Reports of Cases

JUDGMENT OF THE GENERAL COURT (Ninth Chamber, Extended Composition)

23 November 2022 *

(Environment and protection of human health – Regulation (EC) No 1272/2008 – Classification, labelling and packaging of substances and mixtures – Delegated Regulation (EU) 2020/217 – Classification of titanium dioxide in powder form containing 1% or more of particles of a diameter equal to or below 10 μm – Criteria for classification of a substance as carcinogenic – Reliability and acceptability of studies – Substance that has the intrinsic property to cause cancer – Calculation of lung overload in particles – Manifest errors of assessment)

In Joined Cases T-279/20 and T-288/20 and in Case T-283/20,

CWS Powder Coatings GmbH, established in Düren (Germany), represented by R. van der Hout, C. Wagner and V. Lemonnier, lawyers,

applicant in Case T-279/20,

supported by

Billions Europe Ltd, established in Stockton-on-Tees (United Kingdom), and the other interveners whose names are listed in the annex,[1] represented by J.-P. Montfort, T. Delille and P. Chopova-Leprêtre, lawyers,

by

Ettengruber GmbH Abbruch und Tiefbau, established in Dachau (Germany),

Ettengruber GmbH Recycling und Verwertung, established in Dachau,

represented by R. van der Hout, C. Wagner and V. Lemonnier, lawyers,

and by

TIGER Coatings GmbH & Co. KG, established in Wels (Austria), represented by R. van der Hout, C. Wagner and V. Lemonnier, lawyers,

interveners in Case T-279/20,

* Languages of the cases: German and English.

[1] The list of the other interveners is annexed only to the version notified to the parties.

Billions Europe Ltd, established in Stockton-on-Tees, and the other applicants whose names are listed in the annex,[2] represented by J.-P. Montfort, T. Delille and P. Chopova-Leprêtre, lawyers,

applicants in Case T-283/20,

supported by

Conseil européen de l'industrie chimique – European Chemical Industry Council (Cefic), established in Brussels (Belgium), represented by D. Abrahams, Z. Romata and H. Widemann, lawyers,

by

Conseil européen de l'industrie des peintures, des encres d'imprimerie et des couleurs d'art (CEPE), established in Brussels,

British Coatings Federation Ltd (BCF), established in Coventry (United Kingdom),

American Coatings Association, Inc. (ACA), established in Washington, DC (United States),

represented by D. Waelbroeck and I. Antypas, lawyers,

and by

Mytilineos SA, established in Maroussi (Greece),

Delfi-Distomon Anonymos Metalleftiki Etaireia, established in Maroussi,

represented by J.-P. Montfort, T. Delille and P. Chopova-Leprêtre, lawyers,

interveners in Case T-283/20,

Brillux GmbH & Co. KG, established in Münster (Germany),

Daw SE, established in Ober-Ramstadt (Germany),

represented by R. van der Hout, C. Wagner and V. Lemonnier, lawyers,

applicants in Case T-288/20,

supported by

Billions Europe Ltd, established in Stockton-on-Tees, and the other interveners whose names are listed in the annex,[3] represented by J.-P. Montfort, T. Delille and P. Chopova-Leprêtre, lawyers,

by

[2] The list of the other applicants is annexed only to the version notified to the parties.

[3] The list of the other interveners is annexed only to the version notified to the parties.

Sto SE & Co. KGaA, established in Stühlingen (Germany), represented by R. van der Hout, C. Wagner and V. Lemonnier, lawyers,

and by

Rembrandtin Coatings GmbH, established in Vienna (Austria), represented by R. van der Hout, C. Wagner and V. Lemonnier, lawyers,

interveners in Case T-288/20,

v

European Commission, represented in Joined Cases T-279/20 and T-288/20 by S. Delaude, R. Lindenthal and M. Noll-Ehlers and, in Case T-283/20, by A. Dawes, S. Delaude and R. Lindenthal, acting as Agents,

defendant,

supported by

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

by

French Republic, represented in Joined Cases T-279/20 and T-288/20 by T. Stéhelin, W. Zemamta, G. Bain and J.-L. Carré and, in Case T-283/20, by E. de Moustier and W. Zemamta, acting as Agents,

by

Kingdom of the Netherlands, represented in Case T-279/20 by M. Bulterman and C. Schillemans, in Case T-283/20 by M. Bulterman and J. Langer, and in Case T-288/20 by M. Bulterman, J. Langer and C. Schillemans, acting as Agents,

by

Kingdom of Sweden, represented in Joined Cases T-279/20 and T-288/20 by C. Meyer-Seitz and, in Case T-283/20, by O. Simonsson, C. Meyer-Seitz, A. Runeskjöld, M. Salborn Hodgson, H. Shev, H. Eklinder and R. Shahsavan Eriksson, acting as Agents,

by

European Chemicals Agency (ECHA), represented by A. Hautamäki and J.-P. Trnka, acting as Agents,

interveners in Joined Cases T-279/20 and T-288/20 and in Case T-283/20,

by

Republic of Slovenia, represented by V. Klemenc, acting as Agent,

intervener in Case T-283/20,

by

European Parliament, represented by C. Ionescu Dima, W. Kuzmienko and B. Schäfer, acting as Agents,

and by

Council of the European Union, represented by A.-L. Meyer and T. Haas, acting as Agents,

interveners in Joined Cases T-279/20 and T-288/20,

THE GENERAL COURT (Ninth Chamber, Extended Composition),

composed, at the time of the deliberations, of M.J. Costeira (Rapporteur), President, M. Kancheva, T. Perišin, P. Zilgalvis and I. Dimitrakopoulos, Judges,

Registrar: S. Jund and I. Kurme, Administrators,

having regard to the written part of the procedure, in particular the order of 11 March 2022 joining Cases T-279/20 and T-288/20 for the purposes of the oral part of the procedure and the decision closing the proceedings,

further to the hearings on 12 May 2022, in Joined Cases T-279/20 and T-288/20, and on 18 May 2022, in Case T-283/20,

gives the following

Judgment

1 By their actions based on Article 263 TFEU, the applicants, CWS Powder Coatings GmbH ('the first applicant'), Billions Europe Ltd and the other applicants whose names are listed in the annex ('the second applicants') and Brillux GmbH & Co. KG and Daw SE ('the third applicants'), seek annulment of Commission Delegated Regulation (EU) 2020/217 of 4 October 2019 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures and correcting that Regulation (OJ 2020 L 44, p. 1; 'the contested regulation'), as regards the harmonised classification and labelling of titanium dioxide in powder form containing 1% or more of particles of a diameter equal to or below 10 μm.

I. Background to the dispute

2 The applicants are manufacturers, importers, downstream users and suppliers of titanium dioxide.

3 Titanium dioxide is an inorganic chemical substance with the molecular formula TiO_2. It can be found in nature or produced industrially and it is used, in particular in the form of a white pigment, for its colourant and covering properties in various products, such as paints, coating materials, varnishes, plastics, laminated paper, cosmetics, medicinal products and toys.

4 In May 2016, the Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES) (National Agency for Food, Environmental and Occupational Health and Safety (ANSES), France) ('the competent French authority') submitted to the European Chemicals Agency (ECHA), pursuant to Article 37(1) of Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (OJ 2008 L 353, p. 1), a dossier proposing the harmonised classification and labelling of titanium dioxide as a category 1B carcinogen by inhalation (Carc. 1B, H350i) ('the classification proposal').

5 On 31 May 2016, the dossier submitted to ECHA by the competent French authority was published, in accordance with Article 37(4) of Regulation No 1272/2008. A number of parties concerned submitted their comments within the prescribed period.

6 On 14 September 2017, pursuant to Article 37(4) of Regulation No 1272/2008, ECHA's Committee for Risk Assessment ('the RAC') adopted an opinion on titanium dioxide ('the RAC Opinion'). The RAC Opinion, which was adopted by consensus, concluded that the classification of titanium dioxide as a category 2 carcinogen, including the hazard statement 'H351 (inhalation)', was justified.

7 On the basis of the RAC Opinion, the European Commission drew up a draft regulation on the harmonised classification and labelling of, inter alia, titanium dioxide, which was submitted for public consultation between 11 January and 8 February 2019.

8 On 18 February 2020, on the basis of the RAC Opinion, the Commission adopted the contested regulation, by which it proceeded, inter alia, with the harmonised classification and labelling of titanium dioxide (recitals 2 and 5 of the contested regulation).

9 In that regard, first, the contested regulation inserted into Table 3 of Part 3 of Annex VI to Regulation No 1272/2008, which contains the harmonised classification and labelling list, a new row with the chemical name 'titanium dioxide (in powder form containing 1% or more of particles with aerodynamic diameter ≤ 10 μm)', hazard class 'carcinogenicity', hazard category '2', pictogram hazard code 'GHS 08 Wng' and hazard statement code 'H351 (inhalation)' (Article 1(3) of, and Section 2(c) of Annex III to, the contested regulation).

10 In addition, the contested regulation added, in point 1.1.3.1, of Part 1 of Annex VI to Regulation No 1272/2008, the following note (Article 1(3) of, and Section 1(a) of Annex III to, the contested regulation):

'Note W:

It has been observed that the carcinogenic hazard of this substance arises when respirable dust is inhaled in quantities leading to significant impairment of particle clearance mechanisms in the lung.

This note aims to describe the particular toxicity of the substance; it does not constitute a criterion for classification according to this Regulation' ('Note W').

11 Second, the contested regulation added, in Section 1.1.3.2, of Part 1 of Annex VI to Regulation No 1272/2008, the following note (Article 1(3) of, and Section 1(b) of Annex III to, the contested regulation):

'Note 10:

The classification as a carcinogen by inhalation applies only to mixtures in powder form containing 1% or more of titanium dioxide which is in the form of or incorporated in particles with aerodynamic diameter ≤ 10 μm'.

12 Third, the contested regulation inserted, into Part 2 of Annex II to Regulation No 1272/2008, a new Section 2.12 concerning the EUH211 and EUH212 statements that must appear on the label of the packaging of, respectively, liquid and solid mixtures containing titanium dioxide. Section 2.12 is worded as follows (Article 1(1) of, and Annex I to, the contested regulation):

'2.12. Mixtures containing titanium dioxide

The label on the packaging of liquid mixtures containing 1% or more of titanium dioxide particles with aerodynamic diameter equal to or below 10 μm shall bear the following statement:

EUH211: "Warning! Hazardous respirable droplets may be formed when sprayed. Do not breathe spray or mist."

The label on the packaging of solid mixtures containing 1% or more of titanium dioxide shall bear the following statement:

EUH212: "Warning! Hazardous respirable dust may be formed when used. Do not breathe dust."

In addition, the label on the packaging of liquid and solid mixtures not intended for the general public and not classified as hazardous which are labelled with EUH211 or EUH212, shall bear statement EUH210.'

13 Fourth, the contested regulation incorporated, into Part 3 of Annex III to Regulation No 1272/2008, which concerns 'supplemental label elements/information on certain mixtures', the EUH211 and EUH212 hazard statements in all the official languages of the European Union (Article 1(2) of, and Annex II to, the contested regulation).

14 Furthermore, the contested regulation introduced, updated or deleted the harmonised classification and labelling of certain other substances, on the basis of other opinions adopted by the RAC (recitals 3, 4, 6 and 8 and Article 1 of the contested regulation).

15 Under Article 3 of the contested regulation, the amendments to Regulation No 1272/2008 on harmonised classification and labelling of titanium dioxide in powder form containing 1% or more of particles of a diameter equal to or below 10 μm ('the contested classification and labelling') were to apply from 1 October 2021.

II. Forms of order sought

16 The first applicant, supported by the second applicants, Ettengruber GmbH Abbruch und Tiefbau, Ettengruber GmbH Recycling und Verwertung and TIGER Coatings GmbH & Co. KG, the second applicants, supported by the Conseil européen de l'industrie chimique – European Chemical Industry Council (Cefic), the Conseil européen de l'industrie des peintures, des encres d'imprimerie et des couleurs d'art (CEPE), British Coatings Federation Ltd (BCF), American Coatings Association, Inc. (ACA), Mytilineos SA and Delfi-Distomon Anonymos Metalleftiki Etaireia, and the third applicants, supported by the second applicants, Sto SE & Co. KGaA and Rembrandtin Coatings GmbH, claim that the Court should:

– annul the contested regulation in so far as it concerns the contested classification and labelling;

– order the defendant to pay the costs.

17 The Commission, supported by the Kingdom of Denmark, the French Republic, the Kingdom of the Netherlands, the Kingdom of Sweden, the Republic of Slovenia and ECHA, contends that the Court should:

– dismiss the actions;

– order the applicants to pay the costs.

18 The European Parliament and the Council of the European Union contend, in support of the Commission, that the objection of illegality raised in the context of the ninth plea in Case T-279/20 and in Case T-288/20 should be rejected.

III. Law

19 After hearing the parties in that regard and having raised no objections, the Court decided to join Case T-283/20 to Joined Cases T-279/20 and T-288/20 for the purposes of the decision closing the proceedings, in accordance with Article 68(1) of the Rules of Procedure of the General Court.

20 In support of their actions, the first and third applicants put forward, in Case T-279/20 and Case T-288/20 respectively, the same nine pleas in law, which largely overlap with the six pleas in law raised by the second applicants in Case T-283/20. In essence, the pleas may be presented as follows.

21 In the first place, in the context of the second plea, the first and fifth parts of the seventh plea and the eighth plea in Joined Cases T-279/20 and T-288/20 and the arguments raised by the second applicants in their statements in intervention in those cases, as well as in the context of the first plea in Case T-283/20, the applicants and the interveners supporting them claim, in essence, that the contested classification and labelling are vitiated by manifest errors of assessment and that they do not comply with the criteria established by Regulation No 1272/2008 for the classification of a substance as carcinogenic.

22 In the second place, in the context of the third and fourth pleas, the seventh and eighth parts of the seventh plea and the eighth plea in Joined Cases T-279/20 and T-288/20, and in that of the second plea in Case T-283/20, the applicants submit, in essence, that the imposition of the EUH211 and EUH212 statements on the labels of liquid and solid mixtures containing titanium dioxide infringes Article 25(6) of Regulation No 1272/2008 and the principle of legal certainty.

23 In the third place, in the context of the sixth plea and the sixth part of the seventh plea in Joined Cases T-279/20 and T-288/20, and in that of the third plea in Case T-283/20, the applicants claim that the contested classification and labelling infringe the principle of proportionality.

24 In the fourth place, in the context of the fifth plea and the second part of the seventh plea in Joined Cases T-279/20 and T-288/20, and in that of the sixth plea in Case T-283/20, the applicants allege infringement of the Interinstitutional Agreement of 13 April 2016 between the European Parliament, the Council of the European Union and the European Commission on Better Law-Making (OJ 2016 L 123, p. 1) and the absence of an impact assessment prior to the adoption of the contested regulation.

25 In the fifth place, in the context of the third part of the seventh plea in Joined Cases T-279/20 and T-288/20, and in that of the fourth plea in Case T-283/20, the applicants claim that the Commission incorrectly exercised its discretion and that it breached the duty of care. Those pleas overlap for the most part with those referred to in paragraph 21 above, in that they allege manifest errors of assessment.

26 In the sixth place, in the context of the first plea in Joined Cases T-279/20 and T-288/20, the first applicant and the third applicants allege infringement of Article 53c of Regulation No 1272/2008, in the context of the fourth part of the seventh plea, they allege infringement of the principle of equal treatment and, in the context of the ninth plea, they allege, in the alternative and by way of objection, the inapplicability of Regulation No 1272/2008 on account of the infringement of Article 290 TFEU.

27 In the seventh place, in the context of the fifth plea in Case T-283/20, the second applicants allege infringement of Article 37(4) of Regulation No 1272/2008, of the principle of sound administration and of the right to be heard.

A. Preliminary considerations on harmonised classification and labelling of substances in the carcinogenicity hazard class

28 As a preliminary point, it should be noted that, in accordance with recital 1 and Article 1(1) of Regulation No 1272/2008, the purpose of that regulation is to ensure a high level of protection of human health and the environment as well as the free movement of chemical substances, mixtures and certain specific articles on the EU market. As is apparent from, in particular, recitals 5 to 8, 10 and 27 of that regulation, the objective of the latter is to determine the intrinsic properties of the substances which must lead to their classification as hazardous products, so that the hazards posed by those substances (and mixtures containing such substances) can be correctly identified and notified. To that end, in accordance with Article 1(1)(a) thereof, the purpose of that regulation is, inter alia, to '[harmonise] the criteria for classification of substances and mixtures, and the rules on labelling and packaging for hazardous substances and mixtures'.

29 In addition, it is apparent from recitals 4 to 8 of Regulation No 1272/2008 that the EU legislature intended to contribute to the global harmonisation of criteria for classification and labelling, not only at the level of the United Nations Organisation, but also through the incorporation of the internationally agreed Globally Harmonised System of Classification and Labelling of Chemicals ('GHS') into European Union law. To that end, Annex I to that regulation reproduces verbatim almost all of the GHS provisions (judgment of 22 November 2017, *Commission* v *Bilbaína de Alquitranes and Others*, C-691/15 P, EU:C:2017:882, paragraph 42).

30 As regards the classification of hazardous substances and mixtures, it should be recalled that, according to Article 3 of Regulation No 1272/2008, a substance or a mixture fulfilling the criteria relating to physical hazards, health hazards or environmental hazards, as laid down in Annex I, is hazardous and is to be classified in relation to the respective hazard classes provided for in that annex.

31 In that regard, Regulation No 1272/2008 provides, in Title V, for a harmonisation procedure throughout the European Union of the classification and labelling of substances, which concerns substances meeting the criteria set out in Annex I for the hazards listed in Article 36(1) of that regulation, including for the hazard of carcinogenicity. That regulation also lays down, in particular in Articles 5, 9 and 13, a self-classification obligation imposed on manufacturers, importers and downstream users, which relates to substances and mixtures.

32 The procedure for the harmonisation of the classification and labelling of substances is triggered, first of all, by manufacturers, importers and downstream users of a substance or by the competent authority of a Member State, by the submission of a proposal before ECHA, in accordance with Article 37(1) and (2) of Regulation No 1272/2008. Next, the RAC adopts an opinion on the proposal submitted, giving the parties concerned the opportunity to comment, and ECHA forwards that opinion and any comments to the Commission, in accordance with Article 37(4). Lastly, where the Commission finds that the harmonisation of the classification and labelling of the substance concerned is appropriate, it adopts a delegated act, in accordance with Article 37(5) and Article 53a of that regulation, in order to amend Annex VI by including the substance in question together with the relevant classification and labelling elements in Table 3 of Part 3 of Annex VI to that regulation.

33 The purpose of that harmonised classification and labelling of substances, pursuant to Title V of Regulation No 1272/2008, is to determine the intrinsic properties of the substances which must result in their classification as hazardous products, so that the hazards of those substances, and of mixtures containing such substances, can be correctly identified and notified.

34 As regards the hazard of carcinogenicity, Article 36(1)(c) of Regulation No 1272/2008 provides that, if a substance fulfils the criteria set out in Annex I to that regulation for the hazard of carcinogenicity, it is generally subject to harmonised classification and labelling. Those criteria are defined in Section 3.6 of Part 3 of Annex I to Regulation No 1272/2008.

35 In particular, Section 3.6.1.1 of Part 3 of that annex, in its original version, in force on the date of adoption of the contested regulation, provided as follows:

'3.6.1.1. Carcinogen means a substance or a mixture of substances which induce cancer or increase its incidence. Substances which have induced benign and malignant tumours in well performed experimental studies on animals are considered also to be presumed or suspected human carcinogens unless there is strong evidence that the mechanism of tumour formation is not relevant for humans.'

36 Section 3.6.1.1, in the version resulting from Commission Regulation (EU) 2019/521 of 27 March 2019 amending, for the purposes of its adaptation to technical and scientific progress, Regulation No 1272/2008 (OJ 2019 L 86, p. 1), provides as follows:

'3.6.1.1. Carcinogenicity means the induction of cancer or an increase in the incidence of cancer occurring after exposure to a substance or mixture. Substances and mixtures which have induced benign and malignant tumours in well performed experimental studies on animals are considered also to be presumed or suspected human carcinogens unless there is strong evidence that the mechanism of tumour formation is not relevant for humans.

Classification of a substance or mixture as posing a carcinogenic hazard is based on its intrinsic properties and does not provide information on the level of the human cancer risk which the use of the substance or mixture may represent.'

37 In addition, Section 3.6.2.2.1 of Annex I to Regulation No 1272/2008 provides as follows:

'3.6.2.2.1. Classification as a carcinogen is made on the basis of evidence from reliable and acceptable studies and is intended to be used for substances which have an intrinsic property to cause cancer. The evaluations shall be based on all existing data, peer-reviewed published studies and additional acceptable data.'

38 In addition, Section 3.6.2.1 of Annex I to Regulation No 1272/2008 provides that that classification '[allocates substances] to one of two categories based on strength of evidence and additional considerations (weight of evidence)' and that 'in certain instances, route-specific classification may be warranted, if it can be conclusively proved that no other route of exposure exhibits the hazard'. As regards category 2, it is apparent from Table 3.6.1 in Section 3.6.2.1 that 'the placing of a substance in Category 2 is done on the basis of evidence obtained from human and/or animal studies, but which is not sufficiently convincing to place the substance in Category 1A or 1B, based on strength of evidence together with additional considerations [referred to in Section 3.6.2.2]' and that 'such evidence may be derived either from limited evidence of carcinogenicity in human studies or from limited evidence of carcinogenicity in animal studies'.

39 Furthermore, it should be recalled that Regulation No 1272/2008 concerns the assessment of hazards of substances and that that assessment must be differentiated from the risk assessment provided for in 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 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, corrigendum OJ 2007

L 136, p. 3). Hazard assessment constitutes the first stage of the process of risk assessment, which is a more specific concept. Thus, an assessment of the hazards linked to the intrinsic properties of a substance must not be limited in the light of specific circumstances of use, as in the case of a risk assessment, and may be properly carried out regardless of the place where the substance is used (laboratory or elsewhere) or the possible levels of exposure to the substance (see, to that effect, judgment of 21 July 2011, *Nickel Institute*, C-14/10, EU:C:2011:503, paragraphs 81 and 82).

B. Preliminary observations on the intensity of the Court's review

40 As regards the intensity of the Court's review, it should be recalled that, in accordance with settled case-law, if the Commission is to be able to classify a substance pursuant to Regulation No 1272/2008, account being taken of the complex scientific and technical assessments which it must undertake, it must be recognised as enjoying a broad discretion (see judgment of 22 November 2017, *Commission* v *Bilbaína de Alquitranes and Others*, C-691/15 P, EU:C:2017:882, paragraph 34 and the case-law cited).

41 However, the exercise of that discretion is not excluded from review by the Court. It has consistently been held that, in the context of such a review the Courts of the European Union must verify whether the relevant procedural rules have been complied with, whether the facts accepted by the Commission have been accurately stated and whether there has been a manifest error in the appraisal of those facts or a misuse of powers (see judgment of 18 July 2007, *Industrias Químicas del Vallés* v *Commission*, C-326/05 P, EU:C:2007:443, paragraph 76 and the case-law cited).

42 In particular, where a party claims that the institution competent in the matter has committed a manifest error of assessment, the Courts of the European Union must verify whether that institution has examined, carefully and impartially, all the relevant facts of the individual case on which that assessment was based. That duty to act diligently is inherent in the principle of sound administration and applies generally to the actions of the EU administration (see judgment of 22 November 2017, *Commission* v *Bilbaína de Alquitranes and Others*, C-691/15 P, EU:C:2017:882, paragraph 35 and the case-law cited).

43 In addition, the limits to review by the Courts of the European Union do not affect their duty to establish whether the evidence relied on 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 it is capable of substantiating the conclusions drawn from it (see, to that effect, judgment of 6 November 2008, *Netherlands* v *Commission*, C-405/07 P, EU:C:2008:613, paragraph 55 and the case-law cited).

44 Furthermore, as regards the evaluation of scientific studies, the Court has already held that the Commission must be allowed a broad discretion with regard to that assessment, as well as the choice of studies which must take precedence over others, irrespective of their chronology. Thus, it is not sufficient for the applicant to rely on the age of a scientific study to call into question its reliability, but it is also necessary for the applicant to provide sufficiently precise and objective evidence to argue that any recent scientific developments would call into question the soundness of the conclusions of such a study (see, to that effect, judgment of 24 October 2018, *Deza* v *Commission*, T-400/17, not published, EU:T:2018:712, paragraph 95).

45 In the present case, the contested regulation, in so far as it introduces the contested classification and labelling, was adopted by the Commission on the basis of the RAC Opinion and following the classification proposal submitted to ECHA by the competent French authority (see paragraphs 4, 6 and 8 above).

46 The contested classification and labelling concern the substance with the chemical identification 'titanium dioxide (in powder form containing 1% or more particles with aerodynamic diameter ≤ 10 μm)', which was classified as a category 2 carcinogen by inhalation, that is to say, as a substance suspected of being carcinogenic to humans by inhalation (see paragraph 9 above).

47 It is in the light of those considerations that it is appropriate to examine, first, the pleas and arguments alleging manifest errors of assessment and infringement of the criteria laid down, by Regulation No 1272/2008, for the classification of a substance as carcinogenic.

C. The pleas and arguments alleging manifest errors of assessment and failure to comply with the criteria laid down by Regulation No 1272/2008 for the classification of a substance as carcinogenic

48 As stated in paragraph 21 above, by the second plea, the first and fifth parts of the seventh plea and the eighth plea in Joined Cases T-279/20 and T-288/20 and the arguments raised by the second applicants in their statements in intervention in those cases, as well as by the first plea in Case T-283/20, the applicants and the interveners supporting them claim, in essence, first, that the contested classification and labelling are vitiated by manifest errors of assessment and, second, that they fail to comply with the criteria laid down by Regulation No 1272/2008 for the classification of a substance as carcinogenic.

49 The present pleas and arguments can be divided into two parts. The first part alleges manifest errors of assessment and infringement of the criteria laid down, by Regulation No 1272/2008, for the classification and labelling of a substance as carcinogenic, as regards the acceptability and reliability of the Heinrich et al. study (1995) ('the Heinrich study') on which the RAC Opinion was based. The second part alleges manifest errors of assessment and infringement of the criteria laid down, in Regulation No 1272/2008, for the classification and labelling of a substance as carcinogenic, in that the contested classification and labelling do not relate to a substance that has the intrinsic property to cause cancer.

1. The first part, alleging manifest errors of assessment and infringement of the criteria laid down, by Regulation No 1272/2008, for the classification and labelling of a substance as carcinogenic, as regards the acceptability and reliability of the Heinrich study on which the RAC Opinion was based

50 The applicants claim, in essence, that the RAC Opinion is based on the Heinrich study and that the RAC committed several manifest errors in the assessment of the reliability and acceptability of that study. The contested classification and labelling, they submit, are therefore not based on data obtained by reliable and acceptable studies, as required by Section 3.6.2.2.1 of Annex I to Regulation No 1272/2008. They submit, in particular, that the Heinrich study had been considered by the competent French authority to be unreliable, given that it had been conducted solely on female rats and had used a single excessive testing dose.

51 The applicants claim, moreover, that the contested classification and labelling are based on carcinogenicity due to the effects of a lung overload of titanium dioxide particles ('lung overload') and that the RAC committed manifest errors in the assessment of the degree of lung overload which occurred during the Heinrich study by wrongly concluding that it was not excessive.

52 In that regard, the second applicants claim, in their application in Case T-283/20 and their statements in intervention in Joined Cases T-279/20 and T-288/20, that the RAC erred in the density of the particles which it chose to calculate the lung overload. In order to verify the degree of lung overload in the Heinrich study and in the Lee et al. study (1985) ('the Lee study'), the RAC adopted the method proposed by the Morrow studies (1988 and 1992) ('the Morrow overload calculation') and, on that basis, it found that the lung overload of the Lee study had been excessive and that that of the Heinrich study was acceptable. That conclusion, it is submitted, is based on a factual error as regards the density of the particles used by the RAC in the Morrow overload calculation.

53 For the purposes of applying the Morrow overload calculation to the Heinrich and Lee studies, the RAC used the same density value of 4.3 g/cm^3, corresponding to the density of unagglomerated primary particles ('particle density'), whereas it should have used the density of the agglomerates of particles ('agglomerate density'), the value of which is indicated in scientific studies as being 1.6 g/cm^3 for 'P25' grade nano-sized particles. In that regard, it is established, in particular by the Laux et al. (2017), Gebel et al. (2012) and Pauluhn (2011) studies, that nano-sized particles agglomerate and that the agglomerate density is lower than the particle density, given the lower density of void space between particles in the agglomerates. In addition, it is established that the agglomerate density for 'P25' grade titanium dioxide particles is 1.6 g/cm^3. Moreover, in so far as the agglomerate density is lower than that of primary particles, the agglomerates of particles occupy a greater volume than unagglomerated particles. Consequently, the volume of lung overload in the Heinrich study is much higher than that calculated by the RAC. If the RAC had used the correct density in the Morrow overload calculation, namely the agglomerate density, it should have concluded that the Heinrich study had been carried out under excessive lung overload conditions.

54 The Commission disputes those arguments. As a preliminary point, it submits, first, that the applicants' line of argument goes beyond the limits of limited judicial review, given that the applicants do not claim that the RAC or the Commission failed to take into account all the relevant factors, but merely reach a different scientific conclusion from that contained in the RAC Opinion. The Court cannot, however, substitute its own assessment for that of the RAC in respect of scientific and technical facts. Second, the Commission submits that the RAC Opinion is based not only on the Heinrich study but also on the Lee study, as well as on other available evidence and on an approach based on the strength of that evidence, in accordance with Section 3.6.2.1 of Annex I to Regulation No 1272/2008.

55 As regards the manifest error of assessment concerning the particle density, the Commission submits, in essence, that the RAC did not err in calculating the lung overload of the Heinrich study. First, the RAC correctly applied the density value of 4.3 g/cm^3, which is the standard density value of titanium dioxide particles, regardless of their size or form. The RAC is entitled to rely on that value in a context where the actual extent of the agglomeration and the packing of particles in the Heinrich study was not known. Similarly, the larger particles tested in the Lee study are also likely to agglomerate and their actual density is likely to be lower.

56 Second and consequently, by using the standard density of 4.3 g/cm^3, both for the Heinrich study and for the Lee Study, the RAC avoided introducing an element of uncertainty which would have undermined the reliability of the comparisons between those two studies.

57 Third, the Commission submits that, although the density of 1.6 g/cm^3 is indicated in the Pauluhn study (2011) as the value of the agglomerate density of nano-sized titanium dioxide particles, the RAC could not use that density for the Heinrich study, given that there were differences between the studies and that, in the Heinrich study, neither the particle density nor the extent of the agglomeration and the packing of particles were known, with the result that it could not be assumed that the agglomerate density was 1.6 g/cm^3.

58 Fourth, the Commission submits that the lung overload conditions during the Heinrich study were not assessed by the RAC solely on the basis of the Morrow overload calculation, but also on the basis of other reference points. First, the RAC took into account that the lung clearance half-time in that study was barely more than one year and therefore close to the limit recommended by the Organisation for Economic Cooperation and Development (OECD). Second, by comparing the exposure levels in the Heinrich and Lee studies, the RAC took into account the concentration of the substance and the mean mass aerodynamic diameter (MMAD), the latter being included, in both studies, in the range of values recommended in Section 3.1.2.3.2 of Annex I to that regulation.

59 ECHA adds that neither the particle density nor the extent of the agglomeration of particles in the Heinrich study was known, but that those elements were not among the main factors to be taken into consideration. Furthermore, the agglomerate density in the Heinrich study could not immediately be assumed to be 1.6 g/cm^3, given the differences between the scientific study which indicated that value and the Heinrich study. In addition, the micro-sized particles used in the Lee study also tend to agglomerate and, therefore, the agglomerate density, which was also unknown, could also be lower. Thus, in the absence of information on the density of titanium dioxide agglomerates in the Heinrich and Lee studies and in order to calculate the lung overload according to the Morrow overload calculation, the particle density of 4.3 g/cm^3, which is well known for both studies, should be applied.

60 ECHA adds that the degree of lung overload in the Heinrich study could not be greater than in the Lee study, given the lower level of daily exposure to the substance. Furthermore, the values of MMAD are very close to the values set out in Section 3.1.2.3.2 of Annex I to Regulation No 1272/2008, which are recommended values for inhalation studies. Furthermore, a sufficient number of rats in the Heinrich study survived until the end of the experimental period to allow conclusions to be drawn as to carcinogenicity, which is also supported by the clearance half-time at the end of the study, which is close to that recommended by the OECD.

61 The Court considers it appropriate to examine, first, the manifest error of assessment, alleged by the applicants, concerning the particle density value. However, as a preliminary point, it is appropriate to examine certain arguments of the Commission and ECHA relating to the intensity of the Court's review and the relevance of the Heinrich study for the contested classification and labelling, in so far as they are capable of rendering the applicants' arguments ineffective.

(1) The intensity of the Court's review

62 The Commission submits, as a preliminary point, that the applicants' line of argument goes beyond the limits of limited judicial review, since they merely reach a different scientific conclusion from that in the RAC Opinion (see paragraph 54 above). However, contrary to what is claimed by the Commission, the applicants' line of argument is not limited to reaching a different scientific conclusion from that contained in the RAC Opinion.

63 The applicants claim that the RAC Opinion and, consequently, the contested regulation are vitiated by a manifest error of assessment as regards the evaluation of the reliability and acceptability of the Heinrich study and, in particular, the assessment of the degree of lung overload which occurred during that study. In that regard, they allege, inter alia, a material error of fact and a failure to take into account all the relevant factors. In addition, the applicants submit that, as a result of the alleged error, the contested classification and labelling infringe Section 3.6.2.2.1 of Annex I to Regulation No 1272/2008, in so far as that regulation requires that the classification of a substance be based on evidence from reliable and acceptable studies.

64 It follows that the applicants' line of argument raises both a question relating to verification of compliance with the condition laid down in Section 3.6.2.2.1 of Annex I to Regulation No 1272/2008, relating to the reliability and acceptability of the studies on which the classification must be based, and a manifest error in the assessment of that reliability and acceptability as regards the Heinrich study. These are therefore questions which are not exempt from judicial review, the intensity of which has the limits referred to in paragraphs 41 to 44 above.

65 Accordingly, the Commission's argument that the applicants' line of argument in the context of the first part goes beyond the limits of judicial review must be rejected.

(2) The relevance of the Heinrich study for the contested classification and labelling

66 The Commission submits that the RAC Opinion is not based solely on the Heinrich study but also on the Lee study and on other available information (see paragraph 54 above). In addition, in response to a question from the Court, at the hearing on 12 May 2022 in Joined Cases T-279/20 and T-288/20, the Commission claimed that, of the four inhalation studies referred to in the RAC Opinion, the Heinrich and Lee studies were the only ones to find carcinogenic effects and were therefore considered relevant, primarily, for the assessment of the properties of titanium dioxide.

67 In those circumstances, it is necessary to examine whether the Heinrich study was, on its own, decisive for the contested classification and labelling, failing which the applicants' line of argument challenging the reliability and acceptability of that study should be rejected as ineffective.

68 As was pointed out in paragraph 37 above, Section 3.6.2.2.1 of Annex I to Regulation No 1272/2008 provides, inter alia, that the classification of a carcinogen is to be made on the basis of evidence from reliable and acceptable studies and that evaluations are to be based on all existing data, peer-reviewed published studies and additional acceptable data.

69 In the present case and in the first place, it must be noted that both the classification proposal, submitted by the competent French authority, and the RAC Opinion are based, in essence, on inhalation studies carried out on laboratory animals.

70 In the second place, it is apparent from the RAC Opinion that it referred to four animal inhalation studies, including the Lee and Heinrich studies. Those two studies, which were the only studies which reported the development of tumours following exposure to titanium dioxide – for the first study, benign tumours and, for the second study, malignant tumours – were, according to the RAC, the 'key carcinogenicity studies by inhalation' justifying a comparative analysis of their results. By contrast, the other two studies which had not reported tumours, namely the Muhle (1989) and Thyssen (1978) studies, were characterised, according to the RAC, by an insufficient level or duration of exposure.

71 In the third place, as regards the Lee and Heinrich studies, it is apparent from the files in the present cases that the evaluations of those studies by the RAC and by the competent French authority are not the same.

72 As regards the competent French authority, it based its classification proposal for titanium dioxide as a category 1B carcinogen by inhalation, in essence, on the Lee study, to which it gave a Klimisch reliability score of 2, corresponding to 'reliable with restrictions' (as described in the Klimisch, H.J., Andreae, M., and Tillmann, U., article 'A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data', *Regulatory Toxicology and Pharmacology*, Elsevier, 1997, Vol. 25, pp. 1 to 5) ('the Klimisch reliability score').

73 As regards the Heinrich study, the competent French authority found that that study was of 'lower quality', given the lack of information on the degree of purity of the substance and the shortcomings of the exposure protocol, the study having been carried out only on female animals and having tested a single exposure level, which had varied over the experiment. That authority gave the Heinrich study a Klimisch reliability score of 3. According to the applicants, whose view in this regard is not disputed by the Commission or by ECHA, the Klimisch reliability score of 3 corresponds to the 'not reliable' category. However, the competent French authority found that, despite those deficiencies, the carcinogenic effects observed during the Heinrich study should be regarded as 'relevant', given that they were 'consistent' with those of other studies.

74 As regards the RAC, it based its classification proposal for titanium dioxide as a category 2 carcinogen by inhalation, for the most part, on the Heinrich study. It is apparent from the RAC Opinion that the RAC found that the Lee study should not have a 'determining influence' on the classification of titanium dioxide, given that the exposure conditions during that study had been excessive, having led to a complete cessation of the particle clearance mechanisms at the level of alveolar macrophages in the lungs ('the particle clearance mechanisms'), which, according to the RAC, corresponded to 'excessive exposure with questionable relevance for humans'. In addition, it is stated in the RAC Opinion that the RAC found that those excessive exposure conditions in the Lee study 'invalidated the results of [that] study on their own for classification purposes'.

75 As regards the Heinrich study, the RAC found that the degree of lung overload in that study had been significantly lower than that of the Lee study, which did not result in the complete cessation of particle clearance mechanisms and that, although the Heinrich study had not been carried out in accordance with standard testing guidelines, its results were 'sufficiently reliable, relevant and adequate for the assessment of the carcinogenic potential of [titanium dioxide]'.

76 It follows that, of the two studies which, according to the RAC, were the key studies on carcinogenicity by inhalation, the RAC found that the Heinrich study took precedence over the Lee study, the latter not being, in itself, decisive or sufficient to support the classification proposal for titanium dioxide, as, moreover, the Commission acknowledged in reply to a question from the Court at the hearing on 12 May 2022 in Joined Cases T-279/20 and T-288/20.

77 In the fourth place, it should be noted that, in addition to those two key studies, the RAC Opinion refers to other studies, but it does so only as supporting or supplementing the results of the Heinrich study. Thus, the RAC stated, inter alia, that the results of the Heinrich study were 'consistent' with the results of the Gebel study (2012), which concerned the carcinogenicity by inhalation in rats of other substances known as 'poorly soluble low-toxicity particles'.

78 It follows from the foregoing that the Heinrich study was the decisive study on which the RAC Opinion, and therefore the contested classification and labelling, were based. The other studies, including the Lee study, were taken into account purely on a supplementary basis, since the RAC found that those studies were not sufficient, on their own, to support its classification proposal.

79 Consequently, the Commission's argument that the RAC Opinion is not based solely on the Heinrich study must be rejected.

(3) Manifest error of assessment in relation to the particle density value

80 The second applicants claim, in their application in Case T-283/20 and in their statements in intervention in Joined Cases T-279/20 and T-288/20, that the RAC erred in using a particle density value of 4.3 g/cm^3 when applying the Morrow overload calculation to the Heinrich study and that that error led the RAC to conclude, incorrectly, that that study had been conducted under acceptable lung overload conditions.

81 As a preliminary point, and in the first place, it should be noted that that study is entitled 'Chronic inhalation exposure of wistar rats and two different strains of mice to diesel engine exhaust, carbon black and titanium dioxide' and had as its aim the exposure, by inhalation, of rats and mice to diesel engine exhaust, carbon black and titanium dioxide.

82 In the second place, as regards the relevance of lung overload in the context of the contested classification and labelling, it should be noted, first of all, that the classified substance has the chemical identification 'titanium dioxide (in powder form containing 1% or more of particles with aerodynamic diameter ≤ 10μm)' and that it was classified as a substance suspected of being a category 2 carcinogen by inhalation (see paragraph 9 above).

83 Next, it is clear from recital 5 of the contested regulation that the contested classification and labelling are based on carcinogenicity by inhalation combined with the inhalation of respirable titanium dioxide particles, and with the retention and poor solubility of those particles in the lungs. Furthermore, it is stated in Note W that the contested regulation added to Annex VI to Regulation No 1272/2008 (see paragraph 10 above), that 'the carcinogenic hazard of [titanium dioxide arose] when respirable dust [was] inhaled in quantities leading to significant impairment of particle clearance mechanisms in the lung'.

84 Finally, in the RAC Opinion, the RAC acknowledges that tumours observed in rat lungs during the Heinrich and Lee studies developed only under conditions of 'marked reduction of lung clearance'.

85 In the third place, as regards the Morrow overload calculation, the RAC found that, even though that calculation was not generally accepted, it was appropriate to use it in order to assess whether the degree of lung overload to which the animals had been subjected in the Lee and Heinrich studies had been marked or excessive.

86 In that regard, it is apparent from the RAC Opinion, and from the Commission's reply to a question put by the Court by way of a measure of organisation of procedure in Joined Cases T-279/20 and T-288/20, that the Morrow overload calculation links the quantity of inhaled particles and the impairment of the functioning of particle clearance mechanisms with the volume occupied by particles in the alveolar macrophages of the lungs.

87 In addition, the RAC stated, in its Opinion, that the Morrow overload calculation made it possible to determine that an appropriate lung overload in laboratory animals occurred when 6 to 60% of the volume of alveolar macrophages were occupied by particles. First, the volume of the occupied alveolar macrophages had to be greater than 6%, in order to bring about a significant impairment of particle clearance mechanisms, that reduction being essential to the development of chronic inflammation and the carcinogenic effects observed. Second, the volume occupied by the particles had to be lower than 60% since, at that level, there was an almost complete cessation of the particle clearance mechanisms, which demonstrated excessive lung overload, which invalidated the results.

88 In the fourth place, as regards the assessment of the degree of lung overload in the Lee and Heinrich studies on the basis of the Morrow overload calculation, it is apparent from the RAC Opinion that, first of all, the RAC carried out that calculation by taking into account, in essence, two factors, namely, first, the 'exposure level', which takes account of the dose and concentration of the substance in milligrams per cubic metre, and, second, the particle density in grams per cubic centimetre. As regards the Lee study, the RAC stated that the exposure levels were 10, 50 and 250 mg/m^3 and that the particle density was 4.3 g/cm^3. As regards the Heinrich study, the RAC used an exposure level of 10 mg/m^3 and the same density of 4.3 g/cm^3.

89 Next, the RAC stated that, for exposure to titanium dioxide particles of a density of 4.3 g/cm^3, the acceptable lung overload (situated, according to the Morrow overload calculation, at between 6 and 60% of the volume loading of alveolar macrophages, as stated in paragraph 87 above) was equivalent to a burden of between 6.5 and 65 mg of particles per rat lung.

90 Lastly, on the basis of those premisses, the RAC concluded that, in the Heinrich study, the lung overload had been approximately 40% and, therefore, within the acceptable range, whereas, in the Lee study, the lung overload had exceeded 60% of the volume loading of alveolar macrophages, which corresponded to an almost complete cessation of the particle clearance mechanisms.

91 It is in the light of those considerations that the error alleged by the second applicants, concerning particle density, must be examined.

92 In the present case, it is common ground that the Heinrich and Lee studies did not indicate the density of the particles tested. The studies indicated only certain characteristics of those particles, namely, as regards the Lee study, micro-sized particles and, as regards the Heinrich study, 'P25' grade nano-sized particles. Those different characteristics of the particles tested during the Lee and Heinrich studies are, moreover, mentioned in the RAC Opinion, in particular, as regards the 'P25' grade nano-sized particles tested in the Heinrich study.

93 It is also common ground that the RAC used the density value of 4.3 g/cm^3 when applying the Morrow overload calculation to those two studies (see paragraph 88 above).

94 In addition, it is apparent from the written submissions of the Commission and ECHA, and from their answers to the questions put by the Court at the hearings on 12 and 18 May 2022, that the value of 4.3 g/cm^3 is a standard value, usually indicated in the scientific community as the density of titanium dioxide particles, something which, moreover, the applicants do not dispute.

95 However, the applicants claim that the RAC was wrong to use, for the purposes of the Morrow overload calculation, the particle density of 4.3 g/cm^3, when it should have taken account of the agglomerate density of 'P25' grade nano-sized titanium dioxide particles, that density being, according to the scientific studies referred to by the applicants, 1.6 g/cm^3 (see paragraph 53 above).

96 The Commission and ECHA submit, in essence, that the RAC was fully entitled to take into account the particle density, given that the Heinrich study did not indicate the density of the particles tested or the extent of the agglomeration and the packing of those particles and that, in those circumstances, it was appropriate for the RAC to take into account the standard density value of titanium dioxide particles.

97 In that regard, it should be noted that, irrespective of the precise density value that had to be taken into account by the RAC for the purposes of the Morrow overload calculation – a question, in any event, which it is not for the Court to examine – the applicants' line of argument raises above all the question whether the RAC made a manifest error of assessment concerning the type of density used, in that it took into account the particle density instead of using the agglomerate density of nano-sized particles of titanium dioxide.

98 In the present case, the fact, relied on by the applicants, that titanium dioxide particles and, in particular, 'P25' grade nano-sized particles, such as those tested in the Heinrich study, tend to agglomerate is not disputed. The Commission and ECHA do not dispute that specific point, as is apparent from their pleadings and their replies to the questions put by the Court at the hearings on 12 and 18 May 2022. Moreover, as the second applicants submit in Joined Cases T-279/20 and T-288/20, the Heinrich study mentioned the agglomerates of titanium dioxide particles and stated that they were 'particularly suited to exert toxic effects primarily on alveolar macrophages and alveolar lung particle clearance'. Furthermore, with regard to aerosols, that is to say, air-suspended particles, the environment of which is, admittedly, different from that of the lungs, the RAC Opinion also states that 'primary particles … notably nano-sized primary particles tend to agglomerate'.

99 Furthermore, it is common ground between the parties, as is apparent from their pleadings, from their written responses to questions put by way of measure of organisation of procedure in Joined Cases T-279/20 and T-288/20, and from their answers to the questions put by the Court at the hearings on 12 and 18 May 2022, that the agglomerate density of nano-sized particles of titanium dioxide is lower than the particle density, given that the agglomeration creates void spaces which are less dense than the material. Consequently, in so far as the agglomerate density is lower than that of primary particles, the agglomerates of particles occupy a greater volume than unagglomerated particles.

100 It is indeed true, as the Commission and ECHA argue without being challenged by the applicants, that the Heinrich study did not provide any indication as to the density or the extent of the agglomeration and the packing of the titanium dioxide particles tested. However, by applying a density value corresponding to the particle density of 4.3 g/cm^3 and, therefore, a density higher than the agglomerate density of nano-sized titanium dioxide particles (see paragraph 99 above), the RAC did not take into account all the relevant factors of the present case, namely the characteristics of the particles tested in the Heinrich study, in particular their nano size and their 'P25' grade, the fact that those particles tend to agglomerate and the fact that the agglomerate density of the particles was lower than the particle density and that, consequently, the agglomerates of particles occupied more volume in the alveolar macrophages of the lungs (see paragraphs 98 and 99 above).

101 In addition, contrary to what ECHA appears to claim, those factors were relevant for the Morrow overload calculation since the density value was one of the two values necessary to perform that calculation, which was adopted by the RAC in order to assess the degree of lung overload in the Lee and Heinrich studies (see paragraph 88 above). Moreover, in response to a question put by the Court at the hearing on 12 May 2022, the Commission accepted that density was important for the Morrow overload calculation.

102 It follows that particle density was an essential factor for the Morrow overload calculation adopted by the RAC and that that density could not, at the obvious risk of discrediting the results of that calculation, be presumed to be the density of the particles, whereas it was known that the nano-sized particles at issue formed agglomerates, that the agglomerate density was lower and that, consequently, the volume occupied by particles in the lungs was greater.

103 Therefore, by failing to take into account the factors set out in paragraph 100 above, the RAC failed to take into account all the relevant factors in order to calculate the lung overload in the Heinrich study by means of the Morrow overload calculation and therefore committed a manifest error of assessment. That error renders implausible the result of the application of that calculation to that study and, consequently, the RAC's findings that the lung overload in that study was acceptable and that the results of that study were sufficiently reliable, relevant and adequate for the assessment of the carcinogenic potential of titanium dioxide (see paragraphs 75 and 90 above) are also vitiated by a manifest error of assessment. Consequently, in so far as the Commission based the contested classification and labelling on the RAC Opinion (see paragraph 8 above), it committed the same manifest error of assessment when it adopted the contested regulation.

104 The arguments of the Commission and ECHA do not call that conclusion into question.

105 In the first place, it is necessary to reject their arguments that the RAC is entitled to rely on a density corresponding to the particle density because, in the Heinrich study, the particle density and the extent of the agglomerates of particles were not known. Those arguments do not invalidate the fact that the RAC did not take into account all the factors necessary to determine density, in particular the nano size of the particles in question and their tendency to form agglomerates, of which the RAC was aware and which, moreover, was mentioned in its Opinion (see paragraph 98 above).

106 In addition, it should be noted that the question raised by the manifest error of assessment relied on by the applicants is not whether the RAC had in its possession the information necessary to determine the agglomerate density, but, on the contrary, whether the RAC took into account all the relevant factors in order to verify the degree of lung overload in the Heinrich study by means of the Morrow overload calculation.

107 As is apparent from paragraphs 92 and 100 above, the RAC used a value corresponding to the particle density which was not indicated in the study, while disregarding the factors set out in that study, in particular the nano size of the particles and their tendency to agglomerate, even though it was certain that those factors, and in particular the agglomeration, had an impact on the density value and that the density value, in turn, had an impact on the volume occupied by particles in rat lungs, and therefore on the degree of lung overload.

108 Those factors were decisive in the present context, since the Morrow overload calculation, which the RAC decided to adopt, was specifically designed to calculate the volume of alveolar macrophages occupied by particles in rat lungs, in order to determine whether the Heinrich study had been carried out under conditions of marked lung overload or excessive lung overload and therefore to determine whether the results of that study could serve as a basis for classifying titanium dioxide.

109 Accordingly, the argument of the Commission and ECHA that, in the circumstances of the present cases, it would be 'appropriate' for the RAC to take into account the particle density is not convincing and does not make it possible to remedy the failure to take into account all the relevant factors for the purposes of calculating the lung overload, particularly since those elements demonstrated that the density value used by the RAC did not reflect the reality of the particles tested in the Heinrich study.

110 In the second place, contrary to what the Commission and ECHA appear to claim, the objectives of facilitating a comparison between the Lee and Heinrich studies and of avoiding the introduction of a factor of uncertainty in that comparison cannot justify the failure to take into account all the factors necessary to determine the density value. The needs for comparison between those two studies cannot take precedence over the need, put forward by the RAC itself, to examine, in the light of the Morrow overload calculation, whether or not, in those studies, the lung overload had been excessive, since, in the latter case, the results of those studies could not, on their own, justify the classification proposal for titanium dioxide. It is, moreover, for that same reason and following that same calculation that the RAC found that the lung overload in the Lee study had been excessive (see paragraph 74 above).

111 In the third place, as regards ECHA's argument that micro-sized particles, such as those tested during the Lee study, also have a tendency to agglomerate, first, it is sufficient to note that that study was not decisive for the RAC's classification proposal (see paragraph 76 above). Second, the application of the Morrow overload calculation to that study had, according to the RAC, shown that the lung overload was excessive, even taking into account the particle density value, which was always higher than that of the agglomerate density. Accordingly, any errors by the RAC in the assessment of that study cannot have any bearing on the manifest error of assessment found in paragraph 103 above.

112 In the fourth place, as regards the arguments of the Commission and ECHA that the evaluation of the Heinrich study by the RAC was not carried out solely on the basis of the Morrow overload calculation, or even that it was not dependent on that calculation, it must be noted that those arguments are contradicted by the RAC Opinion.

113 Admittedly, the RAC noted a number of factors concerning the exposure conditions in the Lee and Heinrich studies, in particular the lung clearance half-time and the exposure level based on the dose and concentration of the substance. It referred to those factors in a chapter of its Opinion entitled 'Overall conclusion', in which it concluded that the excessive exposure conditions in the Lee study '[invalidated] the results of [that] study on their own for classification purposes' and that the results of the Heinrich study were 'sufficiently reliable, relevant and adequate for the assessment of the carcinogenic potential of [titanium dioxide]' (see paragraphs 74 and 75 above). In particular, as regards the Lee study, the RAC mentioned an excessive lung clearance half-time during the maximum exposure level of 250 mg/m^3 and, as regards the Heinrich study, it noted that the exposure level of 10 mg/m^3 was relatively low.

114 However, in that overall conclusion, the RAC also noted that the lung overload in the Lee study was not in the acceptable range, which led to an almost complete cessation of particle clearance mechanisms, which was not the case with the Heinrich study, in which the lung overload was in the acceptable range (see paragraph 90 above).

115 It follows that, in order to verify the degree of lung overload during the Lee and Heinrich studies and, more specifically, the volume of alveolar macrophages occupied by particles, the RAC adopted the Morrow overload calculation and it was on the basis of that calculation that it drew its conclusions as to whether the lung overload in the Heinrich study had been acceptable (see paragraphs 87 to 90 above).

116 In those circumstances, while it is admittedly true that the RAC referred to the dose and concentration of the substance, as well as to the lung clearance half-time, the fact remains that it was not on the basis of those factors that it drew its conclusions on the degree of lung overload in the Heinrich study and therefore on the acceptability of the results of that study.

117 Similarly, the arguments of the Commission and ECHA alleging that the values of MMAD were comparable between the two studies at issue and that those values were close to those set out in Section 3.1.2.3.2 of Annex I to Regulation No 1272/2008 cannot succeed. Even if it is accepted that, as the Commission submits, the MMAD value may have an influence on the distribution and deposit of particles in respiratory tracts, it must be held that, in any event, the MMAD value was not taken into account by the RAC in order to carry out the Morrow overload calculation and, therefore, it cannot have a decisive influence on the RAC's findings concerning the degree of lung overload in the Heinrich study and the acceptability of its results.

118 In addition, it is necessary to reject ECHA's argument based on the number of rats which survived until the end of the experimental period of the Heinrich study, since it is apparent from the RAC Opinion that the RAC did not take the view that that evidence alone was sufficient to draw a conclusion as to whether the degree of lung overload during that study was acceptable.

119 For the same reasons, it is necessary to reject the Commission's argument that the RAC confirmed the validity of the Heinrich study on the basis of the Thompson et al. study (2016). Even if that study were capable of validating the Heinrich study, which is disputed in the present case, that

validation would not alter the fact that it was on the basis of the Morrow overload calculation that the RAC drew its conclusions on the acceptability of the degree of lung overload in the Heinrich study.

120 Therefore, contrary to what is claimed by the Commission and ECHA, the Morrow overload calculation was decisive in supporting the RAC's findings that the lung overload in the Heinrich study was in the acceptable range and that the results of that study were sufficiently reliable, relevant and adequate, those findings being vitiated by a manifest error of assessment, as noted in paragraph 103 above.

121 It follows from all of the foregoing that, in so far as the contested regulation, as regards the contested classification and labelling, is based on the RAC Opinion (see paragraph 8 above) and in so far as the Heinrich study was decisive for the RAC's classification proposal for titanium dioxide (see paragraph 77 above), the manifest error of assessment referred to in paragraph 103 above renders implausible the RAC's conclusion, which was followed by the Commission when it adopted the contested regulation, that the results of the Heinrich study were sufficiently reliable and adequate, within the meaning of Section 3.6.2.2.1 of Annex I to Regulation No 1272/2008, to support the contested classification and labelling.

122 Accordingly, the first part must be upheld, without it being necessary to examine the other arguments raised by the applicants in the context of that part.

123 However, in the interests of the sound administration of justice, it is appropriate to continue the examination of the action and to give a ruling on the second part in order to provide a complete resolution of the dispute.

2. The second part, alleging manifest errors of assessment and infringement of the criteria laid down, by Regulation No 1272/2008, for the classification and labelling of a substance as carcinogenic, in that the contested classification and labelling do not relate to a substance that has the intrinsic property to cause cancer

124 By the second part, the applicants claim, inter alia, that the contested classification and labelling infringe the criterion laid down by Article 3(1) and Article 36(1)(c) of Regulation No 1272/2008, read in conjunction with Section 3.6.2.2.1 of Annex I to that regulation, for the classification of a substance as carcinogenic, in that it does not relate to a substance that has the intrinsic property to cause cancer.

125 In that regard, the first applicant and the third applicants claim, inter alia, in Joined Cases T-279/20 and T-288/20, that the contested classification and labelling are based solely on the form and size of the titanium dioxide particles, those not being intrinsic properties of titanium dioxide, since they are alterable and stem from the treatment of that substance. Moreover, in its Opinion, the RAC acknowledged that the contested classification and labelling did not relate to an intrinsic hazard in the classical sense of the term. In addition, the fact that the toxicity observed is 'particle toxicity' resulting from the mere accumulation of particles of a certain size in the lungs is apparent from the RAC Opinion and from recital 5 of the contested regulation, from which it follows that the reason for the toxicity observed was the deposited particles and not the solutes of titanium dioxide molecules.

126 In that regard, the second applicants submit, in their application in Case T-283/20 and in their statements in intervention in Joined Cases T-279/20 and T-288/20, that the fact that the reason for the toxicity observed was the deposited particles shows that this is a 'particle toxicity', which does not constitute an intrinsic hazard within the meaning of Regulation No 1272/2008, but which, by contrast, is a new concept, which is not covered by that regulation.

127 In addition, the second applicants claim that the development of tumours in rat lungs, which is at the root of the RAC Opinion and the contested classification and labelling, is a confounding or secondary effect, common, moreover, to other dust, resulting from excessive lung overload and not from an alleged carcinogenic potential for titanium dioxide.

128 The Commission disputes those arguments. In the first place, in Joined Cases T-279/20 and T-288/20, it submits that it is indeed apparent from the RAC Opinion that the form of titanium dioxide was decisive for classification. However, the carcinogenicity of a given form of titanium dioxide powder was to be regarded as an intrinsic property for the purposes of classification under the criteria laid down in Regulation No 1272/2008. The concept of 'intrinsic' property should be understood as referring to the intrinsic hazard emanating from both a substance and a certain form or physical state of a substance, including particle toxicity, in accordance with Article 5(1), Article 6(1), Article 8(6) and Article 9(5) of Regulation No 1272/2008. The systematic framing of that rule in the provisions of that regulation underlines the utmost importance of the forms and physical states and foreseeable use of substances. It is possible that a substance may be hazardous in a specific form and not in any other form, as is the case with titanium dioxide.

129 In addition, the Commission submits that the size of the particles may be relevant for determining the hazard in the context of Regulation No 1272/2008, as is apparent in particular from the part of the ECHA Guidance on the application of the criteria of Regulation No 1272/2008 on the hazard class relating to specific target organ toxicity from repeated exposure, called 'STOT-RE'.

130 In addition, the Commission submits that, although the RAC Opinion noted the lack of intrinsic property in the classical sense of the term, it ultimately concluded that there was an intrinsic toxicity relevant for the harmonised classification and labelling under Regulation No 1272/2008.

131 In addition, the Commission submits, in Case T-283/20, that the carcinogenic effects mentioned in the RAC Opinion are not a 'confounding effect', but that they are due to the physico-chemical characteristics of respirable titanium dioxide particles, in particular to their size and, therefore, to the intrinsic properties of the substance. In addition, the carcinogenicity of titanium dioxide was established, in animal studies, on the basis of a marked, but not excessive, lung overload which is relevant for humans.

132 Furthermore, the Commission maintains, in Joined Cases T-279/20 and T-288/20, that other substances in powder form have already been classified, as is the case with lead powder or nickel powder, which are listed in Part 3 of Annex VI to Regulation No 1272/2008.

133 In that regard, the Kingdom of Denmark and the Kingdom of Sweden add that several substances have been classified as carcinogenic on the basis of their physical properties, in particular refractory ceramic fibres and asbestos fibres, the classification of which is based on their form and their poor solubility.

134 ECHA adds that the examples of lead and nickel cited by the Commission, and the examples of glass microfibres, illustrate cases in which the size of the particles, among other relevant intrinsic properties, was taken into account for classification, without that approach having had the effect of rendering the classification unlawful.

135 As a preliminary point, it should be noted, first of all, that it follows from Regulation No 1272/2008 that the aim of harmonised classification and labelling is to determine the intrinsic properties of the substances which must lead to their classification as hazardous products, so that the hazards of those substances (and of the mixtures containing them) can be correctly identified and notified (see paragraph 28 above).

136 Thus, harmonised classification and labelling under Regulation No 1272/2008 concern the transmission of information on the hazards linked to the substances' intrinsic properties (see, to that effect and by analogy, judgment of 21 July 2011, *Nickel Institute*, C-14/10, EU:C:2011:503, paragraph 81).

137 Next, as regards the classification of a substance as carcinogenic, it should be noted that this relates to substances that have the intrinsic property to cause cancer, in accordance with Article 36 of Regulation No 1272/2008 and Section 3.6.2.2.1 of Annex I to that regulation (see paragraphs 34 to 37 above).

138 Lastly, as regards the concept of 'intrinsic properties', it should be noted that, although that concept does not appear in Regulation No 1272/2008, it must be interpreted in its literal sense as referring to the 'properties which a substance has in and of itself'.

139 That interpretation of the expression 'intrinsic properties' is consistent with the objectives and purpose of harmonised classification and labelling under Regulation No 1272/2008, from which it follows that only the properties specific to a substance must lead to its classification as a hazardous product, so that the hazard associated with such properties can be correctly identified and notified (see paragraphs 135 and 136 above).

140 That interpretation is also consistent with the GHS criteria, which are incorporated into EU law (see paragraph 29 above), of which Section 1.1.1.6 and footnote 1 and Section 1.1.3.1.1, in the 2013 version in force at the date of adoption of the contested regulation, make, inter alia, a distinction between the intrinsic properties of a substance, to which the hazard classification process relates, and other properties which are not specific to the substance.

141 Moreover, that interpretation is consistent with the fact that the harmonised classification and labelling under Regulation No 1272/2008 relate to hazard assessment, and not risk assessment, which is provided for by Regulation No 1907/2006. As is apparent from the case-law referred to in paragraph 39 above, an assessment of the hazards linked to the intrinsic properties of a substance must not be limited in the light of specific circumstances of use, as in the case of a risk assessment, and may be properly carried out regardless of the place where the substance is used or the possible levels of exposure to the substance.

142 It is therefore in the light of that concept of intrinsic properties that it is necessary to interpret Article 3(1) and Article 36(1)(c) of Regulation No 1272/2008, read in conjunction with section 3.6.2.2.1 of Annex I to that regulation, from which it follows that the harmonised

classification and labelling of a substance as carcinogenic can be based only on intrinsic properties of the substance which determine its intrinsic capacity to cause cancer, that is to say, the specific properties of the substance which determine its capacity to cause cancer on its own.

143 In the present case, it should be noted that the contested classification and labelling aim to identify and notify a hazard of category 2 carcinogenicity by inhalation, which was described in the RAC Opinion on the basis, in essence, of the results of the Heinrich study, during which malignant tumours were observed in the lungs of laboratory rats following a lung overload of nano-sized particles of titanium dioxide (see paragraphs 70 and 78 above).

144 The carcinogenic hazard referred to in paragraph 143 above is classified, by the RAC Opinion, as being 'non-intrinsic in a classical sense', the RAC having concluded that 'the mode of action for the rat lung carcinogenicity in rats cannot be considered "intrinsic toxicity" in a classical sense'. Furthermore, it is apparent from Note W that the Commission found it necessary to accompany the contested classification and labelling with a description of the 'particular toxicity of the substance' (see paragraph 10 above).

145 That 'non-intrinsic in the classical sense' or 'particular' nature of the carcinogenicity hazard covered by the contested classification and labelling stems from several factors, referred to in the RAC Opinion and in the contested regulation.

146 In the first place, the carcinogenicity hazard referred to in the contested classification and labelling is linked solely to certain respirable titanium dioxide particles, when they are present in a certain form, physical state, size and quantity. It is for that reason that the Commission found it necessary to 'define respirable titanium dioxide particles in the titanium dioxide entry' (see recital 5 of the contested regulation), departing from the RAC's proposal to classify the substance with the chemical name 'titanium dioxide' without any further physico-chemical description.

147 Thus, it follows from the chemical identification of the substance, which appears in the entry of Table 3 in Part 3 of Annex VI to Regulation No 1272/2008, added by the contested regulation, that the carcinogenicity hazard covered by the contested classification and labelling is linked solely to titanium dioxide particles which, cumulatively, have a given form and physical state (powder), a certain size (aerodynamic diameter equal to or below 10 μm), are present in a certain quantity (1% or more) and are respirable (route of exposure via inhalation).

148 In the second place, the carcinogenicity hazard covered by the contested classification and labelling occurs only in lung overload conditions, that is to say, when large quantities of particles are inhaled, giving rise to a significant impairment of particle clearance mechanisms in the lung.

149 It should be noted that Note W expressly states that carcinogenicity 'arises when respirable dust is inhaled in quantities leading to significant impairment of particle clearance mechanisms in the lung'. Similarly, it is stated in recital 5 of the contested regulation that carcinogenicity is associated with the inhalation of respirable titanium dioxide particles and with the retention and poor solubility of those particles in the lungs (see paragraph 83 above).

150 Furthermore, it is apparent from the RAC Opinion that the tumours in rats were always observed under lung overload conditions. It was, moreover, in the light of that context of lung overload that the RAC found it necessary to use the Morrow overload calculation in order to assess whether the lung overload, to which the animals were subjected in the Lee and Heinrich studies, had been marked or excessive (see paragraph 85 above).

151 In the third place, the carcinogenicity hazard covered by the contested classification and labelling corresponds, according to the actual wording of the RAC Opinion, to 'particle toxicity', the reason for which is 'the deposited particles, but not solutes of [titanium dioxide] molecules'. Furthermore, it is apparent from the RAC Opinion that the development of tumours which was observed in rats was not triggered by the direct contact of titanium dioxide particles with epithelial lung cells, but by the high load of particles in the alveolar macrophages of the lungs and by the resulting significant impairment of particle clearance mechanisms, which led to marked and sustained inflammatory responses.

152 Those assessments are corroborated by Note W, from which it is apparent that carcinogenicity arises following a significant impairment of particle clearance mechanisms in the lung, where particles are inhaled in sufficient quantities to that effect.

153 Furthermore, it is apparent from the RAC Opinion that the toxicity observed, which is not exclusive to titanium dioxide particles, but is common to other poorly soluble low-toxicity particles, is not linked either to the hazards inherent to certain fibres, identified by the World Health Organisation (WHO) ('the WHO fibres'), or to additional specific toxicity of titanium dioxide particles due to surface coatings.

154 It was in the light of the factors set out in paragraphs 146 to 153 above that, first of all, the RAC concluded that 'the mode of action for the rat lung carcinogenicity in rats cannot be considered "intrinsic toxicity" in a classical sense', next, it found that, nevertheless, it had to be taken into consideration in the context of the harmonised classification and labelling under Regulation No 1272/2008 and, lastly, the Commission followed that opinion by adopting the contested regulation and finding that it was necessary to insert Note W to describe the 'particular toxicity of the substance' (see paragraph 144 above).

155 The question that arises in the present cases is whether the Commission, in adopting the contested regulation, made a manifest error of assessment when applying the criterion of 'substance that has the intrinsic property to cause cancer', provided for in Section 3.6.2.2.1 of Annex I to Regulation No 1272/2008.

156 It is true that the carcinogenicity hazard covered by the contested classification and labelling is associated with titanium dioxide particles having certain properties, that is to say, a certain size, a certain form and poor solubility (see paragraph 83 above). However, it must be noted that, according to the RAC Opinion, the reason for the toxicity observed is not the properties of the titanium dioxide particles in themselves, but the deposit and retention of those particles in the alveolar macrophages of the lungs in sufficient quantities to give rise to lung overload leading to a significant impairment of particle clearance mechanisms in the lung (see paragraphs 151 and 152 above).

157 Thus, even if it is accepted that the properties of particles, such as their size, form and poor solubility, play a role in their accumulation in the lung, and irrespective of whether those properties are intrinsic within the meaning of Regulation No 1272/2008, as the Commission maintains, the fact remains that the mode of action of carcinogenicity described in the RAC Opinion, which, according to the RAC, could not be regarded as '"intrinsic toxicity" in a classical sense', does not point to an intrinsic property of titanium dioxide particles to cause cancer.

158 One of the key elements of the toxicity observed is the quantity of inhaled particles, which must be sufficient to bring about a significant impairment of particle clearance mechanisms, and it is that impairment which is essential to the development of chronic inflammation, which, in turn, results in the carcinogenic effects observed (see paragraphs 146 to 153 above). An accumulation of particles in the lung in sufficient quantities to bring about a significant impairment of particle clearance mechanisms, which can be verified only when certain quantities of particles are inhaled, cannot be regarded as forming part of the intrinsic properties of the particles at issue.

159 Thus, contrary to the wording of the second paragraph of Note W, that note does not merely describe a substance's 'particular toxicity', which '[did] not constitute a criterion for classification according to [Regulation No 1272/2008]'. By contrast, that note describes a hazard which is not covered by the classification criterion for the carcinogenicity hazard, referred to in Section 3.6.2.2.1 of Annex I to Regulation No 1272/2008, according to which the substance must have the intrinsic property to cause cancer.

160 Therefore, in accepting the RAC's finding that 'the mode of action for the rat lung carcinogenicity in rats cannot be considered "intrinsic toxicity" in a classical sense', but which had to be taken into consideration in the context of harmonised classification and labelling under Regulation No 1272/2008, the Commission made a manifest error of assessment when applying the criterion for classifying a substance as a carcinogen laid down in Article 3(1) and Article 36(1) of Regulation No 1272/2008, read in conjunction with Section 3.6.2.2.1 of Annex I to that regulation.

161 It must therefore be held that the contested regulation, so far as concerns the contested classification and labelling, was adopted in breach of Article 3(1) and Article 36(1) of Regulation No 1272/2008, read in conjunction with Section 3.6.2.2.1 of Annex I to that regulation.

162 Furthermore, the fact that the contested classification and labelling relate to category 2 of the carcinogenicity hazard class (see paragraph 46 above) does not call those conclusions into question. The criterion of classification for the carcinogenicity hazard class, referred to in paragraph 160 above, is still the same for the two respective hazard categories, those two categories varying only on the basis of the strength and weight of the evidence, in accordance with the provisions of Section 3.6.2.1 and Table 3.6.1 of Annex I to Regulation No 1272/2008, recalled in paragraph 38 above.

163 The arguments put forward by the Commission and by the interveners in support of it do not call those conclusions into question.

164 In the first place, the Commission submits, in essence, that the concept of 'intrinsic' property should be understood as referring to the intrinsic hazard emanating from both a substance and a certain form or physical state of a substance or mixture, in accordance with Article 5(1), Article 6(1), Article 8(6) and Article 9(5) of Regulation No 1272/2008.

165 In that regard, it should be noted that Article 5(1), Article 6(1), Article 8(6) and Article 9(5) of Regulation No 1272/2008, relied on by the Commission, do not directly concern the procedure for the harmonisation of the classification and labelling of substances, laid down in Title V of that regulation, let alone come within the criteria established for the harmonised classification and labelling of a substance as carcinogenic.

166 By contrast, those provisions concern the obligation, referred to in paragraph 31 above, of self-classification of a substance or mixture by the manufacturer, importer or downstream user, where the substance or mixture at issue does not have a harmonised classification and presents hazardous properties. That is why the relevant information for the purposes of determining whether a substance poses a hazard, as well as the assessment of that information, and, where appropriate, the application of the classification criteria for each hazard class must relate to the form or physical state in which the substance is placed on the market or used by individuals or undertakings on which such an obligation is imposed.

167 Furthermore, even if it is accepted that, as the Commission submits, harmonised classification and labelling may relate to an intrinsic hazard emanating from a certain form or physical state of a substance, the fact remains that, in order to comply with the criteria established for harmonised classification and labelling, it is essential that the hazard stems either from the intrinsic properties of the substance or from the intrinsic properties of a certain physical state or a certain form of the substance, which is not the case here for the reasons set out in paragraphs 157 and 158 above.

168 In the second place, the Commission submits that the contested classification and labelling were based on the physico-chemical characteristics of titanium dioxide particles, without, however, putting forward any specific argument capable of calling into question the fact that the toxicity observed is attributed, according to the actual wording of the RAC Opinion, not to the particles in themselves, but to the particles being deposited in the lung in quantities giving rise to a significant impairment of particle clearance mechanisms, which is the case only if a certain threshold of exposure to the particles is reached.

169 Furthermore, as is apparent from the RAC Opinion, the carcinogenicity observed is not attributed to the solutes of the titanium dioxide molecules, to direct contact of the titanium dioxide particles with epithelial lung cells, to fibrous morphology, or to a surface coating of those particles from a toxicological point of view (see paragraphs 151 and 153 above).

170 In the third place, it should be noted that, contrary to the submission of the Commission and the interveners supporting it, the contested classification and labelling are not similar to the harmonised classifications and labelling to which they refer.

171 Thus, as regards lead, it must be observed that both lead massive and lead powder are classified and that, in both cases, the classification was made for the hazard class ‘toxic for reproduction’, with the difference that a specific concentration limit has been established for lead powder (see Table 3 in Part 3 of Annex VI to Regulation No 1272/2008).

172 Similarly, both nickel and nickel powder were classified in the carcinogenicity hazard class, category 2, whereas nickel powder was also classified as ‘hazardous to the aquatic environment’ (see Table 3 in Part 3 of Annex VI to Regulation No 1272/2008).

173 It follows that the classifications of nickel, lead and their respective powders are not comparable to that of titanium dioxide, of which only particles of a certain size, but not the solid substance, are subject to the contested classification and labelling, which, moreover, relate to a different health hazard class.

174 As regards asbestos fibres, it is the substance itself, and not its particles of a given size, which is classified as carcinogenic (see Table 3 in Part 3 of Annex VI to Regulation No 1272/2008).

175 As regards glass microfibres, it follows from the RAC Opinions of 4 December 2014, on the basis of which they were classified (Commission Regulation (EU) 2016/1179 of 19 July 2016 amending, for the purposes of its adaptation to technical and scientific progress, Regulation No 1272/2008 (OJ 2016 L 195, p.11)), that the classification of those fibres as carcinogenic results from a toxicity determined, in essence, by their form and size, but also by their surface chemistry and their biopersistence. It follows that that classification is not comparable to that of titanium dioxide, in respect of which the particles tested had a minor or non-existent surface coating from a toxicological point of view (see paragraph 153 above).

176 As regards refractory ceramic fibres, they were classified as category 1B carcinogens (see Table 3 in Part 3 of Annex VI to Regulation No 1272/2008). As is apparent from the Commission's reply to a question posed by way of a measure of organisation of procedure in Joined Cases T-279/20 and T-288/20, and from its reply to a question from the Court at the hearing on 12 May 2022, that classification was based on a mode of action for carcinogenicity relating to the properties of those fibres, such as the length, diameter and biopersistence, like the WHO fibres. However, unlike the refractory ceramic fibres, the titanium dioxide particles tested did not have the characteristic of biopersistence and had a non-fibrous morphology, which did not fulfil the WHO fibre criteria, as is apparent from the RAC Opinion (see paragraph 153 above).

177 Accordingly, the examples mentioned above illustrate only cases in which the form and size of the particles were, admittedly, taken into account, but where, nevertheless, certain properties specific to the substances at issue were decisive for their classification, which does not correspond to the case here. Thus, the contested classification and labelling are not similar to any of the examples mentioned, contrary to what the Commission contends.

178 In the light of the foregoing, the second part must be upheld, without it being necessary to examine the applicants' other arguments in the context of that part.

179 It follows from all of the foregoing that the second plea in law and the first and fifth parts of the seventh plea and the arguments raised by the second applicants in their statements in intervention in Joined Cases T-279/20 and T-288/20 and the first plea in Case T-283/20, alleging manifest errors of assessment and infringement of the criteria established by Regulation No 1272/2008 for the classification and labelling of a substance as carcinogenic, must be upheld.

180 Consequently, the contested regulation must be annulled as regards the contested classification and labelling, without there being any need to examine the applicants' other pleas and arguments.

Costs

181 Under Article 134(1) of the Rules of Procedure, the unsuccessful party is to be ordered to pay the costs if they have been applied for in the successful party's pleadings. Since the Commission has been unsuccessful, it must be ordered to bear its own costs and to pay those incurred, in Case T-279/20, by the first applicant and by the second applicants, Ettengruber GmbH Abbruch und Tiefbau, Ettengruber GmbH Recycling und Verwertung and TIGER Coatings, in Case T-283/20, by the second applicants and by Cefic, CEPE, BCF, ACA, Mytilineos and Delfi-Distomon and, in Case T-288/20, by the third applicants and by the second applicants, Sto SE & Co. and Rembrandtin Coatings, in accordance with the forms of order which they have sought.

182 Under Article 138(1) of the Rules of Procedure, the Member States and institutions which have intervened in the proceedings are to bear their own costs. Under Article 1(2)(f) of the Rules of Procedure, the term 'institutions' means the institutions of the European Union referred to in Article 13(1) TEU and the bodies, offices or agencies established by the Treaties, or by an act adopted in implementation thereof, which may be parties before the General Court. Under Article 100 of Regulation No 1907/2006, ECHA is a body of the European Union. It follows that the Kingdom of Denmark, the French Republic, the Kingdom of the Netherlands, the Kingdom of Sweden, the Republic of Slovenia, the Parliament, the Council and ECHA must bear their own costs.

On those grounds,

THE GENERAL COURT (Ninth Chamber, Extended Composition)

hereby:

1. **Joins Joined Cases T-279/20 and T-288/20 and Case T-283/20 for the purposes of the judgment;**

2. **Annuls Commission Delegated Regulation (EU) 2020/217 of 4 October 2019 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures and correcting that Regulation, as regards the harmonised classification and labelling of titanium dioxide in powder form containing 1% or more of particles with a diameter equal to or below 10 μm;**

3. **Orders the European Commission to bear its own costs and to pay the costs incurred, in Case T-279/20, by CWS Powder Coatings GmbH, Billions Europe Ltd and the other interveners whose names are listed in the annex, Ettengruber GmbH Abbruch und Tiefbau, Ettengruber GmbH Recycling und Verwertung and TIGER Coatings GmbH & Co. KG, in Case T-283/20, by Billions Europe and the other applicants whose names are listed in the annex, the Conseil européen de l'industrie chimique – European Chemical Industry Council (Cefic), the Conseil européen de l'industrie des peintures, des encres d'imprimerie et des couleurs d'art (CEPE), British Coatings Federation Ltd (BCF), American Coatings Association, Inc. (ACA), Mytilineos SA and Delfi-Distomon Anonymos Metalleftiki Etaireia and, in Case T-288/20, by Brillux GmbH & Co. KG, Daw SE, Billions Europe and the other interveners whose names are listed in the annex, Sto SE & Co. KGaA and by Rembrandtin Coatings GmbH;**

4. Orders the Kingdom of Denmark, the French Republic, the Kingdom of the Netherlands, the Kingdom of Sweden, the Republic of Slovenia, the European Parliament, the Council of the European Union and the European Chemicals Agency (ECHA) each to bear their own costs.

Costeira Kancheva Perišin

Zilgalvis Dimitrakopoulos

Delivered in open court in Luxembourg on 23 November 2022.

E. Coulon S. Papasavvas
Registrar President

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