Orphan medicines. The Court of Justice dismisses the appeal of the European Medical Agency in the *Shire* case

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PHARMACEUTICALS AND LIFE SCIENCES, LITIGATION, EU AND COMPETITION LAW

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On 29 July 2019, the Court of Justice of the European Union adjudged Case C-359/18 P, *European Medicines Agency v Shire Pharmaceuticals Ireland Ltd*, an appeal brought in 2018 by the European Medicines Agency (EMA).

More particularly, the EMA asked the Court to set aside the judgment of the General Court of 22 March 2018, *Shire Pharmaceuticals Ireland* v *EMA*[1], whereby the EMA decision of 15 December 2015 refusing to validate the application submitted by *Shire Pharmaceuticals Ireland Ltd* ("Shire") for the designation of Idursulfase-IT as an orphan medicinal product was annulled ("the contested decision")[2].

On 23 February 2016, Shire had asked the General Court to annul the contested decision by which the EMA had denied the orphan designation to Idursulfase-IT, stating that the former's application did not comply with Article 5(1) of Regulation

[1] General Court 22.05.2018, case T-80/16, *Shire Pharmaceuticals Ireland Ltd v European Medicines Agency*.
[2] For further information, see our previous article, available at the following LINK.

No 141/2000[3]. In its appeal to the Court of Justice, EMA argued that the General Court had erred in law by interpreting separately rather than together Article 5(1) and (2)[4] of Regulation No 141/2000, thus undermining the effectiveness of the provision, and, in the alternative, that the General Court had relied on an incorrect interpretation of the concept of "medicinal product", as defined in Article 1(2) of Directive 2001/83[5].

By the first ground of appeal, the EMA complained of an error of law committed by the General Court in interpreting Article 5(1) and (2). According to the EMA, the aim of Article 5(2) was to enable the EMA Secretariat to verify that the application for designation contains sufficient information for its scientific assessment by the Committee for Orphan Medicinal Products ('COMP')[6] on the basis of easily applied criteria. Therefore, the General Court had erred in accepting that the excipients and the method of administration should be taken into account when examining the risk of an overlap with Article 5(1), inasmuch as, in order to circumvent it, a company could allege inconsequential differences between the product that was the object of the designation and a medicinal product for which an MA application had previously been lodged.

Moreover, the EMA argued that the General Court erred in law by taking the concept of a "medicinal product", defined in Article 1(2) of Directive 2001/83, as the relevant test in order to determine whether there is any overlap between an application for orphan designation and a previous MA application. Indeed, a combined reading of Article 5(1) and (2) clarified that the relevant criteria for assessing whether an application for designation impinged on a previous MA application are the name of the sponsor, the active substance and the proposed therapeutic indication, while the concept of "medicinal product" had a different objective, that is to determine which products fall within the scope of Directive 2001/83.

In adjudging the appeal, the Court of Justice first recalled that, Article 5(1) precludes that a medicinal product for which an MA application has previously been lodged from being the subject of an application for orphan designation.

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[3] Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products, *OJ L 18 of 22.1.2000.* Article 5 of the Regulation, named "Procedure for designation and removal from the register", at paragraph 1 so states: "*... In order to obtain the designation of a medicinal product as an orphan medicinal product, the sponsor shall submit an application to the Agency at any stage of the development of the medicinal product before the application for marketing authorisation is made...*".

[4] Article 5 of Regulation (EC) No 141/2000 at paragraph 2 so states: "*... The application shall be accompanied by the following particulars and documents:*
(a) name or corporate name and permanent address of the sponsor;
(b) active ingredients of the medicinal product;
(c) proposed therapeutic indication;
(d) justification that the criteria laid down in Article 3(1) are met and a description of the stage of development, including the indications expected...".

[5] Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, *OJ L 311 of 28.11.2001*. Article 1 of the Directive at paragraph 2 so states: "*... For the purposes of this Directive, the following terms shall bear the following meanings:*
(...)
2. Medicinal product: Any substance or combination of substances presented for treating or preventing disease in human beings.
Any substance or combination of substances which may be administered to human beings with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in human beings is likewise considered a medicinal product...".

[6] The COMP, established in 2000, is the EMA's committee responsible for recommending orphan designation of medicines to be developed for the diagnosis, prevention or treatment of rare diseases that are life-threatening or very serious.

Furthermore, the information required by Article 5(2)(d) in support of the application for designation aim at establishing that the designation criteria in Article 3(1) are met[7]. Therefore, if for a given therapeutic indication there is already a medicinal product for which an MA has been issued, the sponsor seeking an orphan designation for a further product in respect of that therapeutic indication must not only establish that the latter will be of significant benefit to patients in comparison to the former medicinal product, but also show that the second one is not identical to the first.

The Court of Justice then noted that, despite the EMA's allegations[8], the verification of the Article 3(1) criteria did not fall within the scope of EMA's review of the validity of the application for designation, but rather lied with the COMP in view of their technical and scientific nature. Similarly, the exclusive competence of the COMP extended to verifying the identity of the medicinal product which is the subject of the application for orphan designation with a medicinal product which has already been authorised. Therefore, since such allocation of powers between the EMA and the COMP was without prejudice to the outcome of the designation procedure, and did not undermine the effectiveness of Article 5(1), the Court dismissed the first ground of appeal as partly inadmissible and partly unfounded.

By the second ground of appeal, the EMA had claimed that the concept of 'medicinal product', as defined in Article 1(2) of Directive 2001/83, referred neither to the excipients nor to the method of administration, rather focusing on the active substance. However, the Court of Justice found that the EMA did not put forward any specific argument to prove the alleged error of law committed by the General Court and in consequence rejected this ground of appeal as unfounded. Accordingly, the Court dismissed the appeal in its entirety.

[7] Article 3 of Regulation No 141/2000, named "Criteria for designation", at paragraph one so states: "*... A medicinal product shall be designated as an orphan medicinal product if its sponsor can establish:*
(a) that it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10 thousand persons in the Community when the application is made, or
that it is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the Community and that without incentives it is unlikely that the marketing of the medicinal product in the Community would generate sufficient return to justify the necessary investment;
and
(b) that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorised in the Community or, if such method exists, that the medicinal product will be of significant benefit to those affected by that condition...".
[8] See paragraph 32 of the decision.

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