NIA summary

European Court of Justice (ECJ) – General Court decision of 23 November 2022, annulling Commission Delegated Regulation 2020/217 of 4 October 2019 (harmonised classification and labelling of titanium dioxide as a carcinogenic substance by inhalation in certain powder forms)

Background: in 2019, titanium dioxide (in powder form containing 1% or more of particles with aerodynamic diameter ≤10 µm) was added to Annex VI of the CLP Regulation in the hazard class carcinogenicity, hazard category 2. The Commission act was based on the RAC opinion of 14 September 2017, following the competent French authority's submission of a proposal to ECHA for the classification of titanium dioxide as a carcinogenic substance. The act was subsequently contested in two separate legal cases, which the Court considered jointly.

Summary of the Court decision

Two main arguments are advanced by the applicants seeking a reversal of the titanium dioxide classification and labelling:

1. Manifest (i.e. evident) errors of assessment and infringement of the criteria established in the CLP Regulation, with regard to the acceptability and reliability of the study on which the RAC opinion is mainly based;
2. Manifest errors of assessment and infringement of the criteria established in the CLP Regulation, with regard to the "intrinsic properties" assessment.

The Court assesses these two arguments separately.

Argument 1: the RAC opinion is based on the Heinrich study, on whose reliability and acceptability opinions are divided. The RAC also erred in using a particle density value of 4.3 g/cm³ when applying the Morrow overload calculation to the Heinrich study, leading to the incorrect conclusion that the study had been conducted under acceptable lung overload conditions. Therefore, the classification and labelling of titanium dioxide are not based on data obtained by reliable and acceptable studies, and are therefore in breach of Annex I, Section 3.6.2.2.1 of the CLP Regulation.

Court reasoning:

- Both the French classification proposal and the RAC opinion are based on inhalation studies carried out on laboratory animals. The RAC opinion considered four studies, only two of which (the Heinrich study and the Lee study) reported the development of tumours following exposure to titanium dioxide;
- The French authorities gave the Lee study a Klimisch reliability score of 2 (reliable with restrictions), and the Heinrich study a reliability score of 3 (not reliable);

- Conversely, the RAC considered that the Lee study should not be a determining influence in the decision process due to the excessive exposure conditions, and mainly based its opinion on the Heinrich study;
- 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 excessive, the RAC used the Morrow overload calculation;
- The calculation was done by taking into account two factors: i) exposure level and ii) particle density, which for the Heinrich study were considered to be 10 mg/m^3 and 4.3 g/cm^3 respectively. On the basis of that calculation, the RAC concluded that the lung overload had remained within the acceptable range;
- The value used for the particle density was a standard one, as none was indicated in the study. However, the RAC also disregarded other factors relevant to the calculation, which the study did mention: in particular, i) the fact that the particles were in the nano scale, and ii) their tendency to agglomerate (the particles used were P25 grade, whose agglomerate density is established to be 1.6 g/cm^3);
- Those factors, in particular the agglomeration, have an impact on density value: this in turn impacts the volume occupied by the particles in the animals' lungs, and therefore the degree of lung overload;
- The Court finds that, by using the standard density value of 4.3 g/cm^3 without also considering the particles' size and tendency to agglomerate, the RAC failed to take into account all the relevant factors in performing the calculation and therefore committed a manifest error of assessment in applying the Morrow overload calculation to the Heinrich study;
- This error vitiates the validity of the RAC's conclusion that the lung overload of that study was acceptable, and the study results sufficiently reliable;
- The Commission then repeated the same error of assessment in basing its classification and labelling decision on the RAC opinion.

Argument 2: the contested classification and labelling do not relate to a substance that has the intrinsic property to cause cancer. First, they are based solely on the form and size of the titanium dioxide particles, which are not intrinsic properties as they are alterable, and a result of the substance treatment. Second, the reason for the toxicity observed in the studies was the deposited particles (rather than the solutes of titanium dioxide molecules), and particle toxicity is not an intrinsic hazard covered by the CLP Regulation.

Court reasoning:

- Although the CLP Regulation does not specifically define intrinsic properties, it is not disputed that these can be considered as the properties which a substance has in and of itself;
- It therefore follows that the classification and labelling of a substance as carcinogenic can only be based on specific properties of that substance which determine its capacity to cause cancer on its own;

- The contested classification and labelling refer to a hazard of category 2 carcinogenicity by inhalation, based on the results of the Heinrich study (see also above);
- In that study, malignant tumours were observed in the lungs of laboratory rats following a lung overload of nano-sized particles of titanium dioxide. The RAC opinion acknowledges that the mode of action for the rat lung carcinogenicity cannot be considered "intrinsic toxicity" in a "classical sense";
- This is because the carcinogenicity hazard identified is linked solely to titanium dioxide particles with i) a specific form and physical state i.e. powder; ii) a certain size i.e. aerodynamic diameter ≤10 µm); and which iii) are present in a certain quantity (1% or more), and iv) are respirable;
- Furthermore, the hazard identified corresponds to particle toxicity, caused by deposited particles but not the solutes of titanium dioxide molecules. Finally, the carcinogenicity hazard only occurs in lung overload conditions; and tumours appear to be triggered not by the direct contact of the titanium dioxide particles with epithelial lung cells, but rather by the inflammatory responses triggered by the overload (i.e. the accumulation of particles in the lungs in sufficient quantities to cause overload, leading to a significant impairment of particle clearance mechanisms);
- This mode of action of carcinogenicity as described in the RAC Opinion does not point to an intrinsic property of titanium dioxide particles to cause cancer;
- The RAC opinion proposes that, although this mode of action cannot be considered "intrinsic toxicity", it still has to be taken into consideration for the purpose of classification and labelling of titanium dioxide. This approach however fails to meet the criteria[1] set out in the CLP Regulation for classifying a substance as a carcinogen, and in accepting that conclusion the Commission made a manifest error of assessment;

From the conclusions above, it follows that the contested classification and labelling were adopted in breach of the CLP Regulation and must therefore be annulled.

[1] As laid down in Article 3(1) and Article 36(1) of the Regulation, read in conjunction with Section 3.6.2.2.1 of Annex I