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Enantiomer "Repaglinide" found to lack Inventive Step in Germany

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by Stephan Disser

The German Federal Court of Justice (FCJ) has just issued its written decision in the case “Repaglinid” (X ZR 128/09). As far as can be seen, the decision is not yet available on the FCJ’s website www.bundesgerichtshof.de. The FCJ rejected the patent proprietor’s appeal against the decision of the Federal Patent Court revoking the German part of EP 0 589 874 for lack of inventive step. The decision contains some interesting aspects regarding the assessment of inventive step by the FCJ in the pharma field and in general.

Claimed in the patent-in-suit is the use of an enantiomer (Repaglinide) as active substance in the preparation of a long-term antidiabetic agent characterized in that, compared with double the single dose in the administration of a racemate, unnecessarily high and long-lasting substance loading is avoided, as a result of which substantially lower levels of active substance in the plasma are obtained which go beyond the normal advantage of halving the dose in the administration of enantiomers. As acknowledged in the specification of the patent, the racemate of Repaglinide as such was known. In the prior art, the racemate had been tested, namely, for its overall blood-sugar-lowering effect, in rats but never in humans.

Judging from the Headnotes, the FCJ seems to consider the following two points of the case to be of particular importance from a legal point of view.

The first issue is the definition of the technical problem underlying the invention, or the object of the invention. The specification of the patent-in-suit does not formulate any object. The patent proprietor argued that the object is to provide a long-term antidiabetic agent having beneficial pharmacological properties relative to the prior art, in particular a special pharmacokinetic profile involving a fast onset of effect, low plasma level relative to the blood sugar lowering, and quick elimination from the blood. The FCJ did not accept this and noted that, according to the patent specification, these advantageous pharmacokinetic properties of Repaglinide (in humans) were revealed only during the inventors’ endeavors to further develop the prior art. Therefore, the FCJ defined the object of the invention less ambitiously as the provision of a (long-term) antidiabetic agent having enhanced effect. The FCJ’s findings about the object of the invention are summarized in Headnote (a) of the decision as follows (our English translation):

(a) The technical problem underlying the invention (i.e. the object of the invention) cannot be

determined by means of advantages of the invention, which the person skilled in the art would not have used as a basis when striving to further develop the state of the art since these advantages turned out to be achievable only with the invention.

The second issue addressed in the Headnotes arose from the following situation. Starting from the racemate of Repaglinide, which was considered by the FCJ to be a realistic vantage point, there were several ways other than focusing on the enantiomer Repaglinide to proceed, in particular developing the racemate into a drug, but also developing analogous compounds, modifying the side chain of the molecule, galenic developments or combinations with known antidiabetic agents. Patentee therefore submitted that it was not obvious in which direction the skilled person should go. Moreover, there were major challenges on the way to the enantiomer. For example, an enantiospecific bioassay had to be developed to verify the stability of the enantiomer in the human patient. However, the FCJ held that concentrating on the enantiomer was obvious, because there were no obstacles or circumstance which would have suggested to the skilled person that pursuing the selected enantiomer path is no longer advisable. As the FCJ put it in Headnote (b) of the decision (our English translation):

(b) Depending on the conditions of the technical field and the circumstances of the individual case, it can be obvious to take any of several different ways in order to solve the problem.

Finally, the surprising pharmacokinetic profile of Repaglinide was considered by the FCJ as a bonus effect along the lines of the decision “Kosmetisches Sonnenschutzmittel I” (BGH X ZR 68/99, GRUR 2003, 317) and “Escitalopram” (BGH Xa ZR 130/07, GRUR 2010, 123).

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