IN THE COURT OF JUSTICE OF THE EUROPEAN UNION
CASE: C-557/16

ASTELLAS PHARMA GMBH

-and-

(1) HELM AG
(2) LÄÄKEALAN TURVALLISUUS-JA KEHITTÄMISKESKUS (FIMEA)

WRITTEN OBSERVATIONS OF THE UNITED KINGDOM

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INTRODUCTION

1. The present reference under Article 267 TFEU from the Korkein hallinto-oikeus ("**the referring court**") raises important questions about the operation of the decentralised procedure laid down in Articles 28ff of the Medicines Directive[1] ("**the Directive**").

The decentralised procedure

2. The decentralised procedure applies where an applicant that does not hold a marketing authorisation ("**MA**") for its product applies for MAs in a number of different Member States.

3. Under Article 28(1)[2], the applicant selects one Member State to act as a reference Member State ("**RMS**"), any other Member State to which an application is made being referred to as a concerned Member State ("**CMS**"[3]). Under Article 28(3), the RMS prepares a draft assessment report, a draft summary of product characteristics and a draft of the labelling and package leaflet. The RMS then sends those draft documents to the CMSs and to the applicant.

4. Under Article 28(4), each CMS must, within 90 days of receipt of those documents approve the assessment report, the summary of product characteristics and the labelling and package leaflet and inform the RMS accordingly. The RMS then records the agreement of all parties. Article 28(5) then provides that the CMS "*shall adopt a decision in conformity with the approved assessment report, the summary of product characteristics and the labelling and package leaflet as approved, within 30 days after acknowledgement of the agreement*".

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[1] Parliament and Council Directive 2001/83/EC, OJ L311, 28.11.2001, as amended.

[2] References in these Observations to Articles are, save where otherwise stated, references to [2] References in these Observations to Articles are, save where otherwise stated, references to Articles of the Directive.

[3] To avoid repetition, the terms "CMS" and "RMS" will here be used to refer to the competent authority of the State concerned, save where the context otherwise requires.

5. However, Article 29(1) provides that where, during the 90 day period established by Article 28(4), a CMS "*cannot approve the assessment report, the summary of product characteristics, the labelling and the package leaflet on the grounds of potential serious risk to public health, it shall give a detailed exposition of the reasons for its position to the [RMS], to the other [CMSs] and to the applicant.*" A procedure is then laid down under the remaining provisions of that Article for the resolution of the disagreement between the CMS and the RMS.

The issue that has given rise to the present reference

6. The question that gives rise to the present reference is how those provisions deal with the situation where a third party contends – either in representations to the CMS or in legal proceedings challenging the lawfulness of the decision of the CMS to grant an MA in conformity with the agreed assessment report – that the assessment report prepared by the RMS contains an error of fact or law sufficient to call into question the correctness of that report but which does not raise any issue as to public health that is serious enough to engage Article 29(1).

The facts of the present case

7. In the present case, Finland is a CMS in relation to applications made to a number of Member States under the decentralised procedure by Helm ASG ("**Helm**") for its product, Alkybend. Helm chose Denmark as the RMS.

8. The RMS (Denmark), in preparing the assessment report, has accepted Helm's view that Alkybend is (within the meaning of Article 10(1)) a generic product of another product, Levact, for which MAs are held by Astellas Pharma GmbH ("**Astellas**").

9. Importantly for present purposes, the RMS also accepted that the period of data exclusivity, commencing with the first grant of an MA in relation to the

reference medicinal product ("**RMP**"), has expired, so that, under Article 10(1), Helm is not required to provide the results of pre-clinical tests and of clinical trials.

10. Astellas maintains that that latter conclusion by the RMS is incorrect. The RMS's view is based on the proposition that Levact (which was first granted an MA in 2010) is a "line extension"[4] of another product of Astellas, Ribomustin, which was granted an MA by the German competent authority in 2005. On that basis, the data exclusivity period has expired (since, on that basis, the MA for Levact is part of the same "global MA" as that for Ribomustin). However, Astellas maintains that the 2005 MA granted by the German authority did not amount to a valid decision for the purposes of the Directive. On that basis, Astellas' case is that the RMS should have regarded the data exclusivity period as commencing with the grant of the first MA to Levact, that is to say in 2010: and, on that basis, the data exclusivity period has not expired and Helm was in fact required to provide the results of pre-clinical tests and of clinical trials (which it did not do). According to Astellas, therefore, the assessment report prepared by the RMS is vitiated by what Astellas regards as the erroneous approach of the RMS to the date on which the data exclusivity period commenced.

The issue before the Court of Justice

11. The Court of Justice is not being asked to consider whether the RMS's approach is correct. Nor is it being asked to consider whether the 2005 decision by the German authority amounted to the valid grant of an MA.

12. Rather, the issue that is before the Court of Justice is whether the CMS in this case, the Finnish competent authority, the Lääkealan Turvallisuus-ja

[4] Art.6(1), second paragraph, provides that: "*When a medicinal product has been granted an initial marketing authorisation in accordance with the first subparagraph, any additional strengths, pharmaceutical forms, administration routes, presentations, as well as any variations and extensions shall also be granted an authorisation in accordance with the first subparagraph or be included in the initial marketing authorisation. All these marketing authorisations shall be considered as belonging to the same global marketing authorisation, in particular for the purpose of the application of Article 10(1)*". Products subject to that provision are commonly referred to as "line extensions".

Kehittämiskeskus ("**FIMEA**"), and/or the Finnish courts considering the lawfulness of FIMEA's decisions, are, under the decentralised procedure, entitled, or bound, to decide whether the approach to those issues adopted in the RMS's assessment report was correct (as Astellas maintains) or whether they are bound to accept that the assessment report was correct on that issue, so that the CMS is bound to issue an MA in relation to Ribomustin and that any national court hearing a challenge to that decision is also bound to uphold the CMS's decision based on the Danish report, and to do so even if the national court considers that the approach to the data exclusivity period adopted in the RMS's assessment report was incorrect.

Recent litigation in England and Wales

13. The United Kingdom observes that this issue has arisen on several occasions in litigation before the English courts, although, to date, the English courts have not found it necessary to rule on it.

    13.1. In the recent case of *Reg. (Napp Pharmaceuticals) v Secretary of State for Health* [2016] EWHC 1982 (Admin), the High Court of England and Wales considered an application for judicial review of a decision by the UK competent authority, acting as a CMS under the decentralised procedure, to grant an MA in a case where the RMS (with which the UK competent authority agreed) had proceeded on the basis that the product in question fell under Article 10(3) (the hybrid-abridged procedure). The claimant, which was the holder of the MA for the RMP, alleged that Article 10(3) did not apply. The High Court dismissed the application on the basis that the product at issue did fall within Article 10(3), so it did not need to consider an alternative submission on behalf of the interested party in that case, the applicant for the MA at issue, that the UK competent authority and the High Court were bound by the approach of the RMS[5].

[5] The claimant has sought permission from the Court of Appeal to appeal against that judgment.

13.2. Another recent decision of the High Court relates to the very product at issue in the case now before the Court of Justice, namely *Accord Healthcare v Astellas Pharma GmbH* [2015] EWHC 3676 (Ch). In that case, to which the UK competent authority was not a party, the High Court held (in effect) that the approach of the RMS in the present case was correct in fact and law. However, it does not appear that the question now before the Court of Justice – whether the national court of a CMS has competence to rule on a matter covered in the assessment report prepared by the RMS – was raised by either party in that case and the High Court did not deal with it[6].

THE UNITED KINGDOM'S ANALYSIS OF THE QUESTIONS BEFORE THE COURT OF JUSTICE

14. The first question posed by the referring Court concerns the powers and obligations of the competent authority of a CMS under the decentralised procedure in a case where the CMS considers that the RMS may have erred in calculating the data exclusivity period.

15. The second question assumes that the CMS is not competent to take a different approach to that of the RMS, and raises various questions about the powers and obligations of the national courts of the CMS on an appeal against the decision of the CMS.

16. In the United Kingdom's submission, the two questions – the powers and duties of the CMS and those of the national courts of the CMS – should be considered together.

[6] This judgment is now on appeal to the Court of Appeal. In addition, the decision of the UK competent authority, as a CMS, to grant an MA to Accord Healthcare has been challenged by Astellas by way of judicial review: those proceedings are currently stayed pending the judgment of the Court of Appeal. Further legal proceedings by Astellas challenging the grant of MAs to other products on the basis that they are generics of Ribomustin/Levact have also been stayed.

17. The difficulty in the present case arises because of the tension between two strands of the Court of Justice's case-law.

The Synthon *case-law*

18. The first strand is exemplified by the judgment of the Court in Case C-452/06 *Reg. (Synthon BV) v Licensing Authority* ECLI:EU:C:2008:565 ("***Synthon***"). *Synthon* concerned the mutual recognition procedure under Article 28(2), namely where the applicant for an MA in one Member State (the CMS) already holds an MA for that product in another Member State (the RMS). In that case, the RMS had proceeded on the basis that the product at issue was essentially similar to a RMP for the purposes of what was then Article 10(1)(a)(iii) of the Directive, and had granted an MA on that basis. However, the CMS did not accept that the product was essentially similar to the RMP and refused to validate the application for an MA. The Court held that: -

    18.1. "*In accordance with the objective of abolishing all barriers to the free movement of medicinal products in the [EU] referred to in recitals 12 and 14 in the preamble to the directive, it is apparent from Article 28(4) that a [MA] granted by a [RMS] must, in principle, be recognised by the [CMSs] within 90 days of receipt of the application and the assessment report from the [RMS], and that that recognition is not dependant on the procedure followed by the [RMS] for granting that authorisation*." (§25); and

    18.2. "*such an obligation of mutual recognition is strictly delineated by Article 28 of [the Directive]*" because (a) *an application for mutual recognition must be held to be valid where, in accordance with the requirements of Article 28(2), it is accompanied by the information and particulars referred to in Articles 8, 10(1) and 11 of [the Directive], the dossier submitted is identical to the dossier accepted by the [RMS], and any additions or amendments contained in the file have been identified by the applicant*" and (b) "*it is clear from the wording of Article 28(4) of [the Directive] that the existence of a risk*

> *to public health, within the meaning of Article 29(1) of [the Directive], constitutes the only ground that a [CMS] is entitled to rely on to object to the recognition of a marketing authorisation granted by [an RMS]. In addition, Article 29 provides that a [CMS] wishing to rely on such a ground is required to comply with a specifically prescribed procedure for provision of information, concerted action, and arbitration*." (§§26-28).

19. The Court concluded that:

> "*a [CMS] to which an application for mutual recognition is made pursuant to Article 28 of [the Directive] cannot call into question, on grounds other than those relating to the risk to public health, the assessments carried out by the [RMS] in the context of the procedure for evaluating the medicinal product, such as those concerning essential similarity within the meaning of Article 10(1) of the [Directive]*."

20. A judgment to a similar effect, based on the materially similar provisions of Parliament and Council Directive 2001/82 on veterinary products ("**the Veterinary Directive**") relating to the decentralised procedure, is Case C-145/11 *Commission v French Republic* ECLI:EU:C:2012:490 ("***Commission v France***"). In that case, the RMS had, following the procedures set out in the provisions of the Veterinary Directive equivalent to Article 28(3) (i.e. the decentralised procedure), produced an assessment report and granted an authorisation, equivalent to an MA, to a particular product. However, the French authorities refused to grant equivalent authorisation under the provision of the Veterinary Directive that was equivalent to Article 28(4) of the Directive, claiming that the product did not comply with certain requirements of EU law and that its method of administration failed to comply with provisions of French law.

21. The Court of Justice held that the French authorities had thereby infringed the Veterinary Directive. The Court, first, noted that the provisions of the

Veterinary Directive equivalent to Articles 28 and 29 provided that the only basis on which CMSs could refuse to recognise an assessment report prepared by the RMS was reasons of public health (§34) and that there was no other basis on which a CMS was entitled to make authorisation conditional on supplementary grounds of objection (§35). The Court then held that that approach was confirmed by the consideration that:

> "*une autre approche priverait les dispositions relatives à la procédure décentralisée de leur effet utile, puisque, si un État membre appelé à autoriser un médicament pouvait conditionner la validation de la demande qui lui est présentée à des exigences non prévues par la directive 2001/82, cela reviendrait à priver d'intérêt la procédure décentralisée instituée par le législateur de l'Union et à compromettre sérieusement la réalisation des objectifs visés par ladite directive, au nombre desquels figure, en particulier, la libre circulation des médicaments dans le marché intérieur*"[7].

22. The Court went on to state that that approach was confirmed by its judgment in *Synthon*, and stated that that judgment (which, as noted above, concerned the mutual recognition procedure) also applied to the decentralised procedure (§§38-39).

The Olainfarm *case*

23. The second strand of the Court of Justice's case-law is the Court's judgment in Case C-104/13 *Olainfarm AS v Latvijas Republikas Veselības ministrija* ECLI:EU:C:2014:2316 ("***Olainfarm***").

24. In *Olainfarm*, the Court was asked whether the holder of the MA ('**the RMP MA holder**") for a medicinal product used by another manufacturer ("**the applicant**") as an RMP with a view to obtaining an MA for the applicant's generic product under Article 10 of the Directive enjoyed the right to a judicial

[7] Judgment available only in French. The United Kingdom translates this passage into English as follows: "*any other approach would deprive the provisions relating to the decentralised procedure of their useful effect, since, if a Member State called to authorise a medicinal product could make the grant of the request made to it subject to grounds not foreseen by Directive 2001/82, that would have the effect of depriving the decentralised procedure laid down by the EU legislature of its effect and of seriously compromising the achievement of the objectives pursued by the said Directive, among which is, in particular, the free circulation of medicinal products in the single market*."

remedy in order to determine whether the applicant made lawful, well-founded reference to the RMP, in conformity with the provisions of Article 10.

25. The Court held that it did. The Court first referred to Article 47 of the Charter, which provides that any person whose rights guaranteed by the law of the EU are violated has the right to an effective remedy before a tribunal. It then stated that: -

> "*Article 10 of [the Directive] lays down the conditions under which the [RMP MA holder] is required to accept that the [applicant] is entitled to refer to the results of pre-clinical tests and clinical trials contained in the dossier relating to the application for the MA for the [RMP], rather than perform those tests or trials himself, for the purpose of obtaining a MA for the other medicinal product. It is apparent that that provision confers a concomitant right on the [RMP MA holder] to demand that the rights attaching to him by virtue of those conditions are observed.*" (§37)

26. The Court then went on to hold at §38 that the RMP MA holder must, in the case where the applicant was applying for an MA under Article 10 based on that RMP, have the right to demand that: -

    26.1. the data exclusivity period laid down by Article 10(1) was observed; and

    26.2. its product not be used as an RMP where the conditions of Article 10, including in particular the condition of similarity in Article 10(1), were not, in fact, satisfied.

27. At §§39-40, the Court concluded that in a case where the RMP MA holder asserted a breach of those rights, it was entitled to effective judicial protection, and in particular the right to challenge in judicial proceedings the decision of a competent authority to grant an MA to the applicant.

The tension between the Synthon *and the* Olainfarm *case-law*

28. The tension between the *Synthon* and the *Olainfarm* case-law arises where a CMS, in the course of either the decentralised procedure or the mutual recognition procedure, is faced with the possibility that the grant, under Article 28(5), of the MA sought by the applicant would infringe the rights of the RMP MA holder under Article 10.

29. The United Kingdom notes that *Commission v France* appears to be inconsistent with any distinction in this regard between the decentralised procedure and the mutual recognition procedure.

30. It is evident that, in the case of a grant by the CMS of an MA under Article 28(5), there is an apparent conflict between the two principles: if the CMS can refuse an application for an MA only on limited public health grounds, then the RMP MA holder does not appear, in the CMS, to have the right to effective judicial protection of the rights that Article 10 confers upon it in relation to the use of its dossier by subsequent applicants. After all, a right to judicial protection is nugatory if the CMS has, in law, no power to refuse to issue the MA at issue even if it is convinced that the RMS has erred in law, that the RMP MA holder is correct and that the grant of the MA at issue would infringe the rights of the RMP MA holder. In such a case, the national court would have to reject any appeal by the RMP MA holder even if it, too, agreed with the RMP MA holder that the RMS's decision on the point was wrong in law.

The United Kingdom's approach to resolving that tension

31. In theory, one way of resolving that conflict would be to hold that the *Olainfarm* principle does not extend to the grant of an MA by a CMS under Article 28(5). Such an argument would be based on the fact that neither the decentralised procedure nor the mutual recognition procedure was at issue in *Olainfarm*. The argument would go on to note that the RMP MA holder could, in such a case, seek to challenge the decision of the RMS in the national courts of the RMS. It could also be suggested that, if the RMP MA holder

succeeded in having the decision of the RMS annulled, then decisions of the CMSs under Article 28(5) would also be likely to be void.

32. However, the United Kingdom submits that that would not be the correct approach, for the following reasons.

32.1. As the Court accepted in *Olainfarm*, the RMP MA holder's right to effective judicial protection of its rights under Article 10 is a fundamental right deriving from the Charter.

32.2. That right extends to all cases where the RMP MA holder has rights under Article 10 to prevent the subsequent use of its original dossier relating to the RMP and which are infringed by a decision to grant an MA to an applicant. Examples include: -

32.2.1. cases where the data exclusivity period has in fact not expired (so that use of the RMP MA holder's dossier by the applicant is precluded by Article 10(1)); and

32.2.2. cases where the applicant's product is not, in fact, a generic product of the RMP under Article 10(1) (in which case, the applicant is required to produce its own pre-clinical tests and clinical trials under Article 8(3)(i) and cannot rely on the RMP MA holder's dossier); and

32.2.3. cases where the applicant's product is not, in fact, sufficiently similar to the RMP to engage Article 10(3) (in which case, the applicant is not entitled to rely on the RMP MA holder's dossier and to limit its provision of the results of pre-clinical tests and clinical trials only to what is appropriate under that Article).

32.3. In any of the above cases, a decision by the CMS to grant an MA to an applicant under Article 28(5) has the effect that, in the Member

State concerned, the RMP MA holder's rights have been infringed and that it suffers loss and damage as the result of competition from a product that should not have been granted an MA in that Member State.

32.4. In any of the above cases, limiting the right of the RMP MA holder under the decentralised or mutual recognition procedures, to a right only to challenge the RMS's decision in the national courts of the RMS, fails, in the United Kingdom's submission, to guarantee the RMP MA holder's rights to effective protection.

32.4.1. First, pending the resolution of the appellate procedure in the RMS, the RMP MA holder would appear on that basis to have no possibility of obtaining any relief, including interim relief, in any CMS. Even if the CMS's decision is eventually annulled as the result of proceedings in the RMS, it may be difficult for the RMP MA holder then to obtain compensation for its commercial losses in the interim (since, even if it is entitled under national law to damages from the applicant, such damages are typically very difficult to quantify, and the applicant may be unable to pay such damages). Moreover, in certain cases the structure of the market may irrevocably change as a result of the entry of the applicant's product, leading to irreparable loss to the RMP MA holder.

32.4.2. Second, it is evident and inevitable that the speed and effectiveness of appeals to national courts against the decisions of national competent authorities vary from Member State to Member State. It may be noted in that regard that the applicant decides which Member State will be the RMS, and that the applicant may not have any interest in choosing the Member State with the speediest and most effective appellate procedure.

32.4.3. Third, even when the RMP MA holder succeeds in obtaining the annulment of the decision of the RMS, it may then have to go through further procedures in the CMSs to obtain the annulment of the decisions of the CMSs under Article 28(5), during which time it will suffer further commercial loss and damage in those states.

33. The United Kingdom therefore considers that the correct approach to resolving the tension between the *Synthon* and the *Olainfarm* case law would be to hold that, in a case where the RMP MA holder has rights under Article 10 (such as the cases set out at §32.2 above) it is entitled to the effective judicial protection of those rights, even in a case where the CMS has taken or is considering taking a decision under Article 28(5) in the context of the decentralised or mutual recognition procedures.

34. It is a necessary consequence of that approach that the CMS should have power to refuse to grant an MA under Article 28(5) on the ground that the grant of that MA would infringe the rights of the RMP MA holder under Article 10: otherwise the right to effective judicial protection would be nugatory.

35. It may be noted in that regard that *Synthon* was not a case in which the RMP MA holder's rights to the protection of its dossier under Article 10 were at issue: the United Kingdom's suggested approach would therefore not contradict the Court's judgment in that case[8].

36. However, the United Kingdom accepts the importance of the objective of the mutual recognition procedure recognised in *Synthon* (and indeed of the decentralised procedure, as recognised in *Commission v France*), namely, that of promoting the free circulation of medicinal products within the single market.

[8] Nor did the *Commission v France* case raise any issue about equivalent rights under the Veterinary Directive.

37. The United Kingdom therefore considers that, in taking decisions under Article 28(5), and in reviewing such decisions, CMSs and national courts of CMSs are obliged to have regard to the decisions of the competent authorities and courts of other Member States on the same subject matter, and that (in particular) they should presume that those decisions are correct in the absence of any convincing representations to the contrary by the RMP MA holder.

38. Moreover, if a national court of a CMS considers that the RMS, or the national court of the RMS, has granted (or upheld a decision to grant) an MA on the basis of an incorrect view of the law in relation to the rights of the RMP MA holder under Article 10, then it should, before reaching a different view on that question of law to that of the RMS, refer that question to the Court of Justice for a preliminary ruling under Article 267 TFEU.

The questions posed by the referring Court

39. Against that background, the United Kingdom turns to the questions before the Court of Justice.

40. It follows from the United Kingdom's approach that the answer to the first question (relating to the competence of the authorities of a CMS in granting an MA under Article 28(5) to determine for themselves the correct length of the data exclusivity period) is that, under Article 28(5), the competent authority of the CMS should presume that the RMS has correctly determined the length of the data exclusivity period but that, if representations are made to it to the contrary by the RMP MA holder, it must, after paying due regard to the position taken by the RMS, assess for itself whether the RMS has correctly calculated that period and (if it concludes that the data exclusivity period has in fact not expired) refuse to grant the MA.

41. On that basis, the second question posed by the referring court (which arises only if the national authority has no competence to refuse the MA on that ground) does not in fact arise. However, the United Kingdom would, in

relation to national courts, answer the referring court's questions to the effect that national courts should also presume that the RMS has correctly determined the length of the data exclusivity period but that, if representations are made to it to the contrary by the RMP MA holder, it must, after paying due regard to the position taken by the RMS, assess for itself whether the RMS has correctly calculated that period and (if it concludes that the data exclusivity period has in fact not expired) refuse to grant the MA. But, in the case of national courts, the United Kingdom would also add that a national court that reaches a different view on a question of law relating to the rights of the RMP MA holder under Article 10 to that of the RMS must, before determining the case to that effect, make a reference of that question of law to the Court of Justice under Article 267 TFEU.

42. The United Kingdom would also observe that the above approach applies not just to questions of data exclusivity, but to any other case in which the rights of the RMP MA holder under Article 10 are at issue.

43. The United Kingdom therefore proposes the following answers to the questions posed by the referring court: -

(1) Under Article 28(5) of Directive 2001/83/EC, relating to the grant of marketing authorisations by concerned Member States under the mutual recognition and decentralised procedures established by the preceding paragraphs of the Article, the competent authority of the concerned Member State, or the national court, shall refuse to make such a grant, or (as the case may be) shall uphold such a refusal or annul such a grant, if it is satisfied that that grant would infringe the rights under Article 10 of that Directive enjoyed by the holder of the marketing authorisation of the reference medicinal product.

(2) In taking any such decisions, national competent authorities and national courts must presume that the assessment report prepared by the reference Member State has correctly determined whether that grant would infringe the rights under Article 10 of that Directive

enjoyed by the holder of a marketing authorisation of the reference medicinal product. However, that presumption shall be displaced if, after representations are made by or on behalf of the holder of the marketing authorisation of the reference medicinal product, and after paying regard to the assessment report and any decision of the courts or competent authorities of the reference Member State or any other concerned Member State, the competent authority or court is satisfied that that grant would infringe the rights under Article 10 of that Directive enjoyed by the holder of the marketing authorisation of the reference medicinal product.

(3) A national court must, before deciding any appeal in relation to a decision under Article 28(5) on the basis of a view on a question of law that differs from the view of that question taken by the reference Member State in the assessment report, refer that question to the Court of Justice of the EU for a preliminary ruling under Article 267 TFEU.

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