ASTELLAS - PHARMACEUTICAL REGULATION – IS COMMUNAL COOKING IN THE KITCHEN TOO HOT TO HANDLE?

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Community law has set up a harmonised framework for the regulation of marketing authorisations ("*MA*") for medicinal products to facilitate their free movement within the internal market.[1] Pursuant to that common regulatory framework, a medicinal product cannot be sold within the internal market without a prior authorisation, granted either at EU level by the Commission or by a relevant national competent authority ("*NCA*"). [2] Under the Directive, there are three ways in which an NCA can grant an MA:-

1. By way of a national authorisation;

2. Under the mutual recognition procedure, whereby an NCA from one Member State grants the initial MA which is then recognised in other Member States; or

3. Under the decentralised procedure whereby the application is made to a lead NCA in 'reference Member State' who then co-ordinates with any other NCAs from "*concerned Member States*". [3]

The extent to which one NCA can depart from an MA that has been previously granted by another Member State raises rather dry and technical questions of European law. However, it has huge commercial significance for the entities involved, ie the actual or would be holder of the MA, on the one hand, and generic manufacturers on the other that would like to market and sell their equivalent medicines based on the original relevant medicinal product. The grant of an MA confers a period of data exclusivity on the MA holder, so that generic medicines are not allowed to be marketed or sold within the internal market for a period of eight plus two years (known as the "*data exclusivity period*"). That data exclusivity period effectively excludes generics from the market until that period has expired. The purpose of that exclusivity period is to balance the competing rights of the innovator versus the generic manufacturer. While the innovator has

[1] See Directive 201/83/EC of 6 November 2001 on the community code relation to medicinal products for human use *OJ2001L331*, p.67 (as amended).

[2] This procedure is set out in Articles 3-10 of Regulation 726/2004.

[3] The mutual recognition procedure and decentralised procedure are set out in Article 28 of Directive 2001/83.

to invest substantial sums in research and development and clinical trials, it is entitled to a reasonable reward for that investment in the form of its patent rights and data exclusivity. However that right cannot persist indefinitely, especially when the higher monopoly prices are paid for by national health systems and ultimately the tax payer. The data exclusivity period therefore allows generic manufacturers to market and sell their equivalent drugs at lower prices after a given time. Once the data exclusivity period has expired, generics are entitled to rely on the "*dossier*" of the initial reference product and to avoid the burden and expense of conducting repeated clinical trials and tests.

Before the amendments to the Directive, the authorisation of medicinal products was conducted under national procedures which often resulted in conflicting or inconsistent outcomes. The mutual recognition procedure and decentralised procedure aim to minimise those differences by ensuring that NCAs apply a uniform approach in their assessment of MAs and co-ordinate regarding the grant of the initial MA and/or its recognition and application in other Member States.

The enforcement of the competing rights given to innovators and generic manufacturers has become increasingly adversarial, either with generics seeking multiple authorisations in different Member States or challenging the initial MA that had been granted in favour of the MA holder or the data exclusivity conferred. *Astellas* was one example of such a case. Astellas had received two MAs from two medicinal products: with the German NCA for the first in 2005 for Ribomustin and the second for Levact which had been granted under the decentralised procedure in 2010. In 2012, a generic manufacturer applied for an MA from the Danish NCA under the decentralised procedure for its generic equivalent product, Alkybend, relying on Levact as the reference medicinal product. However, it argued that the data exclusivity period should be taken to start from the time of the Ribomustin MA in 2005. That conclusion was upheld by the Finish NCA who granted the generic MA on that basis. Astellas challenged the generic MA before the Finish courts and the Supreme Administrative Court referred two questions for preliminary ruling to the CJEU. The first question was whether a concerned Member State under the decentralised procedure was competent to determine the time at which the data exclusivity period started to run. The second question was, assuming it was not, whether the national courts could determine the period of data exclusivity and whether the principle of effective legal protection under Article 47 of the Charter required the National Court to scrutinise the original MA granted in another Member State and/or depart from it in order to give effect to the MA holder's rights.

Question 1

The CJEU, adopting the analysis of AG Bobeck, carried out a careful analysis of the decentralised procedure and the role of the reference Member State and

concerned Member States in that process. In his Opinion, AG Bobeck had drawn an analogy with chefs in a kitchen cooking a meal together. In his view, this meant that, as the NCAs were all actively participating in a common procedure which lead to the adoption of the MA under the decentralised procedure, once the relevant agreement had been reached, they were not allowed to turn back and call into question the outcome of that procedure. The CJEU upheld that analysis, holding that once the Member State NCAs had reached a general agreement which had been acknowledged by the reference Member State in its MA, the NCAs in the concerned Member States are required to adopt their own MA decision in conformity with the assessment report that had been reached. They could not subsequently start to unpick the scientific evaluation or try to superimpose their own opinion of the authorisation after the event. The CJEU was clear that, should they try to do so, that would "*deprive the decentralised procedure of all meaning and would, inter alia, compromise the attainment of the objectives of free movement of medicinal products set out in the Directive*". [4]

With regard to the specific issue of data exclusivity, the CJEU made a very clear statement that the data relating to the reference medicinal product is protected for the benefit of the MA holder during the data exclusivity period and therefore cannot be used as the basis for a generic application until the eight plus two year period has expired. [5] As part of the decentralised assessment of the generic application, the NCAs have to verify whether the application complies with the data exclusivity period to check whether the conditions for issuing the generic MA under Article 10 of the Directive have been fulfilled. If the conditions of Article 10 and the documents submitted in support of the application do not comply, the lead NCA "*must*" refuse the MA. [6] The CJEU then went on to hold that as the expiry of the data exclusivity period is a pre-condition for granting the generic MA and the compliance with that condition must be verified by all Member States participating in the decentralised procedure. An NCA is therefore entitled to oppose the application before the agreement has been reached between the Member States if those conditions have not been satisfied. [7] Accordingly, at that point of the co-operation under the decentralised procedure, it is open to an NCA to refuse to approve the assessment report if the data exclusivity condition has not been met. However, once the NCAs have reached an agreement under the decentralised procedure and that agreement has been acknowledged by the reference Member State, it is not open to the concerned NCAs to repeat that verification exercise. That verification should already have been conducted as

[4] The CJEU referred to the Synthon Judgment *C45206EU:C:2008:565 at para 32* which had reached the same conclusion in respect of the national procedure process. A similar outcome has recently been reached by the Administrative Court in respect of the centralised process: see *Teva [1018] EWHC*.

[5] See paragraph 27.

[6] See paragraph 28.

[7] See paragraph 29.

part of the initial assessment as part of the decentralised procedure and should not be duplicated.[8]

Question 2

As to the issue of effective legal protection, the CJEU referred back to its previous jurisprudence concerning the rights granted pursuant to Article 10 of the Directive. In particular the CJEU has held that the data exclusivity period confers a directly enforceable right on the MA holder to demand that a generic product cannot be authorised using its medicinal product as a reference product until the data exclusivity period has expired. That right can be enforced before the national courts. In that sense, it can be said to have vertical direct effect. The MA holder is therefore entitled to effective judicial protection in respect of his rights and has the right to seek a judicial remedy challenging the decision of any NCA which grants a generic MA in contravention of the data protection rights that have been conferred pursuant to Article 10. [9] The CJEU went on to confirm that the rights conferred on the MA holder do not just extend to the protection of its data but also to challenge any determination as to the point in time from which the data exclusivity starts to run. [10]

The problem with the generic applications under the decentralised procedure is that the Directive does not envisage any formal rights of participation for the MA holder in the authorisation procedure. It may not have had any opportunity to submit observations to the NCAs in the reference or concerned Member States at the time of their determination. The MA holder will not be an addressee of that decision, since that will be directed to the generic manufacturer who was the applicant in that procedure. The CJEU noted that the Directive does not provide for any measures whereby the MA holder can bring an action or start court proceedings to assert its rights before the competent authority. The CJEU held, in the absence of such explicit provision, that the principle of effective judicial protection has to create the right for the MA holder to challenge a generic MA granted by an NCA before the court of that Member State. In particular, the MA holder must be able to plead an error of law regarding the time at which the exclusivity period was determined to run. However, that right of action is confined to the national courts of the NCA in question and again will be subject to the procedural rules and time limits applicable within that national regime. The MA holder is not entitled to challenge decisions taken by NCAs in *other Member States* before the courts of a different Member State. The CJEU did not provide specific reasons for this approach, but there is extensive discussion in the Opinion of AG Bobeck who records the principle of judicial comity and the difficulties that would arise if national courts were called upon to adjudicate over decisions taken in other Member States.

[8] See paragraphs 30 to 31.

[9] See paragraphs 34 to 36, referring to case C-104/13 Olainfarm, EU:C:2014:2316 at paragraphs 37 to 40.

[10] See paragraph 37.

This Judgment is to be welcomed as it clearly builds upon the establishment of directly enforceable rights recognised in *Olainfarm*. Although framed solely in terms of the MA holder, the rights that it possesses have a direct impact on the rights and obligations of the generic manufacturer(s) and it is to be assumed that generics have concomitant directly enforceable rights or non-rights (even if qualified or conditional upon the expiry of the data exclusivity period). Although those rights may not (yet) be enforceable horizontally, they can clearly be enforced vertically against the NCAs, as emanations of the Member States.

The Judgment seeks to reconcile the practical realities of enforcing rights within a harmonised regulatory framework. Although the Directive provides for MA decisions to be taken on a harmonised and co-operative basis involving different Member States, it has not provided for a harmonised regime of judicial enforcement. The CJEU has been left to devise one in accordance with the principles of effective judicial protection. However, that piecemeal organic development will inevitably lead to problems. For instance:

- It means that a NCA in a concerned Member State has to follow the approach adopted by the NCA in the Reference Member State regarding the exclusivity period even if it thinks it is wrong. The NCA has to follow that outcome (and cannot gainsay the underlying scientific evaluation) even if, as a matter of domestic law, the complainant has an arguable case.

- If the complainant seeks to challenge, it must bring the action in the "home court" of the NCA concerned – that may involve different courts where there are a number of concerned Member States in the decentralised procedure. Without some mechanism for consolidation or resolving lis alibi pendens [11], that is likely to result in inconsistent rulings.

- A complainant will not be able to challenge the decision of the Reference Member State in the courts of a Concerned Member State. But what is a court to do if it concludes that the decision of the NCA in the Concerned Member State is wrong? That logically entails that the Reference Member State's decision is wrong too: but that decision obviously survives, resulting in conflicting national decisions. Should the national court make a preliminary reference? Would a preliminary reference be admissible if it is essentially asking the CJEU to determine the facts and adjudicate on the scientific evaluations conducted by the lead NCA?

The *Astellas* judgment can therefore be seen as providing a means to an end, although not an ideal one in practice. In resolving one issue, it may give rise to plenty more difficulties. The warnings of AG Bobek may come to pass and

[11] It is not clear whether these proceedings would count as "civil and commercial proceedings" for the purpose of the Recast Brussels Regulation, given their public or regulatory nature.

herald in a new wave of procedural harmonisation for the effective protection of rights in the pharmaceutical field.

George Peretz QC acted for the United Kingdom Government.

The comments made in this case note are wholly personal and do not reflect the views of any other members of Monckton Chambers, its tenants or clients.

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