Reports of Cases

JUDGMENT OF THE COURT (Fourth Chamber)

14 March 2024*

(Appeal – Medicinal products for human use – Application for marketing authorisation – Independence of experts consulted by the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) – Article 41 of the Charter of Fundamental Rights of the European Union – Right to good administration – Requirement of objective impartiality – Criteria for verifying the absence of conflict of interest – EMA's policy on competing interests – Activities as a principal researcher, consultant or strategic adviser for the pharmaceutical industry – Rival products – Re-examination procedure – Regulation (EC) No 726/2004 – Article 56, Article 62, Article 63 – EMA Guidelines – Consultation of a scientific advisory group (SAG) or an ad hoc expert group)

In Case C-291/22 P,

APPEAL under Article 56 of the Statute of the Court of Justice of the European Union, brought on 2 May 2022,

Debrégeas et associés Pharma SAS (D & A Pharma), established in Paris (France), represented by V. Durget, E. Gouesse and N. Viguié, avocats,

appellant,

the other parties to the proceedings being:

European Commission, represented by A. Sipos and G. Wils, acting as Agents,

European Medicines Agency (EMA), represented by C. Bortoluzzi, S. Drosos, H. Kerr and S. Marino, acting as Agents,

defendants at first instance,

THE COURT (Fourth Chamber),

composed of C. Lycourgos (Rapporteur), President of the Chamber, O. Spineanu-Matei, J.-C. Bonichot, S. Rodin and L.S. Rossi, Judges,

Advocate General: L. Medina,

Registrar: C. Di Bella, Administrator,

* Language of the case: French.

having regard to the written procedure and further to the hearing on 11 May 2023,

after hearing the Opinion of the Advocate General at the sitting on 7 September 2023,

gives the following

Judgment

1 By its appeal, Debrégeas et associés Pharma SAS (D & A Pharma) ('D & A Pharma') asks the Court of Justice to set aside the judgment of the General Court of the European Union of 2 March 2022, *D & A Pharma* v *Commission and EMA* (T-556/20, EU:T:2022:111; 'the judgment under appeal'), by which the General Court dismissed its action seeking, inter alia, annulment of the Commission implementing decision of 6 July 2020 ('the decision at issue'), refusing the application for marketing authorisation ('MA') for the medicinal product for human use Hopveus – sodium oxybate ('Hopveus'), under Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency (OJ 2004 L 136, p. 1), as amended by Regulation (EU) 2019/5 of the European Parliament and of the Council of 11 December 2018 (OJ 2019 L 4, p. 24) ('Regulation No 726/2004').

Legal context

Regulation No 726/2004

2 Recitals 19 and 23 of Regulation No 726/2004 state:

'(19) The chief task of the [European Medicines Agency (EMA)] should be to provide [European Union] institutions and Member States with the best possible scientific opinions so as to enable them to exercise the powers regarding the authorisation and supervision of medicinal products conferred on them by [EU] legislation in the field of medicinal products. …

…

(23) Exclusive responsibility for preparing the [EMA]'s opinions on all questions concerning medicinal products for human use should be vested in a Committee for Medicinal Products for Human Use. …'

3 The first paragraph of Article 1 of that regulation provides:

'The purpose of this Regulation is to lay down Union procedures for the authorisation, supervision and pharmacovigilance of medicinal products for human use and to establish [the EMA] which shall carry out the tasks relating to medicinal products for human use and veterinary medicinal products that are laid down in this Regulation and other relevant Union legislation.'

4 Article 5 of that regulation reads as follows:

‘1. A Committee for Medicinal Products for Human Use [(“the CHMP”)] is hereby set up. The Committee shall be part of the [EMA].

2. Without prejudice to Article 56 or to other tasks which Union law may confer on it, the [CHMP] shall be responsible for drawing up the opinion of the [EMA] on any matter concerning the admissibility of the files submitted in accordance with the centralised procedure, the granting, variation, suspension or revocation of an [MA] to place a medicinal product for human use on the market in accordance with the provisions of this Title, and pharmacovigilance. …

…’

5 Article 9 of that regulation provides that:

‘1. The [EMA] shall forthwith inform the applicant if the opinion of the [CHMP] is that:

(a) the application does not satisfy the criteria for authorisation set out in this Regulation;

…

2. Within 15 days after receipt of the opinion referred to in paragraph 1, the applicant may give written notice to the [EMA] that he wishes to request a re-examination of the opinion. In that case, the applicant shall forward to the [EMA] the detailed grounds for the request within 60 days after receipt of the opinion.

…

3. Within 15 days after its adoption, the [EMA] shall send the final opinion of the said [CHMP] to the [European] Commission, to the Member States and to the applicant, together with a report describing the assessment of the medicinal product by the [CHMP] and stating the reasons for its conclusions.

…’

6 Article 10(2) of Regulation No 726/2004 provides:

‘The Commission shall, by means of implementing acts, take a final decision within 15 days after obtaining the opinion of the [CHMP]. …’

7 Article 56 of that regulation provides:

‘1. The [EMA] shall comprise:

(a) the [CHMP], which shall be responsible for preparing the opinion of the [EMA] on any question relating to the evaluation of medicinal products for human use;

…

2. The committees referred to in paragraph 1 … may each establish standing and temporary working parties. The committee referred to in point (a) of paragraph 1 of this Article may establish scientific advisory groups [("SAGs")] in connection with the evaluation of specific types of medicinal products or treatments, to which it may delegate certain tasks associated with drawing up the scientific opinions referred to in Article 5.

…'

8 Article 57(1) of that regulation provides that:

'The [EMA] shall provide the Member States and the institutions of the Union with the best possible scientific advice on any question relating to the evaluation of the quality, safety and efficacy of medicinal products for human use …

To that end, the [EMA], acting particularly through its committees, shall carry out the following tasks:

(a) coordinating the scientific evaluation of the quality, safety and efficacy of medicinal products for human use and of veterinary medicinal products which are subject to Union [MA] procedures;

…'

9 Article 62 of that regulation provides:

'1. …

If there is a request for re-examination of one of its opinions where this possibility is provided for in Union law, the Committee concerned shall appoint a different rapporteur and, where necessary, a different co-rapporteur from those appointed for the initial opinion. The re-examination procedure may deal only with the points of the opinion initially identified by the applicant and may be based only on the scientific data available when the Committee adopted the initial opinion. The applicant may request that the Committee consult a [SAG] in connection with the re-examination.

2. Member States shall transmit to the [EMA] the names of national experts with proven experience in the evaluation of medicinal products for human use and veterinary medicinal products who, taking into account Article 63(2), would be available to serve on working parties or [SAGs] of any of the committees referred to in Article 56(1), together with an indication of their qualifications and specific areas of expertise.

The [EMA] shall establish and maintain a list of accredited experts. That list shall include the national experts referred to in the first subparagraph and any other experts appointed by the [EMA] or the Commission …

…'

10 Under Article 63(2) of Regulation No 726/2004:

'Members of the Management Board, members of the committees, rapporteurs and experts shall not have financial or other interests in the pharmaceutical industry which could affect their impartiality.

They shall undertake to act in the public interest and in an independent manner, and shall make an annual declaration of their financial interests. All indirect interests which could relate to this industry shall be entered in a register held by the [EMA] which is accessible to the public, on request, at the [EMA]'s offices.

The [EMA]'s code of conduct shall provide for the implementation of this Article …

Members of the Management Board, members of the committees, rapporteurs and experts who participate in meetings or working groups of the [EMA] shall declare, at each meeting, any specific interests which could be considered to be prejudicial to their independence with respect to the items on the agenda. These declarations shall be made available to the public.'

The CHMP Rules of Procedure

11 Article 11(2) of the document entitled 'Committee for Medicinal Products for Human Use – Rules of Procedure' ('the CHMP Rules of Procedure') provides:

'The re-examination of the opinion provided for in Article 9(2) of Regulation No 726/2004 may relate only to the points of the opinion initially identified by the applicant and shall be based solely on the scientific data available when the [CHMP] has adopted the initial opinion. The applicant may request that the [CHMP] consult a [SAG] (if and when it is established) in relation to the re-examination. In that case, the [CHMP] shall request the opinion of available additional experts.'

The Rules of Procedure relating to SAGs

12 The third paragraph of Section II of the EMA document entitled 'Mandate, objectives and rules of procedure for the Scientific Advisory groups (SAGs) and ad-hoc experts group' ('the Rules of Procedure relating to SAGs') states:

'When the issues refer to a therapeutic area for which no specific SAG has been constituted, an ad-hoc expert group will be organised and will follow the SAG mandate.'

13 Section IV of the Rules of Procedure relating to SAGs provides:

'…

The SAG will comprise both a core group – which ensures continuity and consistency within the group – and additional experts who may be called upon to participate to a given meeting or series of meetings on a specific issue about which they have relevant professional education, training and experience, therefore bringing additional expertise in specific domains on a case-by-case basis.

…

Appointment of the core members

Twelve core members will be selected for their clinical/technical expertise and independence in the field of interest and will be nominated for a period of 3 years.

The core group should reflect a balanced composition of scientific expertise and therefore members should have diverse professional education, training and experience. The composition of the core group should, as far as possible, reflect different schools of thinking or European therapeutic practices.

An expert in clinical trials methodology and biostatistics should always be one of the core members and may be appointed to more than one SAG.

…'

14 Point 4 of Section VII of the Rules of Procedure relating to SAGs provides:

'Participation of Additional Experts in SAG meetings

CHMP Members, SAG Chair and the EMA will make proposals for additional experts on the basis of their expertise in the therapeutic area or field to be covered by the particular SAG meeting, according to the CHMP List of Questions for the SAG.

…'

The guidelines on the re-examination procedure

15 According to point 6.1 of the document entitled 'Procedural advice on the Re-examination of CHMP Opinions' ('the guidelines on the re-examination procedure'):

'The decision on consultation of the SAG for a re-examination procedure will amongst others depend on the CHMP or the applicant/MAH's request for consultation of the SAG by [the] CHMP.

In case the [applicant] requests [the consultation of] a SAG, the [applicant] will preferably inform the CHMP of this request as early as possible. Such request should be duly motivated. When there is no request from the [applicant] the CHMP will decide on the need for additional expertise. In case of a request for consultation of the SAG coming from the applicant, the CHMP will systematically consult the SAG.

In a therapeutic area where no SAG is established, the advice of additional available expertise will be requested in the form of consultation of an ad hoc expert group meeting.

During the CHMP meeting following receipt of the [applicant's] written notice to the [EMA] or detailed grounds for requesting a re-examination of the opinion, the CHMP decides on the consultation of the SAG and its composition (with regard to experts other than the SAG core group), and the CHMP adopts a List of Questions to the SAG.

…'

The EMA Code of Conduct

16 Under Point 2.3.2 of the EMA Code of Conduct, referred to in the third subparagraph of Article 63(2) of Regulation No 726/2004:

'The definition of what is an interest is set out in the specific EMA policies. …'

17 Under Point 2.3.3 of the EMA Code of Conduct:

'For members of the Management Board or Scientific Committees, rapporteurs and experts as well as EMA staff involvement in the Agency's activities is subject to the availability of a signed declaration of interests form and an assessment of the declared interests. The restrictions that will apply in terms of the individual's activities in the context of the EMA's role and responsibilities will depend on the specific individual's competing interest and their particular role. The details of the relevant restrictions are set out in the EMA policy documents.'

The policy on competing interests

18 In accordance with point 3.2.1 of the document, published by the EMA, entitled 'European Medicines Agency policy on the handling of competing interests of scientific committees' members and experts', in the version of 6 October 2016, applicable to the appellant's request for re-examination ('the policy on competing interests'):

'…

Direct interests in pharmaceutical industry are:

…

– Consultancy to a company

– Strategic advisory role for a company

…

Indirect interests in pharmaceutical industry are:

– Principal investigator

…

'

19 Point 3.2.1.1 of the policy on competing interests reads as follows:

'Consultancy to a pharmaceutical company shall mean: any activity where the concerned expert provides advice (including training on a one to one basis) to a pharmaceutical company regardless of contractual arrangements or any form of remuneration.

…

Strategic advisory role for a pharmaceutical company shall mean: any activity where the expert is participating (with a right to vote/influence the outputs) in a(n) (scientific) advisory board/steering committee with the role of providing advice/expressing opinions on the (future) strategy, direction and development activities of a pharmaceutical company, either in terms of general strategy or product related strategy, regardless of contractual arrangements or any form of remuneration.

…'

20 According to point 3.2.1.2 of that policy:

'…

Principal investigator shall mean: an investigator with the responsibility for the coordination of investigators at different centres participating in a multicentre pharmaceutical industry instigated/sponsored trial or the leading investigator of a monocentre pharmaceutical industry instigated/sponsored trial, or the coordinating (principal) investigator signing the clinical study report.

…'

21 Point 3.2.2 of that policy provides:

'…

Rival product shall mean: a medicinal product that targets a similar patient population with the same clinical objective (i.e. to treat, prevent or diagnose a particular condition), and constituting a potential commercial competition.

…'

22 Point 4.1 of that policy states:

'The main objective of the policy is to ensure that the scientific committees' members and the experts participating in the [EMA]'s activities have no interests in the pharmaceutical industry which could affect their impartiality, as per the requirements of EU legislation. This has to be balanced with the need to secure the best (specialist) scientific expertise for the evaluation and surveillance of medicinal products …

…'

23 According to point 4.2.1.1 of the policy on competing interests:

'In terms of declarations of interests 3 interest levels can be identified:

"direct interests declared" (i.e. interest level 3);

"indirect interests declared" (i.e. interest level 2);

"no interests declared" (i.e. interest level 1).

The primary focus is on direct interests in pharmaceutical industry leading to the most pronounced restrictions on involvement in the [EMA]'s activities.

Indirect interests in pharmaceutical industry will be addressed through mitigating actions to reach the best possible balance between limiting the involvement in the [EMA]'s activities and the need for the availability of the best (specialist) scientific expertise.

…'

24 Point 4.2.1.2 of that policy provides:

'…

Specific case of rival products

For the specific case of rival products (formerly referred to as competitor products) a two tier approach is applied:

The concept of rival products relates to those situations where there are only a very small number (1 to 2) of rival products. …

For broad indications, since many products are authorised for the same indication, the existing volume of competition dilutes adequately potential interests.

In situations characterised by only a very small number of rival products as specified above, consequences will relate to the (vice)-chairpersons of the scientific committees and the working parties, as well as the rapporteurs or other members in a leading/co-ordinating role, or formally appointed peer reviewers.'

25 Point 4.4 of the policy is worded as follows:

'The consequences of the application of the principles laid down in this policy in terms of the allowable interests are summarised in annex 1 "Scientific committees' members and experts allowed involvement in medicinal product related matters".

…'

26 Annex I to the policy on competing interests contains a table which specifies, for each type of participation in the evaluation of pharmaceutical products in the context of procedures before the EMA, the restrictions that apply depending on the nature of the interests declared and the period during which that interest existed.

27 As regards, in particular, experts who have declared a current interest as 'principal investigator', within the meaning of that policy, it is apparent from that table that they may be a member of a SAG or an ad hoc expert provided that their participation is limited in the case of a medicinal product concerned by such an interest:

'Involvement only in discussions with respect to procedures involving the relevant medicinal product, i.e. no part in final deliberations and voting as appropriate as regards the medicinal product.'

28 As regards experts who have declared a current interest as a consultant or strategic advisory role for a pharmaceutical company, that table draws a distinction between, on the one hand, the situation where that interest consists of providing consultancy services which are general or cover several medicinal products and, on the other hand, the situation where that interest consists of providing consultancy services concerning an individual medicinal product. In the first case, any participation in an a SAG or an ad hoc expert group is prohibited, whereas, in the second case, the possibility of being a member of a SAG or an ad hoc expert group is restricted only, as follows:

'No involvement with respect to procedures involving the relevant medicinal product, i.e. no part in discussions, final deliberations and voting as appropriate as regards the medicinal product.'

Background to the dispute

29 The background to the dispute was set out by the General Court in paragraphs 2 to 12 of the judgment under appeal and may, for the purposes of the present proceedings, be summarised as set out below.

30 On 26 June 2018, D & A Pharma filed an application for a conditional MA with the EMA for Hopveus under Commission Regulation (EC) No 507/2006 of 29 March 2006 on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC) No 726/2004 of the European Parliament and of the Council (OJ 2006 L 92, p. 6).

31 Hopveus, which contains sodium oxybate as its active substance, is intended to combat dependence on alcohol.

32 On 17 October 2019, the CHMP issued an unfavourable opinion on that application.

33 On 29 October 2019, D & A Pharma requested a re-examination of the CHMP's opinion pursuant to Article 9(2) of Regulation No 726/2004 ('the request for re-examination').

34 For the purposes of that re-examination, the CHMP convened an ad hoc expert group.

35 Following a new unfavourable opinion from the CHMP dated 30 April 2020, the Commission, by means of the decision at issue, refused the application for a conditional MA.

The procedure before the General Court and the judgment under appeal

36 D & A Pharma brought an action against the Commission and the EMA, seeking annulment of the contested decision and that, following that annulment, the SAG on Psychiatry should be convened in the composition in which it was at the date of the request for re-examination.

37 In paragraphs 21 and 22 of the judgment under appeal, the General Court found that the contested decision emanated from the Commission and that the action was consequently inadmissible in so far as it was directed against the EMA. However, the General Court examined the legality of the procedure before the EMA, since the Commission relied on the opinion provided by the CHMP, which is an integral part of EMA.

38 D & A Pharma put forward six pleas in law in support of its action. The first plea alleged a procedural defect, in that the CHMP had convened an ad hoc expert group and not the SAG on Psychiatry for the purposes of the re-examination of the application for an MA for Hopveus. The second plea alleged a lack of impartiality on the part of two members of that ad hoc expert group (respectively, 'Expert A' and 'Expert B' or, together, 'Experts A and B'). The third plea alleged a procedural defect on account of a failure to comply with the rules governing the operation of the ad hoc expert group and a breach of the principle of adversarial examination of the MA application. The fourth to sixth pleas alleged an error of law, manifest errors of assessment and breaches of the principle of equal treatment.

39 In the judgment under appeal, the General Court, having considered those pleas to be unfounded, dismissed the action.

Procedure before the Court and forms of order sought

40 By document lodged at the Court Registry on 2 May 2022, D & A Pharma brought the present appeal.

41 By this appeal, the appellant claims that the Court of Justice should:

– set aside the judgment under appeal;

– give final judgment on the action brought before the General Court, seeking, in particular, annulment of contested decision, and

– order the Commission and the EMA to pay the costs.

42 The Commission and the EMA contend that the Court of Justice should:

– dismiss the appeal; and

– order the appellant to pay the costs.

43 Following an application made by the appellant on 9 August 2022, the President of the Court of Justice granted it leave to lodge a reply.

44 After the Commission and the EMA lodged their rejoinders, the written part of the procedure in the present case was closed on 25 November 2022.

45 On 14 April 2023, the appellant requested that the written part of the procedure be reopened. In support of that request, it relied on the existence of additional evidence which it considered important for a proper understanding of the file, namely, first, a doctoral thesis concerning the efficacy of sodium oxybate in the treatment of alcohol dependence and, second, the assessment of that thesis by the jury which assessed it.

46 That request was refused by the President of the Fourth Chamber of the Court for the following reasons.

47 Article 128(2) of the Rules of Procedure of the Court of Justice, which appears in the part of those rules dealing with direct actions, provides that the parties to the proceedings may, exceptionally, produce or offer further evidence after the close of the written part of the procedure, which may lead to the prescription of a time limit within which the other party may comment on such evidence. A similar provision is not, however, laid down in the Rules of Procedure in relation to appeals, since in that context the Court of Justice does not, in principle, have jurisdiction to examine such evidence, except where it has been distorted by the General Court, which cannot, by definition, be the case of new evidence submitted to the Court of Justice for the first time.

48 Moreover, since the appellant does not maintain, in the context of the present appeal, that the General Court distorted the facts and evidence submitted for its assessment, by finding, contrary to those facts and evidence, that sodium oxybate was not effective in the treatment of alcohol dependence, the Court of Justice does not have jurisdiction to examine that question. It follows that the additional evidence relied on by the appellant is in any event irrelevant.

49 Accordingly, the President of the Fourth Chamber of the Court decided that the request to reopen the written part of the procedure should be rejected, without having to examine the question, raised by the appellant in its request for such reopening, of whether the non-applicability of Article 128(2) of the Rules of Procedure in appeal proceedings may, in certain circumstances, be contrary to the right to an effective remedy enshrined in Article 47 of the Charter of Fundamental Rights of the European Union ('the Charter').

The appeal

50 The appellant puts forward two grounds in support of its appeal. The first ground of appeal alleges that the General Court erred in law in holding that the CHMP's decision not to convene the SAG on Psychiatry was not unlawful and in its legal characterisation of the facts in holding that that decision could not have influenced the outcome of the contested decision. The second ground of appeal alleges that the General Court erred in law and in its legal characterisation of the facts in so far as it held, in the context of its examination of the requirement of objective impartiality, that Experts A and B were not in a situation of conflict of interest.

Arguments of the parties

51 In the first part of the second ground of appeal, which should be examined at the outset, the appellant claims that the General Court erred in law by requiring proof of bias or personal prejudice on the part of Experts A and B.

52 In that regard, it points out that bias or personal prejudice represents a lack of subjective impartiality. Since it had alleged a lack of objective impartiality, the General Court should have examined whether there were sufficient guarantees to exclude any legitimate doubt as to the impartiality of those experts.

53 Contrary to what the General Court held in paragraphs 132 and 133 of the judgment under appeal, that requirement of objective impartiality, it is argued, applies to any person involved in an administrative procedure and not only to persons vested with particular responsibilities.

54 The General Court, it asserts, wrongly relied on the possible influence – which could not be established, since the deliberations of the expert groups were confidential – exercised by Experts A and B, even though it should have examined whether the links between those experts and the pharmaceutical industry were such as to give rise to objectively justified doubts as to their impartiality.

55 According to the second part of the ground of appeal, that error of law, which constitutes an infringement of the right to good administration enshrined in Article 41 of the Charter, was coupled with an error in the legal characterisation of the facts, since the General Court wrongly held that Experts A and B were not in a situation of conflict of interest.

56 In its examination of the situation of those experts, the General Court, in particular, misinterpreted the concept of 'rival product'.

57 The General Court also failed to have regard to the content of Annex I to the policy on competing interests. According to the appellant, it is apparent in particular from that annex that persons providing consultancy services for several pharmaceutical products, such as Expert A, cannot be members of an expert group consulted by the CHMP.

58 Expert B was a principal investigator for the product AD 04, developed by the company Adial Pharmaceuticals. At the time of Expert B's participation in the ad hoc expert group convened to assess Hopveus, AD 04 was, according to the appellant, the subject of an examination procedure before the EMA. However, AD 04 is intended for the treatment of alcohol dependence and is therefore a rival product to Hopveus, because of the identity of the clinical objective and the similarity of the patients targeted. Paragraph 103 of the judgment under appeal is wrong in law, in that it amounts to artificially partitioning medicinal products intended to treat the same condition, depriving the definition of the concept of 'rival product' of its effectiveness.

59 Paragraph 104 of the judgment under appeal is also wrong in law, it is argued, in that it amounts to saying that only experts who have worked on the product that is the subject of the re-examination procedure cannot be members of the expert group consulted, whereas experts who have worked on rival products may do so.

60 In the appellant's view, if the policy on competing interests were, as the General Court held, to be understood as meaning that the principal investigator for a product may participate in the panel of experts which assesses the suitability of a rival product to be granted marketing authorisation, it would have to be concluded that that policy is contrary to the requirement of objective impartiality as derived from Article 41 of the Charter. The General Court's interpretation of that policy cannot, therefore, be upheld.

61 The Commission and the EMA submit that the requirement of impartiality, enshrined in Article 41 of the Charter, is reflected in Article 63(2) of Regulation No 726/2004 and in the EMA Code of Conduct, adopted pursuant to the latter provision. The decision of the EU legislature to empower the EMA to implement Article 63(2) expresses the fact that that agency is the body best placed to assess the interests involved. The EMA struck a very detailed balance between the need for impartiality and the need for a high level of expertise. That balancing operation is expressed in Annex I to the policy on competing interests.

62 The appellant's argument that the General Court examined the plea alleging infringement of objective impartiality in the light of the applicable criterion for assessing compliance with subjective impartiality is based on a misreading of the judgment under appeal.

63 In particular, the General Court was right to find, in paragraphs 130 and 131 of the judgment under appeal, that the conclusions of the ad hoc expert group were adopted collectively by all its members and that the principle of collegiality guarantees the objective impartiality of the opinions expressed. That assessment is consistent with the case-law of the Court of Justice resulting from the judgments of 1 July 2008, *Chronopost and La Poste* v *UFEX and Others* (C-341/06 P and C-342/06 P, EU:C:2008:375), and of 19 February 2009, *Gorostiaga Atxalandabaso* v *Parliament* (C-308/07 P, EU:C:2009:103).

64 It follows, admittedly, from paragraphs 34 and 38 of the judgment of 27 March 2019, *August Wolff and Remedia* v *Commission* (C-680/16 P, EU:C:2019:257), that, where an expert plays a leading role in the expert group, doubts as to his or her impartiality cannot be dispelled solely on the basis of the principle of collegiality. However, in the present case, Experts A and B did not play such a role in the ad hoc expert group.

65 The General Court was also right to conclude that none of the competing interests of Expert A or Expert B was likely to lead to a conflict of interest.

66 As regards Expert B, the Commission and the EMA maintain that, at the time of the meeting of the ad hoc expert group concerning Hopveus, AD 04 was not yet the subject of an MA application. In any event, the General Court did not err in holding that AD 04 and Hopveus were not rival products, since the patients targeted by AD 04 wish only to limit their alcohol consumption.

67 The Commission and the EMA add that, even if AD 04 were to be regarded as a rival product of Hopveus, the policy on competing interests clearly indicates that an expert who has contributed to the development of a pharmaceutical product is not prohibited from being a member of expert groups convened by the CHMP to examine a rival product. The General Court rightly found, in paragraph 104 of the judgment under appeal, that Expert B would have been prevented from being a member of such a group only if the re-examination procedure concerned the product for which he is the principal investigator.

68 As regards Expert A, the Commission and the EMA argue that the competing interests of that expert, such as his activities as a consultant for the pharmaceutical companies Lundbeck and Janssen, did not lead to a conflict of interest.

69 In that regard, the EMA emphasised, at the hearing before the General Court, that, in his declaration of competing interests, Expert A had clearly specified which individual medicinal products were covered by his consultancy activities carried out for the companies Lundbeck and Janssen. The role of that expert consists of providing advisory services that are not general or cover several medicinal products, within the meaning of Annex I to the policy on competing interests, but in relation to an individual medicinal product, within the meaning of Annex I. It follows that Expert A could be a member of any expert group convened by the CHMP, with the sole exception of those examining the medicinal products concerned by his consultancy activities.

70 Moreover, the appellant has not raised a plea of illegality against the policy on competing interests. The General Court was therefore right to limit itself to finding that that policy did not preclude the participation of Experts A and B in the ad hoc expert group and that that policy, which involved a detailed examination of the interests at stake, was adopted on the basis of the empowerment set out in Article 63(2) of Regulation No 726/2004.

Findings of the Court

71 By the first part of the second ground of appeal, the appellant complains that the General Court erred in law in requiring proof of bias or personal prejudice on the part of Experts A and B.

72 In that regard, it must be borne in mind that the fundamental right to good administration, set out in Article 41 of the Charter, includes, under paragraph 1 of that provision, the right to have one's affairs handled impartially by the institutions, bodies, offices and agencies of the European Union.

73 That requirement of impartiality has a subjective component and an objective component. In accordance with the latter component, on which the appellant relies, each institution, body, office or agency of the European Union must offer sufficient guarantees to exclude any legitimate doubt as to any bias (see, to that effect, judgments of 27 March 2019, *August Wolff and Remedia* v *Commission*, C-680/16 P, EU:C:2019:257, paragraph 27, and of 12 January 2023, *HSBC Holdings and Others* v *Commission*, C-883/19 P, EU:C:2023:11, paragraph 77).

74 The Court has already had occasion to find that the objective impartiality of the CHMP, and therefore of the EMA, is compromised where a conflict of interest on the part of one of the members of the CHMP is likely to result from an overlap of functions, irrespective of the personal conduct of that member. Such a failure is liable to render unlawful the decision adopted by the Commission at the end of the procedure (see, to that effect, judgment of 27 March 2019, *August Wolff and Remedia* v *Commission*, C-680/16 P, EU:C:2019:257, paragraphs 28 and 30).

75 The objective impartiality of the CHMP is also compromised where an expert who is in a situation of conflict of interest is part of the expert group which is consulted by that committee in the context of the re-examination leading to the opinion of the EMA and the Commission's decision on the MA application.

76 It must be observed, in that regard, that the opinion expressed by the expert group convened by the CHMP has a potentially decisive influence on the EMA's opinion and, through that opinion, on the Commission's decision. Each member of that group may, in some circumstances, have a considerable influence on the discussions and deliberations that take place, on a confidential basis, within that group. Accordingly, participation in the expert group consulted by the CHMP of a person who is in a situation of conflict of interest gives rise to a situation that does not offer sufficient guarantees to exclude any legitimate doubt as to possible bias, within the meaning of the case-law referred to in paragraph 73 of the present judgment.

77 Therefore, contrary to what the General Court held in paragraphs 130 to 132 of the judgment under appeal, a conflict of interest on the part of a member of the expert group consulted by the CHMP substantially vitiates the procedure. The fact that, at the end of its discussions and deliberations, that expert group expresses its opinion collegially does not remove such a defect. That collegiality is not such as to neutralise either the influence that the member in a situation of

conflict of interest is in a position to exert within that group or the doubts as to the impartiality of that group which are legitimately based on the fact that that member was able to contribute to the discussions.

78 Those considerations are not invalidated by the principles laid down by the Court in the judgments of 1 July 2008, *Chronopost and La Poste* v *UFEX and Others* (C-341/06 P and C-342/06 P, EU:C:2008:375), and of 19 February 2009, *Gorostiaga Atxalandabaso* v *Parliament* (C-308/07 P, EU:C:2009:103), relied on by the Commission and the EMA. Unlike the present case, the cases which gave rise to those judgments did not concern a conflict of interest that could arise from activities of the person concerned that are unrelated to those he or she carries out in proceedings before an institution, body, office or agency of the European Union.

79 Nor are the considerations set out in paragraphs 75 to 77 of the present judgment invalidated by the fact that the members of the expert group whose participation is challenged in the light of the requirement of objective impartiality do not exercise a management or coordination function in that group. It cannot be accepted, contrary to what the General Court stated in paragraphs 131 and 132 of the judgment under appeal, that only members exercising such a role may have a significant influence on the conduct or outcome of the procedure.

80 Moreover, persons whose affairs are handled by an EU institution, body, office or agency cannot be required to provide, in support of their argument that the requirement of objective impartiality was not complied with during an EU administrative procedure, proof of specific indications of bias, such as statements or positions taken by the expert concerned within the expert group of which he or she is a member. Objective impartiality is to be assessed independently of the specific conduct of the person concerned. In any event, the statements and positions taken in the context of the work of that group are confidential. As the General Court acknowledged in paragraph 132 of the judgment under appeal, it is impossible to determine the influence exercised by the experts concerned. Consequently, the fact that, in the present case, the appellant was unable to adduce evidence of a specific statement or position taken by Expert A or Expert B was irrelevant for the purpose of assessing the merits of the plea alleging infringement of the requirement of objective impartiality, with the result that the General Court was wrong, in paragraph 133 of the judgment under appeal, to rely, inter alia, on such a ground in order to conclude that the appellant's second plea in support of its action for annulment should be rejected.

81 It follows from the foregoing that the first part of the second ground of appeal is well founded.

82 It must be stated, however, that the abovementioned paragraphs 130 to 133 of the judgment under appeal, which are vitiated by the errors of law relied on by the appellant in the first part of the second ground of appeal, constitute only one of the two grounds on which the General Court's reasoning is based. The General Court held, in paragraphs 99 to 129 of that judgment, that Experts A and B were not, in accordance with the policy on competing interests, in a situation of conflict of interest when they participated in the discussions and deliberations of the ad hoc expert committee consulted by the CHMP in the context of the re-examination of the MA application for Hopveus, and that that policy was sufficient to ensure compliance with the requirement of objective impartiality, as follows from Article 41 of the Charter.

83 Therefore, it is necessary to examine the second part of the second ground of appeal, by which the appellant submits that the General Court also erred in law in holding that the competing interests of those experts did not place them in a situation of conflict of interest.

84 In that regard, it should be recalled that the EU legislature chose, as regards the requirement of impartiality of the EMA's experts, to lay down essential criteria in Regulation No 726/2004 and then to entrust that agency with the task of implementing them (see, to that effect, judgment of 22 June 2023, *Germany and Estonia* v *Pharma Mar and Commission*, C-6/21 P and C-16/21 P, EU:C:2023:502, paragraph 50).

85 In that regard, it is for the EMA to reconcile, on the one hand, the twofold requirement of impartiality and independence of its experts, as laid down in Article 63(2) of Regulation No 726/2004, and, on the other hand, the public interest, referred to in Article 57(1) of that regulation, relating to the need for the best possible scientific advice on any question relating to the evaluation of the quality, safety and efficacy of medicinal products for human or veterinary use that is referred to it (judgment of 22 June 2023, *Germany and Estonia* v *Pharma Mar and Commission*, C-6/21 P and C-16/21 P, EU:C:2023:502, paragraph 51).

86 In order to enable the EMA to pursue effectively the objective thus assigned to it, and in view of the complex technical assessments which it must undertake, the broad discretion conferred on it manifests itself in particular in the definition of the criteria which must govern the impartiality and independence of the individuals contributing to the preparation of its scientific opinions (judgment of 22 June 2023, *Germany and Estonia* v *Pharma Mar and Commission*, C-6/21 P and C-16/21 P, EU:C:2023:502, paragraph 52).

87 However, notwithstanding the existence of that broad discretion and the importance of the public interest referred to above, the EMA is required, in the exercise of its powers, under Article 51(1) of the Charter, to respect the rights and principles mentioned therein.

88 That agency is, in particular, bound by the requirements of Article 52(1) of the Charter. That provision states that any limitation on the exercise of the rights and freedoms recognised by the Charter must be provided for by law and respect the essence of those rights and freedoms, and that, subject to the principle of proportionality, limitations may be made only if they are necessary and genuinely meet objectives of general interest recognised by the European Union or the need to protect the rights and freedoms of others.

89 It follows that, while taking care to comply with the objective of general interest referred to in Article 57(1) of Regulation No 726/2004, which may justify, as is apparent from the case-law referred to in paragraph 85 of the present judgment, a mitigation of the requirement of objective impartiality of the persons involved in the processing of an MA application, a requirement which stems from the fundamental right to good administration, the EMA must respect the essence of that fundamental right and the principle of proportionality. In particular, it cannot be accepted that that agency, on the pretext of wishing to maximise the number of experts available, should impose restrictions on the exercise of their mandate that appear insufficient to guarantee, in the context of that exercise, an impartial procedure. That would be the case, in particular, if experts whose activities revealed a current interest in relation to a rival product of the product that is the subject of an MA application were allowed to be members, without restriction or mitigation, of the expert group convened by the CHMP for the purposes of re-examining that MA application.

90 It is therefore important that the criteria formulated in the policy on competing interests and leading to the restrictions and mitigations listed in the table in Annex I to that policy should be commensurate, in particular, with the respective importance of the competing interests concerned (see, to that effect, judgment of 22 June 2023, *Germany and Estonia* v *Pharma Mar and Commission*, C-6/21 P and C-16/21 P, EU:C:2023:502, paragraph 53).

91 It is in the light of the grounds set out in paragraphs 84 to 90 of the present judgment that it is necessary to examine whether, in the present case, the General Court erred in law in its assessment of the appellant's complaints concerning the participation of Experts A and B in the ad hoc expert group consulted by the CHMP in the context of the re-examination of the MA application for Hopveus.

92 As regards Expert B's participation, which the General Court examined first, it is apparent from paragraphs 99, 100, 103 and 105 of the judgment under appeal that that expert was, at the time of the work of the ad hoc expert group concerning the Hopveus, 'principal investigator', within the meaning of the policy on competing interests, for the European Phase III clinical trial of AD 04. That product has been developed by the company Adial Pharmaceuticals and its therapeutic indication, like that of Hopveus, consists of combating alcohol dependence.

93 As is apparent from point 3.2.1.2 of the policy on competing interests, a principal investigator, within the meaning of that policy, is a person who engages in an activity that is induced and/or sponsored by the pharmaceutical industry.

94 In order to determine whether Expert B should have been excluded from the ad hoc expert group, the General Court, first of all, examined whether AD 04 should be classified as a 'rival product' of Hopveus.

95 In the light of the clarification provided by point 4.2.1.2 of the policy on competing interests, according to which 'competitor products' are now called 'rival products', it must be held that the concept of 'competitor product' used by the General Court refers to 'rival product' within the meaning of that policy. Moreover, the General Court expressly referred, in paragraphs 101 and 102 of the judgment under appeal, to the paragraphs of that policy relating to the concept of 'rival product'.

96 In paragraph 103 of the judgment under appeal, the General Court held that AD 04 and Hopveus were not rival products, since AD 04 was aimed at 'patients wishing to control their alcohol consumption, but who cannot or do not want to abstain completely from drinking', whereas Hopveus was intended to 'accompany patients seeking to abstain from alcohol completely'.

97 Section 3.2.2 of the policy on competing interests defines the concept of 'rival product' as a 'medicinal product that targets a similar patient population with the same clinical objective (i.e. to treat, prevent or diagnose a particular condition), and constituting a potential commercial competition'.

98 Although that definition applies, in the present case, to a procedure for re-examining an MA application and does not concern products that are already on the market, it nevertheless reflects the criterion used by the Court's case-law to assess whether two pharmaceutical products are competitors on a given market. According to that case-law, that is the case where, for the same therapeutic indication, those products are interchangeable or substitutable (see in particular, to that effect, judgments of 23 January 2018, *F. Hoffmann-La Roche and Others*, C-179/16, EU:C:2018:25, paragraphs 51 and 65, and of 30 January 2020, *Generics (UK) and Others*, C-307/18, EU:C:2020:52, paragraph 129).

99 It is therefore on the basis of an examination to determine whether, in the event that AD 04 and Hopveus are marketed, those products, both of which have been developed for the purpose of treating alcohol dependence, would present such a degree of interchangeability or substitutability that it would be necessary to determine the existence or absence of potential commercial competition.

100 That assessment of the interchangeability or substitutability of two products intended for a population of patients treated for the same condition need not be carried out solely in relation to the objective characteristics of those products (see, to that effect, judgment of 30 January 2020, *Generics (UK) and Others*, C-307/18, EU:C:2020:52, paragraph 129 and the case-law cited). It is true that the conditions of demand and supply cannot be known before a trade mark is placed on the market. Nevertheless, the examination of potential commercial competition between the products at issue must be based on an overall assessment of the factors that may be taken into account in order to assess whether patients and their prescribing doctors will be able to view one product as a valid alternative to the other.

101 By excluding the possibility of commercial competition on the ground that AD 04 and Hopveus have different clinical objectives and target different groups of patients, namely, as regards the former, those who intend to limit their alcohol consumption and, as regards the latter, those who intend to stop that consumption altogether, the General Court did not carry out such an overall assessment.

102 In that regard, it must be held that the mere difference in intensity in the scope of the therapeutic action between two products intended to treat the same condition is specifically capable of encouraging certain patients suffering from that condition to replace, in the course of their treatment, one of those products with the other depending on the evolution of their symptoms or on considerations by their prescribing doctors regarding their therapeutic appropriateness or efficacy.

103 It follows that the General Court failed to examine whether those products were likely to compete with each other in the light of all the relevant factors, in particular the fact that changes in the treatment of the same patient may lead his or her doctor to prescribe those two products alternately during that treatment, depending on the symptoms and considerations of therapeutic appropriateness and efficacy.

104 Therefore, in concluding that there was no potential commercial competition between AD 04 and Hopveus without making an overall assessment of all the relevant factors, the General Court erred in law.

105 That conclusion is not invalidated by the reference, in paragraph 102 of the judgment under appeal, to point 4.2.1.2 of the policy on competing interests, according to which ‘the concept of rival products relates to those situations where there are only a very small number (1 to 2) of rival products’, the consequences of such a situation concerning, moreover, only ‘the (vice)-chairpersons of the scientific committees and the working parties, as well as the rapporteurs or other members in a leading/co-ordinating role, or formally appointed peer reviewers’.

106 In that regard, it should be noted, without the Court needing to rule on the question whether point 4.2.1.2 of that policy potentially unduly restricts the scope of the principles relating to rival products and the requirement of objective impartiality, that, in its assessment in paragraph 103 of the judgment under appeal, the General Court relied not on point 4.2.1.2 but on the factors mentioned in paragraph 96 of the present judgment.

107 The error of law committed, independently of paragraph 102 of the judgment under appeal, in paragraph 103 of that judgment vitiates the reasoning followed by the General Court, notwithstanding the finding set out in paragraph 104 of the judgment according to which, even assuming that AD 04 and Hopveus constitute rival products, Expert B's participation in the meeting of the ad hoc expert group concerning Hopveus was not be prohibited, since the policy on competing interests prohibits the participation of a principal investigator in the expert group consulted by the CHMP only at the time of the final deliberations and vote in a re-examination procedure concerning the same product as that for which that expert acts as principal investigator.

108 Paragraph 104 of the judgment under appeal is itself vitiated by an error of law, so that it would not, on its own, be sufficient to hold that the operative part of the contested judgment is lawfully justified notwithstanding the error of law in paragraph 103 of that judgment.

109 In paragraph 104, the General Court interpreted the policy on competing interests as meaning that an expert who is principal investigator for a product the development of which is instigated and/or sponsored by the pharmaceutical industry and that is a rival of the product which is the subject of a procedure for re-examination of an MA application before the EMA, may be a member of the expert group consulted by the CHMP in that re-examination procedure.

110 In the same paragraph 104, the General Court also interpreted that policy as meaning that a principal investigator may, moreover, be a member of the expert group that is consulted by the CHMP in the event of re-examination of an MA application submitted for the product for whose development he or she acts as principal investigator, provided only that he or she withdraws from the work of that group during the final deliberations and the vote.

111 Those findings of the General Court must be read in conjunction with paragraphs 127 to 129 of the judgment under appeal, according to which the compliance of the policy on competing interests with the principle of objective impartiality, as it follows from Article 41 of the Charter, should not be called into question since the EMA carried out a detailed examination of all the situations of conflicts of interest likely to arise, and the appellant had not raised a plea of illegality in respect of that policy under Article 277 TFEU.

112 While the General Court was entitled to hold that, since the appellant did not claim that it was unlawful, there was no need to examine the lawfulness of the policy on competing interests, it could not have been unaware that the EMA is bound, when exercising its powers, by the Charter and must therefore, in any event, interpret and apply its policy in a manner consistent with it.

113 In the present case, irrespective of the scope to be given to the undefined concept of 'relevant medicinal product', which appears in the mitigating measure – within the meaning of the third paragraph of Point 4.2.1.1 of the policy on competing interests – that Annex 1 to that policy imposes on experts with a current competing interest as principal investigator, that mitigation measure, according to which those experts may, in procedures concerning the 'relevant medicinal product', be involved 'only in the discussions', which implies that they are only prohibited from

participating in the 'final deliberations and voting', cannot, without disproportionately limiting the protection of objective impartiality, be interpreted or applied as meaning that such an expert may participate in the work of an expert group that is consulted by the CHMP in the procedure for re-examination of an MA application that has been submitted for a product that is a rival of the product for which that expert is at the same time, at the instigation and/or under the sponsorship of the pharmaceutical industry, the principal investigator.

114 Such participation, by its very nature, would be inappropriate in order to ensure that the re-examination procedure in question is conducted impartially. It is sufficient to observe, in that regard, that a refusal to grant an MA for the rival product under re-examination is likely to be of considerable commercial interest to the company at the instigation and/or under the sponsorship of which such an expert carries out his or her activity as principal investigator. His or her participation in the expert group consulted by the CHMP in the context of that re-examination would give rise to a legitimate doubt as to the existence of possible bias.

115 It follows that paragraph 104 of the judgment under appeal is vitiated by an error of law, in that the General Court's interpretation of the policy on competing interests is incompatible with the principle of objective impartiality, as set out in Article 41(1) of the Charter.

116 Similarly, the restrictions – within the meaning of the second paragraph of point 4.2.1.1 of the policy on competing interests – imposed by Annex I to that policy on experts who have declared a current interest as a consultant or strategic adviser for individual medicinal products of one or more pharmaceutical companies cannot, contrary to what the General Court held in paragraph 119 of the judgment under appeal, be interpreted and applied as meaning that such an expert may, unless he or she is the chairperson, vice-chairperson, rapporteur or other member having a leading or coordinating role within that expert group, be a member of the ad hoc expert group convened by the CHMP for the purpose of re-examining the MA application submitted for a product which is a rival of one of those individual medicinal products. Such an interpretation, which the General Court adopted in its analysis of Expert A's participation in the work of the ad hoc expert group consulted on Hopveus, is also incompatible with the principle of objective impartiality.

117 It follows from all the foregoing considerations that the second part of the second ground of appeal is also well founded.

118 Accordingly, the judgment under appeal must, without it being necessary to examine the first ground of appeal, be set aside, except, however, in so far as that judgment declares the action brought against the EMA inadmissible. Since the General Court declared the action inadmissible in so far as it was directed against the EMA and that assessment, which is covered by the operative part thereof, was not challenged on appeal, that part of the judgment under appeal has the force of res judicata (see, by analogy, judgment of 4 March 2021, *Commission* v *Fútbol Club Barcelona*, C-362/19 P, EU:C:2021:169, paragraph 109 and 110).

The action before the General Court

119 Pursuant to the first paragraph of Article 61 of the Statute of the Court of Justice of the European Union, the Court may itself, where the state of the proceedings so permits, give final judgment in the matter.

120 The Court considers it appropriate to give final judgment in the present case. The state of the proceedings so permits, since the appellant's action for annulment before the General Court is based on pleas which were the subject of an exchange of arguments before the General Court and whose examination does not require any further measure of organisation of procedure or inquiry to be taken in the case (see, to that effect, judgment of 8 September 2020, *Commission and Council* v *Carreras Sequeros and Others*, C-119/19 P and C-126/19 P, EU:C:2020:676, paragraph 130).

121 As stated in paragraph 38 of the present judgment, D & A Pharma raised six pleas in law in support of its action before the General Court.

122 Before examining the substance of those pleas, it is appropriate to recall the findings made in paragraph 118 of the present judgment, from which it follows that the action must be held to be inadmissible in so far as it is directed against the EMA.

123 In those circumstances, it is appropriate to give final judgment on the appellant's action for annulment within the limits of the dispute before the Court of Justice.

Arguments of the parties

124 By the first plea in its action, D & A Pharma claims that the decision at issue was adopted following an irregular procedure, on the ground that the CHMP could not refuse to consult the SAG on Psychiatry during the re-examination procedure.

125 It follows from the last sentence of Article 62(1) of Regulation No 726/2004 and from the wording of Article 11 of the CHMP Rules of Procedure, as well as from point 6.1 of the guidelines on the re-examination procedure, that the CHMP must, when the applicant for re-examination so requests, consult a SAG, provided that the product at issue comes within the therapeutic area of competence of such an expert group. Consequently, as regards, in the present case, a product intended to treat a psychiatric condition, it is the SAG on Psychiatry that should have been summoned.

126 That obligation also applies where the members of the SAG core group in the therapeutic area concerned are not, on their own, able to offer exhaustive expertise. Indeed, where an informed opinion on specific issues is required, additional experts could be added to the core group.

127 Those rules make it possible to preserve the continuity and consistency of opinions given on medicinal products in the same therapeutic area. They thus ensure the best possible scientific advice, in accordance with the task entrusted to the EMA under Article 57(1) of Regulation No 726/2004.

128 D & A Pharma states that it repeatedly urged the CHMP to consult the SAG on Psychiatry, particularly after the ad hoc expert group initially convened by the CHMP was dissolved as a result of the irregularities it had complained of. In an email from the EMA of 6 March 2020, that agency stated that the CHMP had decided to convene a second ad hoc expert group, thus persisting in its refusal to comply with the request for consultation with the SAG on Psychiatry.

129 The Commission argues that the applicable legislation does not entitle MA applicants to require the CHMP to consult the scientific group of their choice. The absence of such a right is consistent with the purpose of that legislation, which is to protect public health. In order for the CHMP to be

able, in accordance with Article 57(1) of Regulation No 726/2004, read in the light of recital 19 thereof, to provide the best possible scientific advice, it is imperative for it to convene the most appropriate expert group, according to the particularities of the product in question.

130 With regard to point 6.1 of the guidelines on the re-examination procedure, the Commission submits that, notwithstanding that section, a SAG cannot be consulted systematically where no SAG is established in the therapeutic area in question. Although it may be characterised as a psychiatric disorder, alcohol dependence is a condition affecting several medical disciplines.

131 The Commission states that the purpose of Hopveus is to combat alcohol dependence. The assessment of products intended to treat this condition would require specialised input from experts in the field of addiction studies.

132 Furthermore, comorbidities that may accompany alcohol dependence, such as liver diseases and neurological complications, do not fall within the field of psychiatry.

133 The appellant is also wrong to claim that the consultation of ad hoc expert groups undermines the consistency of opinions. In this respect, the Commission notes that the SAG on Psychiatry was consulted only once for a medicinal product intended to treat alcohol dependence. In any event, the need to give a coherent opinion cannot affect the power, or even the obligation, of the CHMP to consult the expert group most appropriate for providing the best possible scientific opinion. Furthermore, since the members of the SAG on Psychiatry were invited in the present case to take part in the meeting of the ad hoc expert group and three members of that SAG accepted that invitation, there can be no problem of consistency.

Findings of the Court

134 As is apparent from Article 56 of Regulation No 726/2004, the CHMP, which is part of the EMA, may, in connection with the evaluation of specific types of medicinal products or treatments, establish SAGs and delegate to them certain tasks associated with drawing up the opinions referred to in Article 5 of that regulation.

135 It follows from a combined reading of those two articles that the CHMP, which formulates, inter alia, the EMA's opinions on MA applications for medicinal products for human use, may consult, for the purposes of drawing up such an opinion, the SAG that it has established in the therapeutic area to which the product for which a MA is sought belongs.

136 The last sentence of Article 62(1) of that regulation states that, in the event of a request for re-examination of an opinion, the applicant may request that the CHMP consult a SAG. As confirmed by Article 11(2) of the CHMP Rules of Procedure, that possibility exists, inter alia, in the event of a request for re-examination of a negative opinion on an MA application.

137 Regulation No 726/2004 and the CHMP Rules of Procedure make no mention of an obligation on the part of the CHMP to grant such a request for consultation of a SAG. Therefore, it cannot be ruled out from the outset that that committee has discretion as to whether or not it is appropriate to consult the SAG established in the field to which, where appropriate, the product for which the MA is sought belongs.

138 However, it is expressly clear from point 6.1 of the guidelines on the re-examination procedure, as published by the EMA, that the EMA itself has limited that discretion.

139 It is true that the first subparagraph of point 6.1, in stating that the 'decision on consultation of the SAG for a re-examination procedure will amongst others depend on the CHMP or the [applicant's] request for consultation of the SAG by [the] CHMP', does not, in itself, support the conclusion that it is for the CHMP to consult a SAG if requested to do so.

140 The terms of that subparagraph are specified, however, in the second subparagraph of point 6.1. It states that it is preferable that the CHMP be informed as early as possible of the request for consultation of the SAG, that that request should be duly motivated and that, where such a request is made, 'the CHMP will systematically consult the SAG'.

141 The third subparagraph of point 6.1 adds that, in a therapeutic area where no SAG is established, the advice of additional available expertise 'will be requested in the form of consultation of an ad hoc expert group meeting'.

142 It thus follows from point 6.1 of the guidelines on the re-examination procedure, which were published by the EMA, that the EMA undertakes that the CHMP will systematically consult a SAG when the applicant for re-examination requests such a consultation in good time and on a duly motivated basis. It is also apparent from this that the SAG referred to for that purpose must be the one established in the therapeutic area to which the product in question belongs, and that an ad hoc expert group will be convened if no SAG is established in that area.

143 At the risk of infringing the rights that the applicant for re-examination derives from EU law, the CHMP must, in its capacity as the competent committee of the EMA, apply the rules of conduct laid down by that agency, which are set out, inter alia, in point 6.1 of the guidelines on the re-examination procedure. It is settled case-law that, in adopting such guidelines and announcing, by publishing them, that they will apply to the cases to which they relate, an EU institution, body, office or agency imposes a limit on the exercise of its discretion and cannot, as a general rule, depart from those guidelines, at the risk of being found to be in breach of general principles of law, such as equal treatment or the protection of legitimate expectations (see, inter alia, to that effect, judgments of 11 September 2008, *Germany and Others* v *Kronofrance*, C-75/05 P and C-80/05 P, EU:C:2008:482, paragraph 60, and of 10 November 2022, *Commission* v *Valencia Club de Fútbol*, C-211/20 P, EU:C:2022:862, paragraph 35).

144 Therefore, in accordance with point 6.1 of the guidelines on the re-examination procedure, any request, duly motivated and made in good time, for consultation of a SAG obliges the CHMP to refer the matter to the SAG established in the therapeutic area of the product in question or, where no SAG is established in that area, to consult an ad hoc expert group.

145 Accordingly, in the case of such a request, it is for the CHMP to assess whether the therapeutic indication of the product in question falls, at least predominantly, within a therapeutic area for which a SAG is established.

146 Since that assessment is scientific in nature, review by the EU judicature must be limited to ascertaining whether that assessment was in fact made and is not vitiated by a manifest error or misuse of powers, or whether the limits of its discretion have not manifestly been exceeded (see, by analogy, judgment of 9 March 2023, *PlasticsEurope* v *ECHA*, C-119/21 P, EU:C:2023:180, paragraph 46 and the case-law cited).

147 In view of the self-imposed limitation on the EMA's discretion, the contours of which have been set out in paragraphs 140 to 145 of the present judgment and which is equally binding on the CHMP, it must be held that the CHMP manifestly exceeds the limits of that discretion, inter alia, where it decides to convene an ad hoc expert group, even though it has established that the therapeutic indication of the product at issue falls, at least predominantly, within a therapeutic area for which a SAG has been established, or where it decides to convene an ad hoc expert group on the basis not of the fact that no SAG has been established in the therapeutic area to which that product belongs, but on elements that already relate to the substantive treatment, by the CHMP, of the request for re-examination, such as the questions it intends to put to the experts, or on hypothetical considerations, such as the fact that an ad hoc expert group is allegedly better able to answer those questions than the SAG that has been established.

148 It should be noted, in that regard, that it follows from Article 56(2) of Regulation No 726/2004, read in conjunction with Sections IV and VII of the Rules of Procedure relating to SAGs, that consultation of the SAG established in the therapeutic area to which the product at issue belongs enables the CHMP to receive an opinion drawn up by the permanent experts of that SAG, who represent different schools of thinking and European therapeutic practices in that area and provide, inter alia, expertise in clinical trial methodology and biostatistics. Furthermore, that 'core' group of the SAG may be supplemented by additional experts who are specialised in dealing with specific issues raised by the questions that the CHMP intends to ask.

149 Consultation of such an expert group comprising, on the one hand, a group which ensures, by its permanent nature and its balanced composition, continuity and consistency in the treatment of dossiers in the therapeutic area for which the SAG is established and, on the other hand, additional experts specialised in dealing with specific issues raised in the context of the re-examination, ensures, in any dossier in that field, that the 'best possible scientific opinion' is drawn up, and thus enables the EMA to comply with the task entrusted to it, in accordance with Article 57(1) of Regulation No 726/2004.

150 In those circumstances, the convening, in a therapeutic area for which a SAG is established, of an ad hoc expert group cannot, without undermining the useful effect of the establishment of SAGs, the commitments made by the EMA in point 6.1 of the guidelines on the re-examination procedure and consistency in the processing of MA applications, be accepted on the basis of the CHMP's consideration that an ad hoc expert group would be better able to answer its questions than the SAG established, where appropriate reinforced by additional experts.

151 That conclusion is supported by the fourth subparagraph of point 6.1 of the guidelines on the re-examination procedure. As the Advocate General noted, in essence, in point 68 of her Opinion, it is apparent from that provision that the time at which the CHMP decides which type of expert group, permanent or ad hoc, will be consulted, in principle precedes the time at which it determines the questions to be put to the experts. For that reason also, the content of those questions cannot constitute a criterion for assessing whether it is necessary to convene an established SAG rather than an ad hoc expert group. The identification of the type of expert group to be consulted must depend solely on whether the therapeutic indication of the product in question falls within a therapeutic area for which a SAG has been established. That said, the content of the questions formulated by the CHMP may, as is apparent from point 4 of Section VII of the Rules of Procedure relating to SAGs, determine whether it is appropriate, where a SAG is convened, to supplement it by additional experts.

152 In the present case, it is apparent from the documents attached to the application that, following the request for re-examination submitted by D & A Pharma, which included a request for consultation of an expert group, the CHMP convened an ad hoc expert group, the work of which was, however, stopped before that group was able to formulate an opinion. The CHMP subsequently decided to convene another ad hoc expert group. In that regard, the EMA sought to clarify, in an email of 6 March 2020 addressed to D & A Pharma, the reasons why the CHMP had decided, contrary to what D & A Pharma requested, to convene that other ad hoc expert group and not the SAG on Psychiatry.

153 It was apparent from that email, first of all, that the EMA considered that there were, in the present case, 'specific scientific or clinical issues under discussion'. Next, that agency stated that the members of the ad hoc expert group would be selected on the basis of their competency to address the questions asked by the CHMP and that the CHMP was of the opinion that it was more appropriate, in the view of the specific nature of those questions, to consult such a group and not the SAG on Psychiatry. Lastly, the EMA stated that the SAG members would nevertheless be contacted to participate, subject to their availability, in the meeting of the ad hoc expert group scheduled for 6 April 2020.

154 As has been stated in paragraphs 142 to 145 of the present judgment, it follows from the EMA's own code of conduct, and more specifically from point 6.1 of the guidelines on the re-examination procedure, that, where the therapeutic indication of the product at issue falls, predominantly, within the therapeutic area for which a SAG is established, it is for the CHMP, in the event of a request to that effect, duly motivated and made in good time, to consult it, including, where appropriate, experts specialised in dealing with the specific issues raised by the questions that the CHMP intends to put to the SAG.

155 As the Advocate General observed, in essence, in point 59 of her Opinion, neither the Commission nor the EMA disputes the fact, which is moreover consistent with the International Classification of Diseases established by the World Health Organisation (WHO), that the fight against alcohol dependence falls within the therapeutic field of psychiatry. It follows that the CHMP could not refuse to consult the SAG on Psychiatry on the grounds put forward by the EMA in its email of 6 March 2020.

156 Since it is also not disputed that the CHMP's decision to convene an ad hoc expert group was taken after the appellant's clearly expressed and sufficiently motivated request that the SAG on Psychiatry should be consulted, it must be held that that committee would have been justified in taking such a decision and, therefore, in refusing to grant the appellant's request only if it had found, following a detailed examination without any manifest error, that the therapeutic indication of Hopveus, namely the fight against alcohol dependence, did not fall predominantly within the therapeutic field of psychiatry. It is apparent from the documents in the file, in particular the EMA's email of 6 March 2020, that the CHMP did not carry out such an examination nor did it make such a finding.

157 It follows that the decision to convene an ad hoc expert group instead of the SAG on Psychiatry constitutes a defect vitiating the procedure for adopting the opinion of the EMA referred to in Article 5(2) and Article 9 of Regulation No 726/2004. Consequently, the procedure for the adoption of the contested decision is itself vitiated by a formal defect.

158 In that regard, it is settled case-law that failure to comply with the procedural rules relating to the adoption of an act adversely affecting an individual constitutes an infringement of essential procedural requirements within the meaning of the second paragraph of Article 263 TFEU, so that, if the EU judicature finds that the contested measure was not properly adopted, it must draw the appropriate conclusions from the infringement of an essential procedural requirement and, consequently, annul that act (see, inter alia, to that effect, judgments of 24 June 2015, *Spain* v *Commission*, C-263/13 P, EU:C:2015:415, paragraph 56, and of 20 September 2017, *Tilly-Sabco* v *Commission*, C-183/16 P, EU:C:2017:704, paragraph 115). In the present case, since the decision at issue was adopted on the basis of an opinion of the EMA that should have been considered void, that decision is itself void.

159 Consequently, the first ground of the appeal must be declared well founded and the decision at issue must be annulled, in accordance with the form of order to that effect submitted to the General Court by D & A Pharma, without there being any need to examine the other grounds of appeal.

160 On the other hand, in so far as D & A Pharma claimed, in its application before the General Court, that in the event that the decision at issue should be annulled, the SAG on Psychiatry should be convened in its composition on the date of the request for re-examination, that action must be dismissed. It is settled case-law that, when exercising judicial review of legality under Article 263 TFEU, the EU judicature has no jurisdiction to issue directions to the institutions, bodies, offices and agencies of the European Union (see, inter alia, to that effect, judgment of 5 July 1995, *Parliament* v *Council*, C-21/94, EU:C:1995:220, paragraph 33, and order of 22 September 2016, *Gaki* v *Commission*, C-130/16 P, EU:C:2016:731, paragraph 14).

Costs

161 Under Article 184(2) of the Rules of Procedure of the Court of Justice, where the appeal is unfounded or where the appeal is well founded and the Court itself gives final judgment in the case, the Court is to make a decision as to costs.

162 Under Article 138(1) of those rules, applicable to appeal proceedings by virtue of Article 184(1) thereof, the unsuccessful party is to be ordered to pay the costs if they have been applied for in the successful party's pleadings. Article 138(3) of the Rules of Procedure, applicable to appeal proceedings by virtue of Article 184(1) thereof, provides, in addition, that, where each party succeeds on some and fails on other heads, the parties are to bear their own costs. However, if it appears justified in the circumstances of the case, the Court may order that one party, in addition to bearing its own costs, is to pay a proportion of the costs of the other party.

163 In the present case, the appeal is upheld. The contested decision is annulled, and the judgment under appeal is set aside, within the limits of the dispute brought before the Court. In that regard, as noted in paragraphs 118 and 122 of the present judgment, the judgment under appeal is final in so far as it declares the action inadmissible to the extent that it was directed against the EMA.

164 In those circumstances, the EMA, while having participated in the appeal proceedings on the basis of an interest in the dismissal of the appeal, within the meaning of Article 172 of the Rules of Procedure, cannot be regarded as having been unsuccessful and must bear only its own costs relating to the appeal proceedings.

165 Since the Commission has been essentially unsuccessful, notwithstanding what is set out in paragraph 160 of the present judgment, both in the proceedings before the General Court and in the appeal proceedings, it must be ordered to bear its own costs and to pay those incurred by the appellant relating to those proceedings.

166 Since the appellant has been unsuccessful in its action before the General Court in so far as it was directed against the EMA, it must be ordered to pay the EMA's costs relating to the proceedings before the General Court.

On those grounds, the Court (Fourth Chamber) hereby:

1. **Sets aside the judgment of the General Court of the European Union of 2 March 2022, *D & A Pharma* v *Commission and EMA* (T-556/20, EU:T:2022:111), except in so far as it declared the action inadmissible to the extent that it was directed against the European Medicines Agency (EMA).**

2. **Annuls the Commission implementing decision of 6 July 2020 refusing the marketing authorisation application for the medicinal product for human use Hopveus – sodium oxybate pursuant to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency, as amended by Regulation (EU) 2019/5 of the European Parliament and of the Council of 11 December 2018.**

3. **Dismisses the action as to the remainder.**

4. **Orders Debrégeas et associés Pharma SAS (D & A Pharma) to pay the costs incurred by the European Medicines Agency (EMA) relating to the proceedings before the General Court of the European Union.**

5. **Orders the European Commission to bear its own costs, relating to both the proceedings before the General Court of the European Union and to the appeal proceedings, and to pay those incurred by Debrégeas et associés Pharma SAS (D & A Pharma) in those two sets of proceedings.**

6. **Orders the European Medicines Agency (EMA) to bear its own costs relating to the appeal proceedings.**

[Signatures]