EIP

Crystal polymorph patenting becomes more difficult in Europe

The EPO has just officially published (T 777/08 Atorvstatin Polymorphs OJEPO 12/2011 633-643) a decision of the Technical Boards of Appeal which surprisingly finds that, in general, a claim to a crystalline form of a compound lacks inventive step over the compound known only in amorphous form.

Crystalline forms are important in the field of pharmaceuticals and other chemicals. It is not uncommon for new compounds initially to be synthesised in a non-crystalline form and for one or more crystalline forms to be later discovered, or for a later crystalline form to be found to have improved properties compared with an earlier crystalline form. Crystalline forms which are crystallographically different, that is, which differ in the 3-dimensional stacking of the molecules in the crystal lattice, are called polymorphs.

It is also not uncommon for crystal polymorphs to be the subject of patents. A well-known early example relates to ranitidine (Zantac), an anti-ulcer drug. Practitioners in this field have generally considered that crystallisation and polymorphism are largely unpredictable, and that therefore claims directed to crystal polymorphs will frequently fulfil the requirement of an inventive step.

However, as a result perhaps of the evolution of scientific knowledge and predictability, the EPO Board of Appeal has indicated that, in the absence of special and case-specific considerations, such polymorphs are not surprising and cannot be patented.

Referring in particular to a review article published in the same month as the priority date of the patent (July 1995), the BoA considered that, at that date:

- "From his common general knowledge, the skilled person would firstly be

aware of the fact that instances of polymorphism are commonplace molecules of interest for the pharmaceutical industry"

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- "The skilled person would also have known it to be advisable to screen for polymorphs early on in the drug development process"
- "Indeed, the skilled person would also have been aware of regulatory requirements to provide information on the occurrence of polymorphic, hydrated or amorphous forms of a drug substance" and
- "Moreover, he would be familiar with routine methods for screening for polymorphs by crystallisation from a range of different solvents under different conditions"

The Board therefore concluded:

"It follows from the above that, at the priority date of the patent in suit, it belonged to the routine tasks of the skilled person involved in the field of drug development to screen for solid state forms of a drug substance. For the sake of completeness, the board therefore wishes to note that, in the absence of any technical prejudice, which has not been alleged by the appellant, the mere provision of a crystalline form of a known pharmaceutically active compound cannot be regarded as involving an inventive step (contrary to the statement in the patent in suit)"

Because the EPO has no strict doctrine of precedent, both Examining Divisions and Opposition Divisions at first instance, and other Boards of Appeal, can in principle choose whether or not to apply this assessment of the state of scientific knowledge in other cases having a similar or later priority date. However, based on this analysis, it is anticipated to become more difficult to obtain at the EPO patents directed to crystal polymorphs unless in any particular case there is a technical prejudice or unexpected property of the polymorph discovered.