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T 777/08: When is a Polymorph Inventive?

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We report on the recent decision T 777/08 of the Boards of Appeal of the EPO dated May 24, 2011, relating to the issue of inventiveness of (specific) polymorph forms of a drug known in a solid amorphous form.

The relevant claims of the European Patent EP 1 148 049 underlying the decision T 777/08 aim at crystalline forms II and IV of the drug compound atorvastatin hydrate. Novelty thereof was not contested. For the assessment of the inventive step, the closest prior art was considered to be represented by solid forms of atorvastatin obtained from recrystallisation processes disclosed in two prior art documents. The objective problem to be solved by the claimed polymorphs was seen in the provision of an alternative form of atorvastatin having improved filtration and drying properties. That this problem actually was solved by the claimed polymorphs was also not contested during the appeal proceedings.

The Board of Appeal, however, found the claimed solution to be obvious for the skilled person based on common knowledge at the priority date of the patent and thus non-inventive. The major source of information for determining the common knowledge was a review article published shortly before or after the priority date (the exact publication date could not be established). The Board argued that irrespective of the exact publication date the article in any case would reflect the skilled person’s knowledge at the time before the priority date of the contested patent and thus would be a legitimate basis for evidence of common general knowledge. Further considering two additional prior art documents confirming the teaching of the review article that Board came to the conclusion that at the priority date of the patent it was general common knowledge that

– polymorphism is commonplace in molecules of pharmaceutical interest,

– early screening for polymorphs is advisable in a drug development process, and

– crystallisation from different solvents under different conditions is a routine method for screening for polymorphs.

Also, the technical effect achievable by crystalline polymorphs was known, as explicitly stated in one of the additionally considered documents: crystalline products are generally the easiest to isolate, purify, dry and, in a batch process, handle and formulate. As a consequence, the Board held

that a skilled person would attempt obtaining a crystalline form, rather than an amorphous form, in order to achieve the improved filtration and drying properties. Patentee's argument that the skilled person would be dissuaded from attempting to obtain crystalline forms due to their known inferiority as regards solubility and bioavailability was not accepted. Instead, the Board outlined that the skilled person, based on the common knowledge as established, would regard this as a matter of trade-off between the expected advantages and disadvantages of crystalline and amorphous forms of a drug compound.

Thus, in the Board's view, the provision of crystalline polymorphs which do not achieve anything more than the obvious advantages of crystalline materials over amorphous ones is not based on an inventive step. This would apply for the provision of polymorphs in general as compared with amorphous forms, and also for the provision of specific crystalline forms selected from a broader range of polymorphs.

For the future it therefore has to be expected that the inventiveness of a novel polymorph form of a pharmaceutically active compound will be acknowledged only if the novel polymorph form is associated with an unexpected pharmaceutical activity, while improved physical and/or physicochemical properties would not be sufficient. Also, an inventive step might be acknowledged if an inventive activity is required to actually manufacture the polymorph.

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