Generics (UK) limited, The Wellcome Foundation Limited and Glaxo Operations UK limited and Others, 3 December 1998

(Court of Justice of the European Union Case C-368/96**,** reference by the High Court of Justice of England and Wales)

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Summary

This case concerned the protection of pharmaceutical test data under European Union (EU) legislation. The Court of Justice of the European Union (CJEU) interpreted EU law as authorizing generic producers to rely on the test data submitted by an originator firm once the original product has been in the market for at least six or ten years (depending on national law), as long as the generic product is essentially similar to the original product. Such abridged approvals may even include generic versions of indications or dosages of the original products that have been in the market for less than six or ten years.

The facts

This case concerned the marketing approvals of three different products by the UK Medicines Control Agency (MCA), as follows. (1) Captopril is a medicinal product developed by Bristol-Myers Squibb Pharmaceuticals Limited. Generics Limited manufactures and distributes generic medicinal products, and applied for, and was granted, under an abridged application procedure, marketing authorization for a generic version of captopril in respect of all indications which had been authorized at least ten years before. However, the MCA refused market authorization for certain indications whose approval was granted less than ten years before, and which according to the MCA constituted fundamental changes in the terms of the original authorization, thus requiring a new application. (2) Wellcome holds the marketing authorization for aciclovir. A/S GEA Farmaceutisk Fabrik obtained from the MCA marketing authorizations for all the therapeutic indications and dosage forms of aciclovir tablets and intravenous infusion aciclovir for which Wellcome had obtained authorization. Wellcome lodged an application for judicial review of the MCA's decision to grant marketing authorization under the abridged procedure in respect of therapeutic indications, routes of administration and dosage forms. (3) Glaxo obtained from the MCA all marketing authorizations for ranitidine and wrote to the MCA seeking assurance that its right to protection of its own data would be respected. The MCA responded that the subsequent applications for marketing authorizations for products containing ranitidine could rely on all the authorized recommended indications, doses and dosage schedule.

The MCA relied on provisions of European law (Council Directive 65/65/EEC as amended by Council Directive 87/21/EEC). In essence, the underlying law stipulates in relevant part that in order to receive market authorization for a medicinal product, the application must be accompanied by (1) physico-chemical, biological or microbiological tests; (2) pharmacological and toxicological tests; and (3) clinical trials. The applicant is, however, not required to provide the results of the

pharmacological and toxicological tests or the results of clinical trials if he can demonstrate that the medicinal product is essentially similar to a product authorized in the country concerned not less than six or ten years ago (depending on national legislation; the United Kingdom had chosen to provide for a ten-year term of protection). By contrast, if the product is intended for different therapeutic uses than those already approved, then the test and clinical trials need to be provided. The abridged procedure enables a second applicant for marketing authorization for a given product to save time and expenses and also avoids the repetition of tests on humans or animals where not absolutely necessary.

Glaxo applied for judicial review of the MCA's decision. The High Court of Justice of England and Wales referred the matter to the Court of Justice of the European Union (CJEU) for a preliminary ruling.

The legal issues

The legal issues related to the conditions under which a generic competitor may rely on the test data submitted by an originator for the submission of a request for generic marketing approval ("abridged procedure"). The parties agreed on the basic requirement for the abridged procedure, i.e. the need for the original product to have been in the market for at least ten years. Before the expiry of this period of exclusivity, a drug regulator may not rely on the originator's test data for the approval of a generic competing product. The parties also agreed that in order to benefit from the abridged procedure, the generic product had to be essentially similar to the original product.

The parties differed in their interpretation of the law in respect of the extent to which drug regulatory agencies may use the abridged procedure to approve generic versions of indications or dosage forms for which the originator received marketing authorization less than ten years before.[1] In other words, may a European drug regulatory agency approve a generic on the basis of test data supplied by the originator for any new indication or dosage that required a change of the original request or an entirely new request and that was filed after the expiry of the ten-year exclusivity period accorded to the original product?

In the view of the involved originator companies, a generic competitor may only benefit from the abridged procedure if all of the indications or dosages for which generic approval is sought have been marketed by the originator for at least ten years. Generics, by contrast, argued that for essentially similar products, the abridged procedure may be relied on for any indication or dosage for which the original product was authorized, irrespective of when the original marketing authorization was changed or a new marketing authorization was granted. The MCA supported Generic's view, except for cases where the new dosages or indications constitute major therapeutic innovations and require a new application for marketing approval.

The CJEU in its decision confirmed the interpretation advanced by Generics. In essence, the Court considered that for a product to be essentially similar, what mattered is similarity in terms of safety, efficacy and quality of the original and the generic product. By contrast, the question of having the same or different therapeutic

[1] See paragraphs 15-17 of the decision.

indications or dosages, etc., was irrelevant in the Court's view.[2] As long as a generic product may be considered as essentially similar, the CJEU emphasized that it could benefit from the abridged approval procedure even if the request for generic approval included indications or dosages of the original product that were approved less than ten years before. The CJEU in that context clarified that neither the protection of a new indication or dosage by a patent nor its qualification as a fundamental change of the original marketing approval were criteria that can be taken into account, as opposed to essential product similarity in terms of safety, efficacy and quality.[3]

Accordingly, regarding what therapeutic indications may be authorized under the abridged procedure in respect of a medicinal product that is essentially similar to an already authorized medicinal product, the CJEU responded that all therapeutic indications already authorized for that product are included. The same applies to the dosage form, all dosage forms, doses and dosage schedules authorized for that product that can also be authorized under the abridged procedure.[4]

Finally, the CJEU emphasized that the applicable EU legislation struck an appropriate balance between the objective of promoting pharmaceutical innovation on the one hand and the goal of avoiding time-consuming repetitions of clinical trials on the other.[5]

Points of significance

- In the EU, Council Directive 65/65/EEC as amended by Council Directive 87/21/EEC provided for exclusive rights in pharmaceutical test data for six or ten years, depending on national legislation. During that term, a generic company could not rely on the originator's test data to receive generic approval.
- The CJEU clarified that upon expiry of the six or ten-year term of protection, generic competitors may rely on the originator's test data for the approval of essentially similar products, even if the generic request includes indications or dosage forms of the original product that were approved less than six/ten years before. The CJEU emphasized that the essential criterion for the abridged approval procedure to apply was the existence of an essentially similar generic product, no matter whether it included indications or dosages for which the originator had to submit a new marketing request or for which the originator received a separate patent.
- The above means that under Council Directive 65/65/EEC as amended by Council Directive 87/21/EEC, any test data that an originator files in relation to an original product that has been in the market for more than ten years is no longer protected from generic competition in essentially similar products.
- The CJEU defined essentially similar products as those having the same qualitative and quantitative composition in respect of active principles, of having the same pharmaceutical form and of being bioequivalent, unless it is apparent in the light of scientific knowledge that it differs significantly from the original product as regards safety or efficacy.

[2] See paragraphs 36 and 42 of the decision.
[3] See paragraphs 47 - 50 of the decision.
[4] See paragraphs 54 – 56 of the decision.
[5] See paragraphs 83 - 85 of the decision.

- The TRIPS Agreement in Article 39.3 obliges WTO Members to provide protection to pharmaceutical test data against "unfair commercial use". It is controversial whether this obligation requires the protection of test data through exclusive rights. Under a different interpretation, Members may authorize the reliance by generic producers and drug regulatory agencies on original test data, without any waiting period, while prohibiting the misappropriation of protected test data through unfair commercial means. A number of countries have chosen this option to implement Article 39.3 of the TRIPS Agreement.[6] Countries that opt for a data exclusivity regime are also free under TRIPS to define the scope of such exclusivity in accordance with their domestic priorities. The case of *Bayer Inc. v. The Attorney General of Canada and The Minister of Health* [7] illustrates a very narrow interpretation of exclusivity which enables a quicker approval of generics than under the present decision by the CJEU.

Key words: Data exclusivity, market authorization, abridged procedure, bioequivalence.

Available at: http://curia.europa.eu/juris/liste.jsf?language=en&num=C-368/96

[6] See UNCTAD, Using Intellectual Property Rights to Stimulate Pharmaceutical Production in Developing Countries. A Reference Guide, Geneva and New York, 2011, pp. 161, 167 ff.
[7] See the summary available in this database.