in accordance with the provisions of the REACH Regulation and with EU law in general. In the present case, the precise objectives to be achieved were not made clear in the decision-making process, in the Contested Decision or during the appeals procedure. The Board of Appeal considers that the fact that the Study could be conducted yet there remains a realistic probability that the objective of protection of human health might not be promoted to be important in this regard. The lack of clarity over the precise objectives also meant that the design of the Study could not be properly considered by the Appellant. In addition, the required Study is unprecedented, which should have meant that the Agency paid particular attention to ensuring that the basis for its action was carefully considered from a proportionality perspective.

216. On the basis of the extensive and detailed information submitted to it during the present proceedings, the Board of Appeal has formed the view that the main objectives pursued in this case are the protection of human health and to identify the cause of the death of pregnant rabbits in the PNDT study. The Agency concluded that there was toxicity of particular concern and that there was insufficient information for toxicological evaluation and/or risk characterisation. However, trying to identify the cause of death of animals in a test is a very different challenge from identifying a study to address a particular end-point. In evaluation decisions addressing a standard information requirement it would be usual to require a study which addresses a particular end-point. In this particular case, it is the Board of Appeal's view that the Agency required the performance of a test with open-ended objectives, related to the repeated dose toxicity end-point. This is a different objective to the generation of information to identify specifically the cause of death of pregnant rabbits in the PNDT study.

217. Pursuant to Article 25(1) of the REACH Regulation, the Board of Appeal finds that one of the responsibilities that the Agency should have assumed in this case is to ensure that testing on vertebrate animals is only undertaken as a last resort.

Where the Agency itself is considering whether to place demands on a registrant for testing on vertebrate animals under Section 8.6.4 of Annex X it must also comply with Article 25(1) of the REACH Regulation with regard to the 'last resort' principle. In this case the Agency did not take all necessary steps to ensure that testing on vertebrate animals was undertaken only as a last resort. Furthermore, the Agency failed to ensure a test using the minimum number of vertebrate animals would be used.

218. For the reasons explained in this Decision, and having regard in particular to the unprecedented nature of the Study, the Board of Appeal concludes that in the present case the Agency's decision breaches the principle of proportionality. As detailed in this Decision, there are reasons to doubt that the Study will actually provide useful information, as it is not certain for example:

(i) whether and how the required Study can be performed;

(ii) whether the results arising would be reliable and useful; and

(iii) whether the Study is the least onerous way of addressing the concerns identified as, for example, a step-wise approach may be more appropriate in this particular case.

219. The Board of Appeal's findings do not mean that a requirement for a registrant to perform a 90-day sub-chronic test by inhalation in rabbits is a breach of the proportionality principle per se. However, in order for such a requirement to comply with the proportionality principle, the concerns over its appropriateness and whether it is the least onerous option to achieve the objective(s) pursued must be addressed. To this end, the Board of Appeal considers that the Agency should examine whether an investigation of the death of pregnant rabbits in the PNDT study requires a rigorous step-wise approach. Furthermore, if the objectives pursued were wider than considering the cause of death of pregnant rabbits in the PNDT study, in addition to possible reproductive toxicity, for example carcinogenic effects, then this must be made explicit in the decision making process and the decision itself. This will ensure that the Appellant, the MSCAs and the MSC can comment appropriately. Furthermore, it allows the design of a study or studies (or other ways of generating the information required) that reflect the objectives pursued.

220. The Board of Appeal finds that the Contested Decision breaches Article 25(1) of the REACH Regulation in that it failed to ensure testing on vertebrate animals was a last resort. In addition, the Agency failed to ensure a test using the minimum number of vertebrate animals would be used. Furthermore, the Board of Appeal finds that the Contested Decision breaches the principle of proportionality. Common to all of these failings, the Agency failed to assess '*all the information which must be taken into account in order to assess a complex situation*' (see paragraph 76) exceeding in this way its margin of discretion.

221. Consequently, the Board of Appeal annuls the Contested Decision, as sought by the Appellant, and remits the case to the Agency for a re-examination, in accordance with Article 93(3) of the REACH Regulation.

Refund of the appeal fee

222. In accordance with Article 10(4) of Commission Regulation (EC) No 340/2008 on the fees and charges payable to the European Chemicals Agency pursuant to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) (OJ L 107, 17.4.2008, p. 6), the appeal fee shall be refunded if the appeal is decided in favour of an appellant.

223. As the Board of Appeal has decided the appeal in favour of the Appellant in the present case, the appeal fee shall be refunded on that basis.

ORDER

On those grounds,

THE BOARD OF APPEAL

hereby:

Annuls Part 2 of Section II of Decision CCH-D-0000001396-72-03/F of 22 March 2011 adopted by the European Chemicals Agency, to the extent that the Agency required the Appellant to conduct a 90-day repeated dose toxicity study in the rabbit by inhalation (Test Method B.29 of Regulation (EC) No 440/2008 or OECD Test Guideline 413) as modified by the additional clinical pathology and histopathological evaluations to evaluate effects on reproductive organs; specifically as described in OECD Test Guideline 416, paragraphs 29-32, 39, 41-45.

Remits the case to the competent body of the Agency for further action consistent with this Decision.

Orders the refund of the appeal fee.

Mercedes ORTUÑO
Chairman of the Board of Appeal

Sari HAUKKA
Registrar of the Board of Appeal