Reports of Cases

JUDGMENT OF THE GENERAL COURT (Fourth Chamber)

29 March 2023 *

(REACH – Evaluation of registration dossiers and compliance check of information provided by registrants – Request for further studies for the purposes of the registration dossier for dimethyl ether – Pre-natal developmental toxicity study – Extended one-generation reproductive toxicity study – Dose-range finding study – Article 51(7) of Regulation (EC) No 1907/2006 – Animal testing – Article 25 of Regulation No 1907/2006 – Manifest error of assessment – Proportionality)

In Case T-868/19,

Nouryon Industrial Chemicals BV, established in Amsterdam (Netherlands),

Knoell NL BV, established in Maarssen (Netherlands),

Grillo-Werke AG, established in Duisburg (Germany),

PCC Trade & Services GmbH, established in Duisburg,

represented by R. Cana, Z. Romata and H. Widemann, lawyers,

applicants,

v

European Commission, represented by R. Lindenthal and K. Mifsud-Bonnici, acting as Agents,

defendant,

supported by

Kingdom of Denmark, represented by M. Søndahl Wolff, acting as Agent,

by

Kingdom of the Netherlands, represented by M. Bulterman, A. Hanje and J. Langer, acting as Agents,

by

* Language of the case: English.

Kingdom of Sweden, represented by A. Runeskjöld, C. Meyer-Seitz, M. Salborn Hodgson, H. Shev, H. Eklinder, R. Shahsavan Eriksson and O. Simonsson, acting as Agents,

and by

European Chemicals Agency (ECHA), represented by M. Heikkilä, W. Broere, S. Mahoney and N. Herbatschek, acting as Agents,

interveners,

THE GENERAL COURT (Fourth Chamber),

composed, at the time of the deliberations, of S. Gervasoni, President, L. Madise (Rapporteur) and P. Nihoul, Judges,

Registrar: M. Zwozdziak-Carbonne, Administrator,

having regard to the order of 30 April 2020, *Nouryon Industrial Chemicals and Others* v *Commission* (T-868/19 R, not published, EU:T:2020:171), by which the applicants' application for interim measures was dismissed,

having regard to the written part of the procedure,

further to the hearing on 15 September 2022,

gives the following

Judgment [1]

1 By their action based on Article 263 TFEU, the applicants, Nouryon Industrial Chemicals BV, Knoell NL BV, Grillo-Werke AG and PCC Trade & Services GmbH, seek annulment of Commission Implementing Decision C(2019) 7336 final of 16 October 2019 on the compliance check of a registration of dimethyl ether, adopted on referral by the European Chemicals Agency, on the basis of Article 51(7) of Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) ('the contested decision').

Background to the dispute

...

4 The applicants are manufacturers or importers of dimethyl ether established in the European Union or exclusive representatives acting on behalf of manufacturers of that chemical substance established outside the European Union. In accordance with the principle of 'no data, no market' laid down in Article 5 of Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending

[1] Only the paragraphs of the present judgment which the Court considers it appropriate to publish are reproduced here.

Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC (OJ 2006 L 396, p. 1) ('the REACH Regulation'), the applicants, together with other registrants, on 30 November 2010, filed with the European Chemicals Agency (ECHA) an application for registration of dimethyl ether for manufactured or imported quantities of 1 000 tonnes or more per year per manufacturer or importer. Akzo Nobel Industrial Chemicals BV, subsequently renamed Nouryon Industrial Chemicals ('the first applicant'), acted as the lead registrant for the joint registration dossier, in accordance with Article 11 of the REACH Regulation.

5 On 29 March 2016, ECHA initiated a procedure for a compliance check of the registration on the basis of Article 41 of the REACH Regulation.

...

15 In the operative part of the contested decision, the Commission concluded that the registration of dimethyl ether did not comply with the information requirements as regards two different effects relating to reproductive toxicity, namely effects on pre-natal development and effects on one-generation reproduction (Article 1 of the contested decision). Consequently, in the contested decision, the Commission requires the registrants to provide information on the effects of dimethyl ether, based, in the first place, on a pre-natal developmental toxicity study as referred to in Section 8.7.2. of Annex X to the REACH Regulation (hereinafter, the annexes to the REACH Regulation are referred to solely by their Roman numeral), to be carried out, via inhalation, on a second animal species, namely rabbits (Article 2 of the contested decision) and, in the second place, on an extended one-generation reproductive toxicity study as referred to in Section 8.7.3. of Annex X, to be carried out on rats via inhalation. As regards that second study, the Commission states that a preliminary 'dose-range finding' study, conducted for example in accordance with the guideline of the Organisation for Economic Co-operation and Development (OECD) for the testing of chemicals No 421, intended in particular to detect possible narcotic-type effects (namely, sleepiness), must be carried out, in particular in order to determine whether it is necessary, depending on whether or not such effects are observed at any of the concentrations chosen for that extended study, to include, in that study, cohorts 2A and 2B which are intended specifically for the developmental toxicity study (Article 3 of the contested decision). The contested decision requires the applicants to submit, within 36 months of the date of notification of that decision, an updated version of the registration of dimethyl ether to ECHA, together with the results of the requested studies and, where relevant, to submit an update of the chemical safety report (Article 4 of the contested decision).

Forms of order sought

16 In the application, the applicants claim that the Court should annul the contested decision and order the Commission to pay the costs.

17 The Commission contends that the Court should dismiss the action as unfounded and order the applicants to pay the costs.

18 The Kingdom of Denmark, the Kingdom of the Netherlands, the Kingdom of Sweden and ECHA, intervening in support of the Commission, contend that the Court should dismiss the action as unfounded. The Kingdom of the Netherlands and ECHA also contend that the applicants should be ordered to pay the costs of the proceedings.

Law

The first plea in law, alleging that the Commission infringed Article 51(7) of the REACH Regulation by adopting the contested decision which covers aspects on which the Member State Committee reached a unanimous agreement

19 As a preliminary point, it is necessary to note the circumstances in which the Commission was called upon to adopt the contested decision.

20 The contested decision was adopted under the procedural mechanism laid down in Article 51 of the REACH Regulation, which provides:

‘1. [ECHA] 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 [ECHA].

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

4. If [ECHA] receives a proposal for amendment, it may modify the draft decision. [ECHA] 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. [ECHA] 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, [ECHA] 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).

8. An appeal may be brought, [before the Board of Appeal of ECHA], against [ECHA’s] decisions under paragraphs 3 and 6 of this Article.’

21 After ECHA sent its revised draft decision to the Member State Committee (see paragraph 8 above), the latter agreed that it was necessary to require information on studies carried out under Sections 8.7.2. and 8.7.3. of Annex X, as requested by ECHA, namely a pre-natal developmental toxicity study carried out on rabbits, representing a second animal study species, and an extended one-generation reproductive toxicity study carried out on rats. However, it did not reach a unanimous agreement as regards the content of the second of those studies.

...

23 In that situation, referring to Article 51(7) of the REACH Regulation, ECHA sent its revised draft decision to the Commission so that the latter could adopt a final decision in the case. If, conversely, the Member State Committee had reached a unanimous agreement on the revised draft decision of ECHA, the latter would have '[taken] its decision accordingly', in accordance with Article 51(6) of the REACH Regulation, in other words ECHA would itself have adopted the final decision.

...

27 Contrary to what is claimed by the applicants, it is not apparent from Article 51(7) of the REACH Regulation that if a disagreement within the Member State Committee concerns only part of ECHA's draft decision, ECHA must divide the final decision into one part that would be adopted by it on the basis of paragraph 6 of that article and into another part, the subject matter of the disagreement, which would be adopted by the Commission in accordance with paragraph 7 of that article.

28 Article 51 of the REACH Regulation, which is a procedural article and is entitled 'Adoption of decisions under [registration] dossier evaluation', lays down in its various provisions the conditions for the examination of draft decisions prepared by ECHA for that purpose, first by the competent authorities of the Member States and then, where appropriate, by the Member State Committee, and it also determines the conditions for the adoption of the final decisions that are the subject of its heading in different situations. Paragraph 7 of that article refers to the specific situation where there is a lack of unanimous agreement within that committee on the 'draft decision' of ECHA, by providing that, in that case, the Commission is to prepare 'a draft decision'.

29 In interpreting that provision, it is necessary to consider not only its wording but also the context in which it occurs and the objectives pursued by the rules of which it is part (judgments of 17 November 1983, *Merck*, 292/82, EU:C:1983:335, paragraph 12, and of 19 July 2012, *ebookers.com Deutschland*, C-112/11, EU:C:2012:487, paragraph 12). Reference is made in that regard to the literal, contextual (or systematic) and teleological interpretations respectively.

30 In the first place, in the context of a literal approach, it must be observed that that procedural provision does not state that the Commission should prepare a draft decision 'on the aspects on which the Member State Committee has failed to reach a unanimous agreement'. In addition, Article 41(3) of the REACH Regulation, on the 'compliance check of registrations', which, for its part, determines the subject matter of a draft decision and then of a decision, which may be drawn up when such a compliance check is carried out, states in the last sentence that 'such a decision', that is to say, the decision following a draft decision, 'shall be taken in accordance with the procedure laid down in [Article 51]'. None of the wording of the paragraphs of Article 51, where a 'draft decision' is mentioned, gives the impression that the purpose of those drafts differs from the purpose referred to in Article 41(3), namely an invitation to provide any information necessary to bring the registration into compliance. That wording therefore supports the interpretation that Article 41(3) of the REACH Regulation refers to the adoption of a single decision at the end of the procedure laid down in Article 51 of that regulation.

31 In the second place, in the context of a contextual approach, it must be observed that Article 51(6) of the REACH Regulation gives ECHA the power to adopt a decision the draft of which has been communicated to the Member State Committee only if, within 60 days of that communication,

that committee reaches a unanimous agreement on that draft (see paragraph 20 above). It follows that, in the absence of such unanimous agreement within that period, as in the present case, ECHA loses the power to adopt a decision under Article 51 of the REACH Regulation following a compliance check in respect of a registration and that, consequently, the Commission's power provided for in Article 51(7) of that regulation covers all of the aspects which have been examined by the Member State Committee, whether or not they gave rise to unanimous agreement within that committee.

32 In the third place, from a teleological perspective, in the light of the principle of good administration laid down in the Charter of Fundamental Rights of the European Union and of the principle of legal certainty, which is a general principle of EU law that requires, inter alia, that those concerned know precisely the extent of the obligations which are imposed on them (see, to that effect, judgment of 29 March 2011, *ArcelorMittal Luxembourg* v *Commission* and *Commission* v *ArcelorMittal Luxembourg and Others*, C-201/09 P and C-216/09 P, EU:C:2011:190, paragraph 68 and the case-law cited), it is more rational that, in the event of a disagreement within the Member State Committee, that is to say, under Article 76 of the REACH Regulation, within one of the components of ECHA, the Commission is to exercise its power over the entire compliance check in respect of the registration under consideration, in order to prevent the preparation, and then second-level review, of assessments regarding the evaluation of the effects and hazards of a chemical substance from being shared amongst several bodies (ECHA and the Commission, the Board of Appeal of ECHA and the General Court, respectively), which might lead to inconsistencies, when those assessments concern the same dossier for the registration of a substance and must retain their overall consistency.

33 Therefore, Article 51(7) of the REACH Regulation can be understood only as meaning that any disagreement within the Member State Committee on an aspect of a draft ECHA decision examined in the context of a compliance check of registrations constitutes a disagreement on that draft considered as a whole, which confers on the Commission the power to prepare a new draft decision evaluating a registration dossier and then to adopt a final decision in that regard under a 'comitology' procedure. Consequently, the Commission is right to submit that that provision does not limit its power solely to the specific parts of the draft ECHA decision which is the subject of a disagreement within the Member State Committee, but grants the Commission the power to take a decision on all the aspects addressed in that draft decision.

34 That analysis is not called into question by the applicants' other arguments.

…

36 The applicants also state that they would have benefited from more guarantees if the final decision, as regards the aspects on which the Member State Committee had reached a unanimous agreement, had been adopted by ECHA. The review carried out by the Board of Appeal of ECHA differs from the review carried out by the General Court and is not limited, as in the case of the latter, to verifying whether there are manifest errors.

37 As the Commission and the Kingdom of the Netherlands submit in essence, the distinction drawn between situations in which the Board of Appeal of ECHA may intervene in the process for the review of an administrative decision requesting registrants to supplement the dossier for the registration of a chemical substance and situations in which there is no provision for that board to intervene, and the consequences which may ensue as regards the scope of that review, stem from the FEU Treaty and from the legislative framework of the REACH Regulation, more specifically

from Article 51 thereof, which lays down, in one case, which is the subject of paragraph 6 of that article, an ECHA decision, and in the other case, which is the subject of paragraph 7 of that article, a Commission decision where there is a disagreement within the Member State Committee, that is to say, a disagreement within ECHA. First, the legislature provided for the possibility, for the Board of Appeal, as an administrative body of ECHA empowered to review a first decision adopted by ECHA, to exercise any power which lies within the competence of ECHA or to remit the case to the competent body of ECHA for further action, in accordance with Article 93(3) of the REACH Regulation. Secondly, Article 263 TFEU provides that Commission decisions are to be subject to judicial review by the EU judicature. The different nature of those reviews justifies the procedural differences between them and the different powers of the bodies which exercise them.

38 In that regard, the EU law applicable in the present case has the effect of differentiating between, on the one hand, an administrative review carried out, with regard to a first ECHA decision, by a higher authority, namely the Board of Appeal of ECHA, and, on the other hand, a judicial review in which, in the context of an action for annulment based on Article 263 TFEU, the review is carried out by the EU Courts in respect of a Commission decision. It has already been held that, in an action for annulment brought under Article 263 TFEU, the review carried out by the EU Courts consists, where it involves the assessment of highly complex scientific and technical facts, as may be so in the present case, in reviewing whether they are vitiated by a manifest error, a misuse of powers or whether the author of the decision clearly exceeded the limits of its discretion (see judgment of 20 September 2019, *BASF Grenzach* v *ECHA*, T-125/17, EU:T:2019:638, paragraph 87 and the case-law cited; see also, to that effect, judgment of 15 October 2009, *Enviro Tech (Europe)*, C-425/08, EU:C:2009:635, paragraph 47). That limitation does not apply to the intervention by the Board of Appeal of ECHA, which is also a component of ECHA, as has already been pointed out. In that intervention, the Board of Appeal does not confine itself to reviewing the legality of the decision taken by ECHA, in view of, in particular, the latter's discretion, but examines, in the context of the criteria set out in the legislation, whether it is appropriate to review the assessments which ECHA made. That is why the EU legislature made sure to include, in the composition of that Board of Appeal, persons with the necessary technical and scientific expertise to carry out that new assessment and why the nature of that board's review of the scientific and technical assessments previously carried out within ECHA differs from the nature of a review carried out by the EU judicature (see, to that effect, judgments of 20 September 2019, *BASF Grenzach* v *ECHA*, T-125/17, EU:T:2019:638, paragraphs 88 and 89, and of 20 September 2019, *Germany* v *ECHA*, T-755/17, EU:T:2019:647, paragraph 55). It is not for the Court to call into question that difference and to confer on itself the powers of a body such as the Board of Appeal of ECHA (see, to that effect and by analogy, judgment of 25 July 2002, *Unión de Pequeños Agricultores* v *Council*, C-50/00 P, EU:C:2002:462, paragraphs 44 and 45).

39 Furthermore, although the applicants have not raised a plea of illegality against Article 51(7) of the REACH Regulation, that difference in the review of the assessment of highly complex scientific and technical facts cannot make it possible, contrary to that provision as interpreted in the present judgment (see paragraph 33 above), to restrict the Commission's power to take a decision, pursuant to that provision, on all the aspects of a draft ECHA decision that has been submitted to the Member State Committee where a disagreement arises within that committee on one or more aspects of that draft decision.

...

The second plea in law, alleging that the Commission infringed Article 13(3) of the REACH Regulation and made a manifest error of assessment by requesting tests which run counter to the applicable legal requirements and which are not technically feasible

41 The applicants submit that the Commission infringed Article 13(3) of the REACH Regulation and made a manifest error of assessment by requesting 'test[s] at concentrations that could produce effects while being safe' and, more specifically, as regards the extended one-generation reproductive toxicity study, by requesting 'a dose level set to induce some toxicity at the highest dose level'.

...

47 It may be stated, at the outset, that nowhere in the contested decision does the Commission require that concentrations of dimethyl ether for the requested tests be exceeded in such a way as to render those tests dangerous, in breach of the applicable safety rules. It is true that the Commission requests, in the contested decision, in Article 3 of the operative part, that the extended one-generation reproductive toxicity study be conducted at a 'dose level set to induce some toxicity at the highest dose level', moreover by reproducing an instruction which appears, in essence, both in Section 21 of test method B 56 of the regulation on test methods as regards that study and in the second paragraph of Section 1.6.3 of test method B 31 of that regulation as regards the pre-natal developmental toxicity study. However, the Commission expresses that request in the general framework applicable to acute inhalation toxicity tests, by which it is bound, as are the registrants. That framework does recommend that a certain concentration of the tested substance not be exceeded based on that substance's characteristics. The abovementioned two methods, which are explicitly referred to in the operative part of the contested decision, themselves state in their abovementioned provisions: 'the dose levels should be based on toxic effects, unless limited by the physical/chemical nature of the test chemical' (test method B 56) and 'unless limited by the physical/chemical nature or biological properties of the test substance, the highest dose should be chosen with the aim to induce some … toxicity' (test method B 31).

...

49 In that regard, it must be noted that OECD GD 39, the application of which is not disputed by the Commission in its pleadings, states, in paragraph 67, under Section 5.1.4, that 'in the case of potentially explosive test chemicals, care should be taken to avoid conditions favourable for an explosion' and that 'for safety reasons[,] it is generally advisable to not exceed 50% of the [LEL]'. It is apparent from that wording that that limit, in this case 1.65%, is not a universal limit which must not be exceeded under any circumstances. Moreover, in paragraph 61 of the application and paragraph 15 of the reply, the applicants accept that tests on dimethyl ether may be possible up to a maximum of 2%.

50 It follows from the foregoing that the Commission left it to the registrants, of course in conjunction with the laboratories which they might use, to determine the maximum concentration to be used to produce a certain toxicity, but within the limits of the concentrations that might prove dangerous in view of the physicochemical properties of dimethyl ether.

51 It has therefore not been demonstrated in any way that, in the contested decision, the Commission required, contrary to the legally applicable provisions, that dangerous concentrations be reached for acute inhalation toxicity tests.

52 Furthermore, it is apparent from the documents produced by the applicants (Annexes A12 and A13) that there are at least two laboratories which consider that they are capable of carrying out the tests in question at a concentration of 1.65%, or even one of the tests at a concentration of up to 2%. The applicants' argument calling into question the technical feasibility of the studies requested in the contested decision must therefore be rejected.

...

The third plea in law, alleging that the Commission made a manifest error of assessment in requiring tests that do not provide any relevant information on dimethyl ether

...

61 It must first be observed that, of the studies requested in the contested decision, some seek to obtain standard information which, in all cases, it is necessary to provide in the registration dossier for dimethyl ether under Annex X, which is applicable in view of the declared level of manufacture or importation per year per manufacturer or per importer, in quantities of 1 000 tonnes or more. The applicants do not dispute that that is the case for the extended one-generation reproductive toxicity study in its basic configuration including only cohorts 1A and 1B but they argue, for questions on the interpretation of Annexes IX and X, that that is not the case for the developmental toxicity study carried out on a second animal species; the latter argument is rejected in the context of the examination of the eighth plea (see paragraph 168 below). In particular with regard to the studies which in all cases have to be carried out under Annex X, in so far as they seek to obtain standard information, the applicants consider, in essence, as indicated in paragraph 57 above, that the requirements under that annex should not be applied too strictly in order to prevent registrants from being required to provide information that is manifestly irrelevant by carrying out unnecessary tests on animals.

62 In order to examine that argument, it is necessary, first of all, to note the layout and role of the annexes to the REACH Regulation.

...

69 It is apparent from that presentation that the information requested from the registrants under Annexes VII to X, in particular the standard information in column 1 of those annexes, which must in all cases be provided except where such information may be adapted under a provision in column 2, is requested incrementally based on the manufactured or imported quantities of substance. It must also be pointed out that those information obligations concern chemical substances and are intended, as set out in Article 1 of the REACH Regulation, to ensure that the hazards associated with those substances, when manufactured, placed on the market and used, are known and that those substances, when used, do not adversely affect human health or the environment. Consequently, in the light of the potential hazards of chemical substances and applying the precautionary principle, but also taking into account the objective of preventing unnecessary testing on vertebrate animals, that principle and that objective both also being referred to in that article, the legislature has already made choices in order to request registrants to carry out studies on vertebrate animals only if those studies appear relevant in view of the relevant quantities of substance. Moreover, Annex XI also provides for possibilities of adaptation which are additional to those provided for in column 2 of Annexes VII to X, which the registrants may put forward if they consider that a study provided for in those annexes serves no purpose.

70 Since the applicants do not challenge the validity of those choices, in other words the legality of the provisions under which, in the contested decision, they were requested to carry out studies, more specifically the provisions in Annex X, and since, under the plea currently being examined, they do not rely on the possibility of adaptation provided for in Annex XI, they cannot validly claim that they are not required to carry out studies which must in all cases be carried out under Annex X, which concerns the obtaining of standard information, on the ground that those studies are irrelevant.

...

72 Since the applicants' argument of principle referred to in the last sentence of paragraph 57 above, which advocated a purely legal analysis, has been rejected, it must be observed that, for the remainder, the arguments put forward in support of the third plea seek to call into question the Commission's assessment relating to the usefulness of the various studies that it requested, in so far as those studies are not in any event mandatory under Annex X, that is to say, the Commission's assessment relating to the usefulness of the part of the extended reproductive toxicity study including cohorts 2A and 2B in order to assess developmental neurotoxicity and relating to the usefulness of the preliminary dose-range finding study.

73 Such an assessment falls within the category of assessments of highly complex scientific and technical facts by an administrative authority. As has already been pointed out in paragraph 38 above, if the EU judicature is called upon to examine such assessments, it must confine itself to ascertaining whether they are vitiated by a manifest error or a misuse of powers, or whether that authority has manifestly exceeded the limits of its discretion. In that regard, it has been consistently held that, in order to establish that the administrative authority made a manifest error in assessing those elements such as to justify the annulment of the contested measure, the evidence adduced by the applicant must be sufficient to make the factual assessments used in that measure implausible. Without prejudice to that examination of plausibility, it is not for the Court to substitute its assessment of highly complex facts for that of the institution which adopted the measure (see, to that effect, judgments of 12 December 1996, *AIUFFASS and AKT* v *Commission*, T-380/94, EU:T:1996:195, paragraph 59, and of 19 September 2019, *Arysta LifeScience Netherlands* v *Commission*, T-476/17, EU:T:2019:618, paragraph 87 and the case-law cited). In the light of the scientific and technical arguments put forward by the applicants, it is therefore necessary to ascertain whether those arguments render implausible the Commission's assessment that, by carrying out the studies in conditions intended to ensure that the tests are not dangerous, that is to say by not exceeding a concentration of 1.65%, or even 2%, it is possible that some toxicity may manifest itself at the highest dose (for the sake of simplicity, reference will be made hereinafter only to the value of 1.65%).

74 Before beginning that verification, it is appropriate, however, to state the position taken by the Court with regard to the applicants' request, expressed in the application, that the Court appoint an independent expert responsible for examining and clarifying certain complex scientific issues, which, moreover, relate to most of the applicants' pleas, as they stated in the reply. The General Court would have availed itself of that possibility, provided for in Article 25 of the Statute of the Court of Justice of the European Union, only if that had proved necessary in order to decide whether or not certain pleas were well founded, given the nature of the review which it carries out in respect of the assessment of highly complex scientific and technical facts by an administrative authority, referred to in paragraph 73 above. However, as shown in the assessment of the present and the following pleas, that has not proved necessary in the present case.

...

83 In the third place, as regards the arguments relating to specific uses in humans and relating to the assessment and management of risks in that regard, which seek to demonstrate that, where the substance is used in its industrial, professional or domestic applications, it cannot lead to narcotic effects in humans, the Commission, the Kingdom of Denmark, the Kingdom of the Netherlands, the Kingdom of Sweden and ECHA rightly state that registration of a substance is not intended solely to ensure non-hazardous use in its normal applications, but also to know about the substance and its effects on living organisms and on the environment as such, in other words, to know its intrinsic characteristics, which may require tests recreating conditions that differ from those in its normal applications. In that regard, Annexes VII to X specifically define the information to be provided in order for the intrinsic properties of a substance to be known. Therefore, the fact that a substance is not hazardous for humans in its normal applications, in particular the fact that there are no narcotic effects in humans during such uses, even if established, cannot remove the need to carry out studies which are required under Annexes VII to X, unless an adaptation is possible under Annex XI. ECHA also rightly states that applications of a substance may evolve over time, whereas its intrinsic properties remain the same. In addition, in the present case, the applicants' demonstration is based in particular on the premise of a NOAEC of 2.5%, which is uncertain for reproductive toxicity studies, as noted in paragraph 81 above.

...

88 In the light of the foregoing, even though there may be uncertainties as to the concentration at which harmful effects of dimethyl ether could be observed in reproductive toxicity studies and even though there are scientific debates in that regard, it does not appear to be a manifest error of assessment to have requested the tests listed in the contested decision, particularly as the Commission requested that the extended one-generation reproductive toxicity study be preceded by a preliminary dose-range finding study. In that context, it cannot be ruled out that the tests requested in the contested decision demonstrate toxicity below the concentration level of 1.65% which, in OECD GD 39, it is recommended not to exceed. Even if there were no toxicity below that level, those tests would not be futile and would enable the debates referred to above to be settled in part.

...

The fourth plea in law, alleging that the Commission made a manifest error of assessment and infringed column 2 of Section 8.7.3. of Annex X by requiring the addition of cohorts 2A and 2B to the extended one-generation reproductive toxicity study

90 In the fourth plea, the applicants put forward arguments which are divided, in essence, into two parts, one alleging that the Commission erred in law by distorting the scope of the words 'particular concerns' in the second paragraph of column 2 of Section 8.7.3. of Annex X, and the other alleging that it made a manifest error of assessment in finding that dimethyl ether presents 'particular concerns' associated with neurotoxicity on the basis of the first and third indents of that provision.

91 As a preliminary point, it should be noted that column 1 of Section 8.7.3. of Annex X requires, by way of standard information, an extended one-generation reproductive toxicity study covering cohorts 1A and 1B, carried out on a single species. According to the second paragraph of column

2 of that section, the inclusion of cohorts 2A and 2B in an extended one-generation reproductive toxicity study in order to assess developmental neurotoxicity may be required by ECHA, or where appropriate by the Commission, in the event of particular concerns on (developmental) neurotoxicity justified by any of the following:

– existing information on the substance itself derived from relevant available *in vivo* or non-animal approaches (e.g. abnormalities of the [central nervous system], evidence of adverse effects on the nervous or immune system in studies on adult animals or animals exposed prenatally), or

– specific mechanisms/modes of action of the substance with an association to (developmental) neurotoxicity and/or (developmental) immunotoxicity (e.g. cholinesterase inhibition or relevant changes in thyroidal hormone levels associated to adverse effects), or

– existing information on effects caused by substances structurally analogous to the substance being studied, suggesting such effects or mechanisms/modes of action.

...

The first part, alleging that the Commission erred in law by distorting the scope of the words 'particular concerns' in the second paragraph of column 2 of Section 8.7.3. of Annex X

95 The applicants submit that, in so far as the second paragraph of column 2 of Section 8.7.3 of Annex X does not define the concept of 'particular concerns' associated with developmental neurotoxicity, that concept should be defined in the light of the other provisions of the REACH Regulation and point R.7.6.2 of Chapter R.7a of the ECHA guidance entitled 'Guidance on Information Requirements and Chemical Safety Assessment' ('the ECHA Guidance'). On those bases, they are 'strong' concerns showing a certain level of severity revealed by serious and severe neurotoxicity effects.

...

103 Having noted those interpretations, it appears that, despite the lack of a precise definition as to what is a particular concern on developmental neurotoxicity, within the meaning of the second paragraph of column 2 of Section 8.7.3. of Annex X, it follows from the very wording used in that provision (see paragraph 91 above), in particular from the word 'concern', which, in the context in question, means 'worry', that, for such a concern to exist, information of a certain nature held by the registrants or by the competent authority must establish that the substance in question has developmental neurotoxic effects, irrespective of effects that result from a more general toxicity, or even merely gives reasonable grounds for fearing that that substance might have those effects. Where there is such information, the purpose of the extended one-generation reproductive toxicity study including cohorts 2A and 2B is then to clarify, confirm or disprove the developmental neurotoxic effects of the substance.

104 Therefore, as the Kingdom of the Netherlands submits, in a specific case, it is for the competent authority, in the absence of a spontaneous initiative to that effect by the registrants, to consider, in the light of the existing data and on the basis of the principles referred to in paragraph 103 above, whether concerns on developmental neurotoxicity exist.

105 Thus, in order to reach the conclusion that dimethyl ether gives rise to 'particular concerns', the Commission was not required, contrary to what the applicants claim (see paragraph 95 above), to put forward evidence, at that stage, that dimethyl ether has serious and severe neurotoxicity effects. It is sufficient that one of the elements mentioned in the first to third indents of the second paragraph of column 2 of Section 8.7.3. of Annex X exists and gives reasonable grounds for fearing that there are sufficiently serious or severe harmful effects that justify the possibility of developmental neurotoxicity.

...

The fifth plea in law, alleging that the Commission infringed column 1 of Section 8.7.3. of Annex X to the REACH Regulation, and Article 25 of that regulation, by requiring that the extended one-generation reproductive toxicity study be preceded by a preliminary dose-range finding study

...

133 Section 8.7.3. of Annex X must therefore be interpreted as authorising the Commission to request a preliminary dose-range finding study to be carried out prior to an extended one-generation reproductive toxicity study and it therefore appears that the Commission did not err in law in that regard.

134 In the second place, as regards the argument that, in Section 8.7.1. of Annex VIII, it is stated that a dose-range finding study is not required if a pre-natal developmental toxicity study is already available, it is appropriate to note the following, already mentioned in paragraph 65 above. In accordance with the 'Guidance note on fulfilling the requirements of Annexes VI to XI', which is the introductory part of Annex VI, 'for the lowest tonnage level, the standard requirements are in Annex VII, and every time a new tonnage level is reached, the requirements of the corresponding Annex have to be added' and 'for each registration the precise information requirements will differ, according to tonnage, use and exposure'. In addition, the introductory parts of Annexes VIII, IX and X each indicate that 'the information required in column 1 of this Annex is additional to that required in column 1 of [the preceding annexes]'. It may be inferred from this that Annexes VII to X are not superfluous as regards column 1, in the sense that column 1 of the annex with the highest figure does not repeat all the elements in column 1 of the preceding annexes. However, if the pieces of information to be provided corresponding to the standard requirements in column 1 of the relevant annexes are added to each other when the level of quantity manufactured or imported per year per manufacturer or per importer reaches the level referred to in a given annex, the possible adaptations mentioned in column 2 of those annexes are not retained from one annex to the next, unless they are repeated (the opposite principle). An adaptation may be envisaged for a certain level of manufacture or importation and no longer be envisaged at a higher level.

135 In other words, since, in view of the quantities declared in the present case, the level referred to in Annex X, namely that of substances manufactured or imported per year per manufacturer or per importer in quantities of 1 000 tonnes or more has been reached, the applicants cannot rely on the adaptation possibilities set out in column 2 of Section 8.7. of Annex VIII, which refers to the level of substances manufactured or imported in quantities of 10 tonnes or more, in order to reject a request made to them under Annex X. The applicants' argument that the Commission infringed that provision is, therefore, unfounded and the error of law alleged in that regard has not been established.

136 In the third place, as regards the argument that the carrying out of a preliminary dose-range finding study disregards the objective, set out in Article 25(1) of the REACH Regulation, of carrying out tests on vertebrate animals only if there is no other solution, the following factors must be taken into consideration.

137 First, the objective of avoiding animal testing must be applied in the light of the other principles underlying the REACH Regulation, in particular in the light of the precautionary principle. Article 1(3) of the REACH Regulation states that its provisions 'are underpinned by the precautionary principle'. It has been held that that principle entails that, where there is uncertainty as to the existence or extent of risks to human health, protective measures may be taken without having to wait until the reality and seriousness of those risks become fully apparent (see, to that effect, judgments of 5 May 1998, *National Farmers' Union and Others*, C-157/96, EU:C:1998:191, paragraphs 63 and 64, and of 1 October 2019, *Blaise and Others*, C-616/17, EU:C:2019:800, paragraph 43 and the case-law cited). It has also been held that a correct application of the precautionary principle in respect of a substance whose effects are not fully determined presupposes (i) identification of the potentially negative consequences for health of the proposed use of the substance at issue, and (ii) a comprehensive assessment of the risk to health based on the most reliable scientific data available and the most recent results of international research (see by analogy, as regards substances used in plant protection products, judgment of 22 December 2010, *Gowan Comércio Internacional e Serviços*, C-77/09, EU:C:2010:803, paragraph 75 and the case-law cited). In the present case, the request for a preliminary dose-range finding study in the context of the carrying out of an extended one-generation reproductive toxicity study has made it possible to reconcile the precautionary principle with the requirement to reduce animal testing. As the Commission explains, since no narcotic effect would be found at concentration levels that are compatible with carrying out hazard-free tests, cohorts 2A and 2B would not be included in the extended one-generation reproductive toxicity study.

...

The sixth plea in law, alleging that the Commission infringed Article 41 of the REACH Regulation and Annex XI to that regulation, on the ground that the contested decision does not allow the applicants to remedy the non-compliance of the registration of dimethyl ether by submitting adaptations of the studies requested in that decision

142 The applicants complain, in essence, that the contested decision obliges them, as well as the other registrants, to have the studies mentioned in that decision carried out by providing the results of those studies (see paragraph 15 above), without allowing them to provide appropriate information from other sources instead. According to the applicants, following a decision such as the contested decision, adopted pursuant to Article 41 of the REACH Regulation, ECHA must examine any information submitted by the addressees of that decision, as indicated in Article 42 of that regulation. Article 13(1) of the REACH Regulation itself states that 'information on intrinsic properties of substances may be generated by means other than tests, provided that the conditions set out in Annex XI are met'. Column 2 of Section 8.7. in Annexes IX and X also provides for the possibility of adaptation of what is requested exclusively in the contested decision.

...

144 As has already been held, the relevant general provisions of the REACH Regulation and the objective of limiting animal testing set out in those general provisions mean that a registrant whom ECHA has requested to supplement its registration dossier on the basis of a study involving animal testing has, in so far as possible from a scientific and technical perspective, the option and even the obligation to respond to that request by providing appropriate information in the light of the grounds on which that request was based, but from sources other than that study. It has also been held that, in such a situation, ECHA is under a corresponding obligation to check the compliance of such alternative information with the applicable requirements and, more specifically, to determine whether it is to be classified as adaptations in accordance with the rules laid down in the relevant annexes to the REACH Regulation (see, to that effect, judgment of 21 January 2021, *Germany* v *Esso Raffinage*, C-471/18 P, EU:C:2021:48, paragraphs 132 to 136).

145 There is no reason why a different solution should be used where, as in the present case, the decision requesting the registrant to supplement its registration dossier on the basis of a study involving animal testing is adopted, in the context of the procedure laid down in Article 51 of the REACH Regulation on the adoption of decisions under dossier evaluation, not by ECHA, but by the Commission because of the lack of unanimity in the Member State Committee on the draft ECHA decision.

146 In spite of the wording used in the imperative in the contested decision for the purposes of the carrying out of the studies referred to in the operative part of that decision, the latter cannot therefore be interpreted, in its regulatory context well known to the applicants, as prohibiting them and the other registrants from responding to that decision by proposing in the technical dossier, in accordance with the relevant general provisions of the REACH Regulation and its objective of limiting animal testing, appropriate information in the light of the grounds which justified the requests for studies on animals made in that decision, but from sources other than those studies. It must, however, be stated that those adaptations of the tests requested in the contested decision must not be manifestly unreasonable in the light of the possibilities for adaptation provided for in the REACH Regulation, in particular in Annex XI, and in view of the exchanges which have already taken place between the registrants, ECHA and the Commission. Otherwise, ECHA could simply, in order to prevent the procedure from becoming unjustifiably prolonged, once more find that the registration is not compliant, but without having to use the procedure laid down in Article 42(1) of the REACH Regulation, which itself refers in that regard to Article 41 of that regulation (see, to that effect, judgment of 8 May 2018, *Esso Raffinage* v *ECHA*, T-283/15, EU:T:2018:263, paragraphs 62 and 112).

...

148 It follows from the foregoing that, contrary to what the applicants submit, the contested decision does not prohibit them from proposing adaptations of the studies requested in that decision. The sixth plea must therefore be rejected.

The seventh plea in law, alleging that the Commission infringed Article 41 of the REACH Regulation and Annex XI to that regulation on the ground that, in the contested decision, the Commission prematurely rejected any adaptation of the studies requested in that decision

...

152 It is apparent, first, that the position taken in the contested decision concerning a possible adaptation of the pre-natal developmental toxicity study carried out on rabbits, based on the similar ongoing study concerning the structural analogue diethyl ether, responded to a need to state reasons in the light of the arguments put forward by the applicants and, secondly, in view of what is set out in paragraphs 144 to 146 above, that such a position does not lead to the advance rejection of any adaptation proposal made in the technical dossier following the contested decision in relation to the studies requested in that decision, in particular any proposal that would use the results of the pre-natal developmental toxicity study carried out on rabbits in respect of dimethyl ether which became available in the meantime, where serious arguments are put forward in support of that proposal in addition to those already put forward prior to the adoption of the contested decision.

153 The seventh plea, based on the argument that the Commission prematurely rejected any adaptation of the studies requested in the contested decision, must therefore be rejected.

The eighth plea in law, alleging that, by requesting that a pre-natal developmental toxicity study be carried out on rabbits, the Commission made a manifest error of assessment, failed to take into account all the relevant information and infringed column 2 of Section 8.7.2. of Annex IX

...

The first part, alleging that the Commission erred in law by infringing Annex IX

...

160 It must be concluded from that, in the light of the general principle of construction and application of Annexes VII to X, that the standard requirements and adaptations under Annex X are independent of those in Annex IX. It may already be inferred that the rules in Annex IX for Section 8.7.2. do not make it possible to determine which are the standard requirements and possible adaptations defined in Annex X for that section, which are applicable for a substance manufactured or imported in quantities of 1 000 tonnes or more per year per manufacturer or per importer. In that regard, the provision according to which 'the study shall be initially performed on one species' and 'a decision on the need to perform a study at this tonnage level or the next on a second species should be based on the outcome of the first test and all other relevant available data, highlighted by the applicants, which appears in column 2 of Annex IX, means only that the requirement for a study on a second species for a substance manufactured or imported in quantities between 100 tonnes and 999 tonnes per year per manufacturer or per importer may, where the conditions for carrying out such a study are met, possibly be postponed until such time as the substance comes under the 'next level', namely when the substance is manufactured or imported in quantities of 1 000 tonnes or more per year per manufacturer or per importer.

161 The applicant's allegation that the Commission erred in law for having infringed the provisions of Annex IX has therefore not been established.

The second part, alleging that the Commission made a manifest error of assessment by requesting a pre-natal developmental toxicity study on a second species when the conditions set out in column 2 of Section 8.7.2. of Annex IX were not met

162 In order to assess this second part of the eighth plea, it must be pointed out at this stage of the analysis that no adaptation equivalent to that provided for in column 2 of Section 8.7.2. of Annex IX applies to Annex X in respect of that section, for the reasons set out in paragraphs 159 and 160 above, in particular because column 2 of Annex X is blank for that section. In order to determine the scope of the obligations based on Annex X for Section 8.7.2. and to determine, at the same time, the discretion which the Commission had in that regard, it is next necessary to ascertain which standard requirement is requested in column 1 of Annex X.

163 As stated in paragraph 158 above, the wording of column 1 for Section 8.7.2. is essentially identical in Annexes IX and X in that it refers to 'toxicity study … one species'. As already stated in the same paragraph, those texts, read in isolation, might suggest a mere repetition of the same requirement, that is to say, be interpreted as requiring only that a pre-natal developmental toxicity study be conducted on one species, whether the substance concerned is produced or imported at the levels covered by Annex IX or at the levels covered by Annex X.

164 However, in the light of the general principle of construction and application of Annexes VII to X set out in paragraphs 159 and 160 above, which means that column 1 in one of those annexes is not superfluous in relation to column 1 in the other, there would be no sense in repeating the same standard requirement in column 1. As much as the option of adaptation set out in column 2 may be repeated from one annex to another if that option is valid with regard to different standard requirements set out in different annexes, such a repetition is not conceivable for the same standard requirement already set out in column 1 of a preceding annex for a lower level of production or importation. The requirement in column 1 of Section 8.7.2. of Annex X to have a 'toxicity study … single species' carried out must therefore be interpreted as differing from the requirement set out in similar terms in column 1 of Annex IX for the same section, which can mean only one thing: both studies in question must each concern a different species. In other words, the requirement in column 1 of Section 8.7.2 of Annex X to have a 'toxicity study … one species' carried out must be understood as referring to a study on a species other than that used for the similar study carried out under Annex IX. As no adaptation is provided for in that regard in Section 8.7.2. of Annex X, as stated in paragraph 162 above, it follows that the pre-natal developmental toxicity study carried out on a second species is mandatory where the substance is produced or imported at the levels referred to in Annex X, unless adaptations are possible under the provisions set out elsewhere.

…

On those grounds,

THE GENERAL COURT (Fourth Chamber)

hereby:

1. Dismisses the action;

2. Orders the applicants to bear their own costs and to pay those incurred by the European Commission, including the costs relating to the proceedings for interim relief;

3. Orders the Kingdom of Denmark, the Kingdom of the Netherlands, the Kingdom of Sweden and the European Chemicals Agency (ECHA) to bear their own costs.

Gervasoni Madise Nihoul

Delivered in open court in Luxembourg on 29 March 2023.

[Signatures]