Reports of Cases

OPINION OF ADVOCATE GENERAL
RICHARD DE LA TOUR
delivered on 12 January 2023 [1]

Joined Cases C-6/21 P and C-16/21 P

Federal Republic of Germany (C-6/21 P),
Republic of Estonia (C-16/21 P)
v
Pharma Mar SA,

European Commission

(Appeal – Public health – Medicinal products for human use – Regulation (EC) No 726/2004 – Refusal of a marketing authorisation for the medicinal product for human use Aplidin – plitidepsin – Action for annulment – Concept of 'pharmaceutical company' – Conflict of interest – Concept of 'rival product')

I. Introduction

1. In the two joined appeals, the Federal Republic of Germany (Case C-6/21 P) and the Republic of Estonia (Case C-16/21 P) ask the Court of Justice to set aside the judgment of the General Court of the European Union of 28 October 2020, *Pharma Mar* v *Commission*,[2] by which the latter annulled Commission Implementing Decision C(2018) 4831 final of 17 July 2018 [3] refusing to grant a marketing authorisation ('MA') to the company Pharma Mar, SA for Aplidin – plitidepsin, a medicinal product for human use.

2. As requested by the Court of Justice, I will not address the questions relating to the admissibility of the appeals in this Opinion. I will set out the reasons why I propose that the Court of Justice should set aside the judgment under appeal and refer the case back to the General Court.

1 Original language: French.

2 T-594/18, not published, EU:T:2020:512 ('the judgment under appeal').

3 'The decision at issue'.

II. Legal context

A. Regulation (EC) No 726/2004

3. Recitals 7, 8, 13, 19, 23 and 24 of Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency,[4] as amended by Regulation (EU) No 1027/2012 of the European Parliament and of the Council of 25 October 2012,[5] provide:

'(7) Experience gained since the adoption of Council Directive 87/22/EEC of 22 December 1986 on the approximation of national measures relating to the placing on the market of high-technology medicinal products, particularly those derived from biotechnology [[6]] has shown that it is necessary to create a centralised authorisation procedure that is compulsory for high-technology medicinal products, particularly those resulting from biotechnical processes, in order to maintain the high level of scientific evaluation of these medicinal products in the European Union and thus to preserve the confidence of patients and the medical professions in the evaluation. This is particularly important in the context of the emergence of new therapies, such as gene therapy and associated cell therapies, and xenogenic somatic therapy. This approach should be maintained, particularly with a view to ensuring the effective operation of the internal market in the pharmaceutical sector.

(8) With a view to harmonising the internal market for new medicinal products, this procedure should also be made compulsory for orphan medicinal products and any medicinal product for human use containing an entirely new active substance, i.e. one that has not yet been authorised in the [European Union], and for which the therapeutic indication is the treatment of acquired immune deficiency syndrome, cancer, neurodegenerative disorder or diabetes. Four years after the date of entry into force of this Regulation, the procedure should also become compulsory for medicinal products for human use containing a new active substance, and for which the therapeutic indication is for the treatment of auto-immune diseases and other immune dysfunctions and viral diseases. …

…

(13) In the interest of public health, authorisation decisions under the centralised procedure should be taken on the basis of the objective scientific criteria of quality, safety and efficacy of the medicinal product concerned, to the exclusion of economic and other considerations …

…

(19) The chief task of the [European Medicines] Agency [('the Agency' or 'the EMA')] should be to provide [EU] 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. Only after a single scientific evaluation procedure addressing the quality, safety and efficacy

4 OJ 2004 L 136, p. 1.

5 OJ 2012 L 316, p. 38, 'Regulation No 726/2004'.

6 OJ 1987 L 15, p. 38.

of high-technology medicinal products has been conducted by the Agency, applying the highest possible standards, should marketing authorisation be granted by the [European Union], and this should be done by means of a rapid procedure ensuring close cooperation between the Commission and Member States.

…

(23) Exclusive responsibility for preparing the Agency's opinions on all questions concerning medicinal products for human use should be vested in a Committee for Medicinal Products for Human Use. [7] … As regards orphan medicinal products, the task should fall to the Committee on Orphan Medicinal Products set up under Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products [8] …

(24) The creation of the Agency will make it possible to reinforce the scientific role and independence of the committees, particularly through the setting-up of a permanent technical and administrative secretariat.'

4. Title IV of Regulation No 726/2004, entitled 'The European Medicines Agency – Responsibilities and administrative structure', includes a Chapter 1 on 'Tasks of the agency', comprising Articles 55 to 66.

5. Article 62(2) of that regulation provides:

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

The Agency shall keep an up-to-date list of accredited experts. The list shall include the experts referred to in the first subparagraph and other experts appointed directly by the Agency. The list shall be updated.'

6. In accordance with Article 63(2) of that regulation:

'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 Agency which is accessible to the public, on request, at the Agency's offices.

The Agency's code of conduct shall provide for the implementation of this Article with particular reference to the acceptance of gifts.

Members of the Management Board, members of the committees, rapporteurs and experts who participate in meetings or working groups of the Agency shall declare, at each meeting, any

7 'The CHMP'.

8 OJ 2000 L 18, p. 1.

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.'

B. The Code of Conduct of the EMA

7. The second subparagraph of Section 2.3.3. of the European Medicines Agency Code of Conduct ([EMA] Code of Conduct), [9] of 16 June 2016, states as follows:

'The restrictions that will apply [to members of the Management Board, members of the committees, rapporteurs and experts] 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.'

C. The policy of the EMA

8. According to first and fourth bullet points under Section 3.2.2. of the European Medicines Agency policy on the handling of competing interests of scientific committees' members and experts, [10] of 6 October 2016:

'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.

…

Pharmaceutical Company shall mean: any legal or natural person whose focus is to research, develop, manufacture, market and/or distribute medicinal products. For the purpose of this policy, the definition includes companies to which activities relating to the research, development, manufacturing, marketing and maintenance of medicinal products (which might also be carried out in house) are outsourced on a contract basis.

In this regard CROs [clinical research organisations] or consultancy companies providing advice or services relating to the above activities, fall under the definition of a pharmaceutical company.

Legal or natural persons which do not fall within the scope of the above definition but (i) control (i.e. own a majority stake in, or otherwise exercise a significant influence in the decision-making processes of the relevant pharmaceutical company), (ii) are controlled by or (iii) are under common control of a pharmaceutical company, shall be considered as pharmaceutical companies for the purposes of this policy.

Independent researchers and research organisations including universities and learned societies are excluded from the scope of the present definition.'

[9] EMA/385894/2012 rev.1.

[10] EMA/626261/2014, Rev. 1; 'the EMA policy'.

9. Section 4.1. of the EMA policy, entitled 'Objectives of the policy', provides as follows:

'The main objective of the policy is to ensure that the scientific committees' members and the experts participating in the Agency'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 for human and veterinary use. It is, therefore, of utmost importance to strive for the optimal balance between the cooling-off period for the declared interests versus maintaining the experts' knowledge.

In order to achieve this objective and to strike the aforementioned balance the focus will first be on the nature of the declared interest before determining the length of time any restrictions will apply.'

10. Section 4.2.1.2 of that policy is worded as follows:

'Involvement of the individual in the Agency's activities is restricted taking into account three factors: the nature of the declared interest, the timeframe during which such interest occurred, as well as the type of activity. The following methodology applies: first the nature of the declared interest within the frame of the specific Agency activity will be looked at, before determining the length of time any restrictions will apply.

As a general rule, current employment with a pharmaceutical company or current financial interests in pharmaceutical industry are incompatible with involvement in the Agency's activities. One exception to this general rule relates to the concept of expert witness. Current financial interests are compatible with this concept.

The requirements for membership of decision-making bodies (i.e. scientific committees) are stricter than for advisory bodies (i.e. [scientific advisory groups [11]] and ad hoc expert groups).

The requirements are also stricter for chairpersons/vice-chairpersons of the scientific committees compared to the chairpersons/vice-chairpersons of other fora and compared to the members of the scientific committees and the other fora. Likewise the requirements are stricter for rapporteurs (or equivalent leading/co-ordinating role) and formally appointed peer reviewers compared to the other members of the scientific fora.

The timeframe to be considered depending on the declared direct or indirect interest is either current, or within the past three years, or in certain cases, as stated before, for a longer period (see Section 4.2.1.1. for further details). As already mentioned before, the nature of the declared interest will be considered first before deciding on the duration of any restrictions. However, individuals can always declare any interests beyond those periods limited in time (i.e. current, or within the past three years). They can always also restrict on their own initiative their involvement in the Agency's activities as a result of such declaration.

Furthermore, if a scientific committee/working party/SAG/ad hoc expert group member intends to be engaged (either solicited or not) in occupational activities with a pharmaceutical company (such as employment) during the term of the mandate (irrespective if an employment contract with a company has been signed or not), the member shall immediately inform the Agency. The

[11] 'SAGs'.

Agency will fully restrict the member from further involvement in the Agency's activities from the date of notification. The Nominating Authority will be informed by the Agency that the member can no longer be involved in the Agency's activities.

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 (one to two) of rival products. The same would apply for the brand leader when a generic product is under consideration;

– 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.'

III. Background to the dispute

11. Pharma Mar is a company operating in the oncology research sector. On 16 November 2004, it obtained, in accordance with Regulation No 141/2000, designation of the medicinal product Aplidin as an orphan medicinal product for the treatment of a serious cancer of the bone marrow.

12. On 21 September 2016, Pharma Mar submitted to the EMA an application for marketing authorisation for Aplidin. The procedure for the EMA's assessment of the application for marketing authorisation commenced on 27 October 2016.

13. During that procedure, the CHMP, which is responsible, under Article 5(2) of Regulation No 726/2004, for drawing up the EMA's opinion on any matter concerning, inter alia, the granting of marketing authorisation for a medicinal product for human use, issued a negative opinion on 14 December 2017 recommending that the Commission reject the MA application submitted by Pharma Mar, considering, primarily, that the efficacy and safety of the product were not sufficiently demonstrated and that, therefore, the benefits did not outweigh the risks.

14. On 3 January 2018, Pharma Mar submitted to the EMA a request for re-examination of the CHMP's opinion of 14 December 2017, pursuant to Article 9(2) of Regulation No 726/2004. Pharma Mar also requested that, the EMA consult a SAG as part of the re-examination, in accordance with Article 62(1) of that regulation.

15. On 7 March 2018, a meeting of the SAG for oncology was therefore held to answer the various questions that had been put to it. The SAG consisted of five core members, six additional experts and two patient representatives.

16. On 22 March 2018, the CHMP upheld its negative opinion of 14 December 2017 on the MA application submitted by Pharma Mar. At the same time, a draft Commission decision rejecting the MA application was drawn up. The Commission therefore adopted the decision at issue refusing the MA application for Aplidin, in accordance with Regulation No 726/2004. An action was brought before the General Court in relation to that decision, resulting in the judgment under appeal.

IV. The procedure before the General Court and the judgment under appeal

17. By document lodged at the Registry of the General Court on 1 October 2018, Pharma Mar brought an action for annulment of the decision at issue.

18. The General Court ruled on the first part of the first plea in law, alleging a lack of objective impartiality on the part of two members of the SAG [12] in the light of the provisions of the EMA policy or of the more general principle of impartiality based on Article 41(1) of the Charter of Fundamental Rights of the European Union. [13]

19. The General Court first examined the allegation of conflict of interest concerning the two experts employed by both a university institute and a university hospital that collaborate on research and teaching and share staff and equipment, especially for clinical research.

20. The General Court noted that the university hospital is home to a cell therapy centre falling within the definition of 'pharmaceutical company' under the EMA policy, because that centre makes research infrastructure and personnel available to pharmaceutical companies, carries out clinical trials at the request of pharmaceutical companies and manufactures medicinal products as outsourced by pharmaceutical companies. The General Court considered that the EMA policy provided for an extension of the definition of 'pharmaceutical company' to include a natural or legal person controlled by or controlling a pharmaceutical company and held that the university hospital controlling the cell therapy centre should itself be considered a pharmaceutical company and that it was up to the Commission to prove the contrary.

21. The General Court added that that cell therapy centre is responsible for carrying out clinical trials and for manufacturing a product that is a rival product to the product examined by the SAG, which is an orphan medicinal product for which there is no alternative treatment on the market. However, under current activities, the second expert declared a consultancy in relation to that rival product and activities as principal investigator and investigator for two other rival medicinal products.

22. Second, the Court ruled on the effect of the alleged conflicts of interest concerning both experts on the validity of the procedure.

23. On the one hand, after noting that the requirement of impartiality to which the EU institutions, bodies, offices and agencies are subject also extends to experts consulted, the General Court held that the SAG was involved in the procedure to re-examine the application, in the context of a guarantee provided to Pharma Mar, as a group of experts highly specialised in the

[12] 'The first expert' and 'the second expert', respectively, or collectively 'the two experts'.

[13] 'The Charter'.

field of the medicinal product at issue, and that because its opinion was taken into consideration by the CHMP, the SAG could have had an influence on the conduct and outcome of the procedure that led to the adoption of the decision at issue.

24. On the other hand, the General Court found that the first expert had responsibilities of his own as vice-chairperson in the SAG meeting, including the proposing of additional experts, one of whom was the second expert.

V. Procedure before the Court of Justice and forms of order sought

25. By its appeal in Case C-6/21 P, the Federal Republic of Germany claims that the Court of Justice should:

– set aside the judgment under appeal;

– confirm the decision at issue and dismiss the action;

– in the alternative, refer the case back to the General Court; and

– order Pharma Mar to bear the costs.

26. By its appeal in Case C-16/21 P, the Republic of Estonia claims that the Court of Justice should:

– set aside the judgment under appeal; and

– order each of the parties to bear its own costs incurred in the appeal proceedings.

27. Pharma Mar claims that the Court of Justice should declare the appeals inadmissible or dismiss them and order the applicants to bear the costs incurred in the appeal proceedings.

28. By decision of the President of the Court of Justice of 30 March 2021, Cases C-6/21 P and C-16/21 P were joined for the purposes of the written and oral procedure and of the judgment.

29. By decision of 8 July 2021 and by order of 17 September 2021, leave to intervene was granted to the Kingdom of the Netherlands and the EMA in support of the forms of order sought by the Federal Republic of Germany and the Republic of Estonia in the two joined proceedings.

VI. Analysis

30. Before examining the grounds of appeal, I would like to briefly recall that the EMA has broad regulatory powers of harmonisation.

31. Indeed, Regulation No 726/2004, which created the EMA, is based, in particular, on Article 95 EC, now Article 114 TFEU, which aims to establish the functioning of the internal market and which the Court of Justice has already ruled gives the EU legislature a margin of discretion that can be used ‘in particular to choose the most appropriate harmonisation technique where the proposed approximation requires physical, chemical or biological analyses to be made and

scientific developments in the field concerned to be taken into account'.[14] Furthermore, recital 8 of that regulation refers to 'a view to harmonising the internal market for new medicinal products'. Thus, the EMA has broad general powers of harmonisation.

32. On the other hand, an analogy can be made with the EMA's policy on transparency and access to documents with regard to the EMA policy (on conflicts of interest).[15] Indeed, the doctrine would argue that this policy could be seen as a regulatory measure implementing the right of access to documents, as established in Article 15(3) TFEU and Article 42 of the Charter.[16] Furthermore, the General Court has held on several occasions that, in application of Article 73 of Regulation No 726/2004, the EMA has adopted detailed rules for the implementation of Regulation (EC) No 1049/2001,[17] and those rules are reflected in that policy.[18] As with the EMA policy (on conflicts of interest), the policy on transparency and access to documents provides for a table of results that is updated as the EMA gains experience with requests for access to documents.[19]

33. I conclude that Regulation No 726/2004 represents a translation of the principle of sound administration and of Article 42 of the Charter on the right of access to documents and, since the EMA policy was adopted on the basis of the same regulation, it can also be viewed as an explicit and harmonised implementation of primary legislation.

34. I would add that this broad power of harmonisation goes hand in hand with an extensive discretionary power for the EMA in preventing conflicts of interest. As the EMA noted in its observations, Article 63(2) of Regulation No 726/2004, giving competence to the EMA to draw up a code of conduct on preventing conflicts of interest, was added by the European Parliament during the discussion of the draft document in order 'to introduce the appropriate level of openness and transparency, which is especially necessary in the pharmaceutical sector. Additionally an extra paragraph concerning the code of conduct needs to be added'.[20]

14 Judgment of 6 December 2005, *United Kingdom* v *Parliament and Council* (C-66/04, EU:C:2005:743, paragraph 46).

15 European Medicines Agency policy on access to documents (related to medicinal products for human and veterinary use) (EMA/110196/2006) of 30 November 2010. That policy was replaced by the European Medicines Agency policy on access to documents (EMA/729522/2016) of 4 October 2018.

16 See Kim, D., 'Transparency Policies of the European Medicines Agency: Has the Paradigm Shifted?', *Medical Law Review*, Oxford University Press, Oxford, 2017, vol. 25, No 3, pp. 456 to 483, in particular p. 463.

17 Regulation of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents (OJ 2001 L 145, p. 43).

18 See judgments of 5 February 2018, *Pari Pharma* v *EMA* (T-235/15, EU:T:2018:65, paragraphs 58 and 59); of 5 February 2018, *PTC Therapeutics International* v *EMA* (T-718/15, EU:T:2018:66, paragraphs 54 and 55); of 5 February 2018, *MSD Animal Health Innovation and Intervet international* v *EMA* (T-729/15, EU:T:2018:67, paragraphs 39 and 40); and of 25 September 2018, *Amicus Therapeutics UK and Amicus Therapeutics* v *EMA* (T-33/17, not published, EU:T:2018:595, paragraphs 48 and 49).

19 See document EMA/127362/2006, Rev. 1, of 4 October 2018.

20 See draft legislative resolution of the European Parliament on the proposal for a regulation of the European Parliament and of the Council laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products [COM(2001) 404 – C5-0591/2001 – 2001/0252(COD)], incorporated into the report on the same proposal of 7 October 2002; available at: https://www.europarl.europa.eu/doceo/document/A-5-2002-0330_EN.html. See, in particular, amendment 111 to that proposal.

A. The first ground of appeal in Cases C-6/21 P and C-16/21 P: infringement of the concept of 'pharmaceutical company', within the meaning of Section 3.2.2. of the EMA policy

1. Arguments of the parties

35. In their first grounds of appeal, the Federal Republic of Germany and the Republic of Estonia assert that the General Court, by classifying the university hospital as a whole as a pharmaceutical company whose employees cannot be experts, violated Section 3.2.2. of the EMA policy and misapplied the right to sound administration guaranteed by Article 41(1) of the Charter. They believe, and are supported in this by the EMA, that the EMA has significant discretion to develop a code of conduct on the independence of experts in accordance with Article 63 of Regulation No 726/2004, since it is the authority best placed to strike the right balance in terms of rules for managing conflicts of interest with regard to the need to have the best possible expertise for evaluating medicinal products for human use. They add that university hospitals, despite hosting a cell therapy centre that meets the definition of 'pharmaceutical company', are included, because of their research mission, in the category of independent researchers and research organisations, including universities and learned societies, and, as such, are excluded from that definition. The EMA clarifies that that exclusion of independent researchers and others applies irrespective of their degree of control or ownership of a pharmaceutical company. It adds that the interpretation adopted by the General Court would have disproportionate consequences on the quality of scientific advice, even though experts from hospitals or universities are subject to strict ethical rules. The Kingdom of the Netherlands agrees, stating that the interpretation adopted by the General Court would drastically restrict the possibility of recruiting independent experts and, moreover, would only work to the detriment of experts of a SAG appointed by the EMA and not for those participating in a SAG meeting at the request of a pharmaceutical company.

36. On the other hand, Pharma Mar argues that the EMA's margin of discretion in establishing a conflict of interest policy is not unlimited and that, if a situation is not foreseen by that policy (university hospitals or rival products), the case-law principles relating to compliance with the requirement for objective impartiality intended to exclude any legitimate doubt as to possible prejudice should be applied. In the present case, the cell therapy centre within the university hospital is involved in the development of a rival product to Aplidin, without a third-party observer being able to easily assess whether objective impartiality is being observed, as that centre is not legally distinct from the university hospital, and the Commission has not proven the absence of control between the university hospital and the centre.

2. Assessment

37. The analysis of this ground of appeal requires a ruling on two elements: on the one hand, the scope of application of the concept of 'research organisations' mentioned as being excluded from the definition of 'pharmaceutical company' in the fourth paragraph of the fourth bullet point of Section 3.2.2. of the EMA policy and, on the other hand, the application of the concept of 'control' laid down in the third paragraph of that fourth bullet point to the persons falling within the scope of the exception to the concept of 'pharmaceutical company'.

38. Before addressing these two points, I would like to reiterate that all the parties agree that the cell therapy centre at issue in this case is a pharmaceutical company, within the meaning of Section 3.2.2. of the EMA policy, and that, consequently, the persons working within it cannot be appointed as experts on the basis of the second bullet point of Section 4.2.1.2. of that policy.

39. First, regarding the scope of the concept of 'research organisations', it is common ground that university hospitals are not mentioned as such in the list of organisations excluded from the definition of 'pharmaceutical company' in the fourth paragraph of the fourth bullet point of Section 3.2.2. of the EMA policy, which only mentions 'independent researchers and research organisations, including universities and learned societies'. However, this literal argument does not seem to me to be sufficient to decide the issue.

40. Indeed, on the one hand, the explicit objective of the EMA policy is stated in Section 4.1. and consists in guaranteeing the impartiality of experts through the absence of interests in the pharmaceutical industry while preserving the need to obtain the best specialised scientific expertise. Thus, that policy is characterised by a balance between the absence of conflicts of interest and the requirement for a high level of scientific expertise. It is undeniable that the exception for research organisations, including universities, is based on that requirement. Moreover, the case-law requires that, in order to carry out its task, a committee of experts must be 'composed of persons possessing the necessary scientific knowledge in the various fields in question or [that] its members are advised by experts having that knowledge'. [21]

41. In that respect, the requirement for scientific quality would justify considering university hospitals as research organisations or universities.

42. On the other hand, there is a classification of university hospitals, in the same way as research institutes, as research organisations in recital 12 of Directive (EU) 2019/790 of the European Parliament and of the Council of 17 April 2019 on copyright and related rights in the Digital Single Market and amending Directives 96/9/EC and 2001/29/EC, [22] which states that 'research organisations across the Union encompass a wide variety of entities the primary goal of which is to conduct scientific research or to do so together with the provision of educational services. … They should for example cover, in addition to universities or other higher education institutions and their libraries, also entities such as research institutes and hospitals that carry out research'. Thus, in the field of intellectual property, a university hospital is considered a research organisation.

43. Consequently, it is possible to draw the conclusion, from the purpose of requiring scientific quality and the intent of the EU legislature in another area, that university hospitals should be considered research organisations within the meaning of the fourth paragraph of the fourth bullet point of Section 3.2.2. of the EMA policy.

44. Second, the next step in the reasoning is whether the research organisations excluded from the definition of 'pharmaceutical company' are subject to the test of ascending, descending or common control provided for in the third paragraph of the fourth bullet point of Section 3.2.2. of the EMA policy. That provision concerns natural or legal persons who do not fall under the definition of 'pharmaceutical company' but who control, are controlled by or are under the common control of a pharmaceutical company and, as such, are considered to be pharmaceutical companies.

45. That paragraph refers to persons that do not, as such, meet the definition of 'pharmaceutical company', but are considered to be pharmaceutical companies because of their control structures for the purposes of preventing conflicts of interest. The fourth paragraph of the fourth bullet point

[21] Judgment of 9 September 2010, *Now Pharm* v *Commission* (T-74/08, EU:T:2010:376, paragraph 76), with regard to a procedure for the designation of orphan medicinal products.

[22] OJ 2019 L 130, p. 92.

of Section 3.2.2., on independent researchers and research organisations, lays down the inverse rule, namely that persons or entities that could be considered as pharmaceutical companies (including by way of control) are excluded from the scope of that definition.

46. In this case, at the hearing, the Republic of Estonia stated that if the criterion of control of a cell therapy centre led to a university hospital being considered a pharmaceutical company, it would no longer be able to continue proposing the experts currently proposed to the EMA, in accordance with Article 62(2) of Regulation No 726/2004, since all of them were employees of the country's sole university hospital. And yet, that hospital has a cell therapy centre with four staff, while the hospital employs 4 800 people, including 200 doctors and 197 interns.[23] Thus, applying the control criterion would result in the exclusion from consideration as an expert for the EMA of a very large number of people in proportion to the number of people actually working in the structure classified as a 'pharmaceutical company', which would adversely impact the scientific qualification requirement. Consequently, the exclusion of all hospital staff, like the exclusion of all employees of a pharmaceutical company, solely on the basis of their employment by an organisation, seems to go beyond the balance sought by the EMA policy on conflicts of interest, even though the main purpose of a university hospital is not the manufacture of medicinal products, in contrast to a pharmaceutical company.

47. As the wording of Section 3.2.2. of the EMA policy stands, it does not seem possible to me to distinguish between the different types of control described in the third paragraph of the fourth bullet point of that section, even if, in the present case, it is only the control of the cell therapy centre – described as a 'pharmaceutical company' – by the hospital that is at issue, and not the control of a hospital by a pharmaceutical company, for example. If we were to determine that the criterion of control does not apply to classify a university hospital as a 'pharmaceutical company', this would therefore result in the exclusion of all types of control.

48. However, that interpretation does not result in an absence of any control over a possible conflict of interest for the staff of a university hospital employed outside the cell therapy centre. Indeed, any EMA expert remains individually subject to the rules governing conflicts of interest. Thus, the balance between the prevention of conflicts of interest and the scientific level of the experts is preserved.

49. Similarly, it seems to me that it is sufficient for the department in question to be distinctly identifiable, along with the staff assigned to it, without requiring legal autonomy. Since the entire system for preventing conflicts of interest, as organised by the EMA, is based on the declarations of experts, it does not seem any more complicated for a third party to obtain information on the position held by an employee within a hospital where the departments are clearly identified than within another organisation. It is the responsibility of the EMA to ensure that the declarations of experts make it clear whether the person concerned is working in a pharmaceutical company within the meaning of its policy.

50. I conclude from all these considerations that the General Court erred in law in holding that the university hospital was a pharmaceutical company solely by virtue of its control over a cell therapy centre, itself classified as a 'pharmaceutical company' within the meaning of Section 3.2.2. of the EMA policy.

[23] Similarly, at the hearing, the Federal Republic of Germany explained that Germany's largest university hospital (the Charité in Berlin) employed 20 900 people, of whom only 100 worked in a commercial drug manufacturing unit.

B. The second ground of appeal in Case C-6/21 P: infringement of the rules governing the burden of proof

1. Arguments of the parties

51. With regard to the second ground of appeal in Case C-6/21 P, the Federal Republic of Germany considers that the General Court reversed the burden of proof by accusing the Commission of failing to present evidence of the existence of a separate legal structure housing the cell therapy centre and of the absence of control over that centre by the hospital, whereas, in the absence of evidence of such control, the General Court should not have classified the university hospital as a 'pharmaceutical company'.

2. Assessment

52. Because of the interpretation of Section 3.2.2. of the EMA policy proposed during consideration of the previous ground of appeal, I consider that the General Court has reversed the burden of proof by inferring, from the absence of evidence that the hospital did not have control over the cell therapy centre, that the former did indeed have control over the latter. In any event, that ground can be regarded as not applicable, since the criterion of control is not being applied with regard to research institutes.

C. The third ground of appeal in Case C-6/21 P and the second ground of appeal in Case C-16/21 P: infringement of the concept of 'rival product'

1. Arguments of the parties

53. The third ground of appeal in Case C-6/21 P and the second ground of appeal in Case C-16/21 P allege infringement of the concept of 'rival products' within the meaning of Section 4.2.1.2. of the EMA policy.

54. By the first part of these grounds of appeal, the Federal Republic of Germany and the Republic of Estonia, supported by the EMA, consider that the General Court erred in law by not finding that the second expert was only an ordinary (mere) member of the SAG, and was not therefore subject to the conflict of interest rule relating to participation in the development of a rival product. They point out that, according to Annex 1 to the EMA policy, restrictions on the development of a rival product apply only to certain persons with well-defined functions, in particular the chairpersons and vice-chairpersons of scientific committees, given their decisive role in the outcome of the evaluation.

55. Conversely, Pharma Mar submits that those grounds of appeal relate to a superfluous element in the General Court's reasoning and that an error on this point would be of no consequence. In the alternative, it notes that the conclusion concerning the first expert has not been contested. It adds that this part of the ground of appeal is inadmissible as it is intended solely to obtain a new examination of the facts. It also contests the classification of the second expert as an ordinary member of the SAG, since he was appointed as an additional member, because of the rarity of the disease, and, as such, his appointment should have been subject to more guarantees than for an ordinary member.

56. The second part of the ground of appeal alleges an error of law committed by the General Court with regard to the concept of 'rival products', within the meaning of Section 4.2.1.2. of the EMA policy, and the misapplication of that concept. The Federal Republic of Germany and the Republic of Estonia, supported by the EMA, point out that the EMA policy lays down a conflict of interest rule for the expert involved in the development of a rival product only if there are one or two rival products for the therapeutic indication for which marketing authorisation is sought. They add that the General Court was wrong to find that, because Aplidin is an orphan medicinal product, there were few, if any, alternative treatments on the market. The EMA states that there are at least 15 medicinal products for the requested therapeutic indication and that, under its discretionary power, it considers that orphan medicinal products should be subject to the same evaluation rules as other medicinal products.

57. Pharma Mar maintains that this part of the ground of appeal is not well founded, since, where the EMA policy makes no provision for orphan medicinal products, a verification of a potential conflict of interest should be more rigorous in the case of a marketing authorisation for such a medicinal product. In the alternative, it disputes the allegation that the General Court made a manifest error of assessment concerning the number of rival products to Aplidin.

2. Assessment

58. As a preliminary point, it should be noted that, in Section 4.2.1.2. of the EMA policy, the term 'competitor products' has been replaced by 'rival products'.

59. Furthermore, that section makes it clear that where there are only one or two rival products, the consequences in terms of conflicts of interest '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'. Thus, the mere fact of working on a rival product is not sufficient to qualify as a conflict of interest. The grounds of appeal therefore relate to the two cumulative conditions of that rule, namely, on the one hand, the function of the expert in question within the working group and, on the other, the number of rival products in question.

60. First, the EMA policy only lays down rules for certain functions that give the holder, a priori, more weight in the decision-making process than an ordinary member. Furthermore, that text does not distinguish between core members and additional members, all of whom are considered to be simple members. The second expert, an additional member of the SAG, does not therefore meet the first condition required for the rival product rules to apply.

61. As a result, the General Court erred in law by applying the specific rules for rival products, even though the second expert was merely an ordinary member of the SAG.

62. Second, the mere fact that Aplidin is an orphan medicinal product is not sufficient to trigger the application of the rival product rules, since the EMA policy does not lay down specific rules for orphan medicinal products. Rather, the EMA takes the view, by virtue of its discretion resulting from its broad powers of harmonisation,[24] that orphan medicinal products should be subject to the same requirements as any other medicinal product during the examination prior to placing on the market.[25]

[24] See points 30 to 34 of this Opinion.

[25] See recital 8 of Regulation No 726/2004 and points 3 and 4 of the Annex to that regulation.

63. Conversely, neither is the mere fact that CellProtect, a medicinal product produced within the cell therapy centre in question and having been subject to guidance from the second expert, meets the definition of 'rival product' laid down in the first bullet point of Section 3.2.2. of the EMA policy sufficient to trigger the application of those rules. Again, those rival products must exist in very small numbers, namely one or two. And yet, according to the General Court's own findings in paragraph 69 of the judgment under appeal, there are three rival products to Aplidin on which the second expert is working (CellProtect, Daratumumab, Isatuximab). In addition, the EMA recalls that the CHMP report on Aplidin, submitted to the General Court, states that the treatment landscape for multiple myeloma includes at least 15 medicinal products.

64. Thus, the General Court erred in law in holding that the mere fact of working on rival products placed the second expert in a conflict of interest situation, without establishing that there were only one or two such products. Furthermore, by not taking into account the fact that 15 medicinal products existed for the therapeutic indication requested by Pharma Mar for its product, the General Court committed a manifest error of assessment.

65. The third ground of appeal in Case C-6/21 P and the second ground of appeal in Case C-16/21 P must therefore be upheld in their entirety.

D. The fourth ground of appeal in Case C-6/21 P and the third ground of appeal in Case C-16/21 P: failure to understand the role of the experts and their influence on the SAG and absence of a decisive influence of the second expert

1. Arguments of the parties

66. The fourth ground of appeal in Case C-6/21 P and third ground of appeal in Case C-16/21 P relate to the absence of a decisive influence on the part of the two experts. The Republic of Estonia argues that, since the university hospital is not considered to be a pharmaceutical company, the mere fact that the first expert, who had chaired a meeting of the SAG in his capacity as vice-chairperson of the group, is an employee of that hospital is not sufficient to create a conflict of interest situation. As regards the second expert, the Federal Republic of Germany and the Republic of Estonia contend that, as an ordinary member of the SAG, he had no leading role, even though the impartiality of the SAG was guaranteed by its collegial structure.

67. Conversely, Pharma Mar disputes the classification of the second expert as an ordinary member, as he was appointed as an additional member of the SAG, due to the need for specific expertise.

2. Assessment

68. Since the reasons why the General Court questioned the impartiality of the two experts – namely that they were employees of the university hospital and, in the case of the second expert, that they had worked on rival products – have been rejected in the light of the reasoning I proposed in my analysis of the first ground of appeal in Cases C-6/21 P and C-16/21 P and of the third ground of appeal in Case C-6/21 P and the second ground of appeal in Case C-16/21 P, it is therefore unnecessary to consider the fourth ground in Case C-6/21 P and the third ground in Case C-16/21 P.

69. In conclusion, the judgment under appeal must, in my view, be set aside.

VII. Referral of the case back to the General Court

70. In accordance with the first paragraph of Article 61 of the Statute of the Court of Justice of the European Union, that Court may, where a decision of the General Court has been set aside, either itself give final judgment in the matter, where the state of the proceedings so permits, or refer the case back to the General Court for judgment.

71. In the present case, I consider that the Court of Justice does not have at its disposal the elements necessary to give a final ruling on the merits of the action, which would involve an examination of elements that were neither assessed by the General Court in the judgment under appeal nor argued before the Court of Justice.

72. Accordingly, I consider it necessary to refer the case back to the General Court, with costs reserved, so it can rule on the dispute in its entirety.

VIII. Conclusion

73. In the light of all of the foregoing considerations, I propose that the Court of Justice should rule as follows:

(1) The judgment of the General Court of the European Union of 28 October 2020, *Pharma Mar* v *Commission* (T-594/18, not published, EU:T:2020:512), is to be set aside.

(2) The case is to be referred back to the General Court of the European Union.

(3) The costs are reserved.