

Analysis on Supreme Court's Decision No. 2018Hu10923 dated March 31, 2022

1. Overview of the case

Case No.: 2018Hu10923 Final Rejection (patent)

Related patent application: Patent Application No. 10-2010-7003939

Date of decision: March 31, 2022

2. Gist of the decision

(1) Determination of inventive step of a crystalline invention

Polymorph screening, which examines whether a compound has various crystalline forms, i.e., polymorphs, for the formulation design of a pharmaceutical compound, is commonly performed. In the field of pharmaceutical compounds, it is necessary to consider this particular characteristic when determining the inventive step of the so-called crystalline invention, which claims a compound of a specific crystalline form having the same chemical structure as a compound known in the prior invention but having a different crystalline form. However, based on the foregoing alone, it cannot be concluded that the difficulty in constitution of the crystalline invention is denied. This is because the fact that polymorph screening is a commonly conducted experiment and whether a specific crystalline form of a crystalline invention can be easily reached through the experiment are separate issues. Meanwhile, since the effect of an invention in the field of pharmaceutical compounds, such as a crystalline invention, cannot be easily predicted based on constitution alone, it is necessary to consider the effect of the invention when determining the difficulty in constitution, and if the effect of the invention is remarkable compared to the prior art invention, it can be powerful data to infer difficulty in constitution (Supreme Court Decision No. 2010Hu2865 dated July 14, 2011, etc.)

(2) Determination of difficulty in constitution of a crystalline invention

When determining difficulty in constitution of a crystalline invention, the technical significance and specific effect of the crystalline invention, the structure of the specific crystalline form claimed in the invention and manufacturing method thereof, the contents and characteristics of the prior invention, the technical level of those skilled in the art, and the polymorph screening methods that are general at the time of filing should be understood based on the data shown in the records. Then, it should be considered whether the crystalline form of the compound of the prior art invention has been taught or expected, the prior art invention or reference discloses any teachings, hints, motives, etc., that the specific crystalline form claimed by the

crystalline form invention can be reached, whether the specific crystalline form of the crystalline form invention is included in the scope of polymorphs that could be reviewed by general polymorph screening for compounds of the prior art invention, and whether the specific crystalline form has an unpredictable advantageous effect. In consideration of all the above, it should be reviewed whether a person skilled in the art can easily derive the constitution of the crystalline invention from the prior art invention.

(3) Determination of remarkability in effect of a crystalline invention

If an effect of a crystalline invention is qualitatively different or has a quantitatively remarkable difference from that of the prior art invention, inventive step is not denied (refer to Supreme Court Decision No. 2010Hu2865 dated July 14, 2011, etc.). Remarkability in effect of a crystalline invention should be determined with a focus on an effect disclosed in the specification of the invention such that it can be recognized or inferred by a skilled person in the art, and if the effect is in doubt, it is allowed to argue and prove the effect in detail by submitting additional experimental data after the filing date within the scope of the disclosed content, etc. (refer to Supreme Court Decision No. 2019Hu10609 dated April 8, 2021, etc.).

3. Details of the case

(1) Facts

- A. The plaintiffs filed a patent application directed to a crystal form of 20,23-dipiperidiny-5-O-mycaminosyl-tylonolide (hereinafter, referred to as 'tylosin') (priority date: July 26, 2007).
- B. The prior art invention (US Patent No. 6,514,946; February 24, 2003) discloses that tylosin has selectively high antibacterial activity against *Pasteurella*.
- C. The examiner of the Korean Intellectual Property Office (KIPO) issued final rejection to the plaintiffs on the ground of lack of inventive step over the prior art invention, and the plaintiffs filed an appeal against the final rejection along with submitting an Amendment to the specification, etc. for re-examination. However, the examiner of the KIPO maintained the final rejection, and the Intellectual Property Trial and Appeal Board (IPTAB) also rejected the appeal against the final rejection. In response, the plaintiffs filed a petition for cancellation of the trial decision.

(2) Determination of the original decision (Patent Court)

- A. It is well known in the field of pharmaceutical compound that the same compound may have various crystalline forms and that pharmaceutical properties such as solubility and stability may differ depending on the crystalline form. Therefore, it is general to check the presence of such polymorph for the formulation design of a pharmaceutical compound. Accordingly, in the field of pharmaceutical compound, so-called crystalline invention which claims a compound of a specific crystalline form that differs only in crystalline form from a known compound cannot be denied inventive step as long as there is a qualitatively different effect from the effect of the known compound of the prior art invention or there is a quantitatively remarkable difference, if no qualitatively different effect, unless there are no special circumstances. Here, the effect can be considered for determining inventive step, only if its effect is clearly described in the specification of the crystalline invention, not to the extent of comparative experimental data with prior art inventions, and if the effect is in doubt, the applicant or the patentee should prove the effect in detail by submitting reliable comparative experimental data after the filing date (refer to Supreme Court Decision No. 2010Hu2865 dated July 14, 2011, etc.).
- B. It is common technical knowledge in this art that the same compound may have various crystalline forms and that pharmaceutical properties such as solubility and stability may differ depending on the crystalline form. Accordingly, even if the prior art invention does not suggest or imply the presence of the crystal form of tylosin, a skilled person in the art can sufficiently recognize the possibility that tylosin disclosed in the prior art invention may present in various crystal forms.
- C. It is common technical knowledge widely known in this art that the most thermodynamically stable polymorph is selected by identifying whether polymorphs of which pharmaceutical compound are in a thermodynamically monotropic or enantiotropic relationship. Accordingly, it is hard to deem that the thermodynamic stability of tylosin type I crystal form is a qualitatively different effect that cannot be predicted by a skilled person in the art.

Hygroscopicity is a significant factor in the process of formulating a pharmaceutical, and the stability of a drug becomes an issue as the solubility to water is higher. In this regard, it is common technical knowledge in this art to select a crystal form having non-hygroscopicity as possible by making a change in the crystal form in order to solve the aforementioned problem, and it is a widely-known fact that the most

thermodynamically stable crystal form generally has low water absorption. In this light, type I crystal form of tylosin exerting lower water absorption than other crystal forms cannot be deemed as a qualitatively different effect that cannot be predicted by a skilled person in the art.

Upon review on whether the low water absorption of tylosin type I crystal form is a quantitatively remarkable effect, the specification (Figs. 5, 12, and 19) of claim 1 of the present case indicates respective dynamic vapor sorption (DVS) result values of types I to III crystal forms as respective changes in mass (dm%) of types I to III crystal forms with respect to relative humidity (RH%), from which the fact that type I exerts about 1% change, type II exerts about 2% change, and type III exerts about 6% change can be acknowledged. According to this, it can be understood that type I crystal form with the lowest change in mass has the lowest water absorption, but the fact alone is not sufficient to acknowledge that the low water absorption of tylosin type I crystal form has reached a quantitatively remarkable level compared to other crystal forms.

(3) Decision of the Supreme Court

- A. The present invention has the same chemical structure as tylosin, which is the compound of the prior art invention, but is different in terms of constitution from the prior art invention in that it is an invention relating to tylosin type I crystal form having a feature specified with a powder X-ray diffraction spectrum value comprising peaks of 5.0, 9.0 and 10.5° 2 θ . In addition, according to the specification of the present case and the experimental data submitted after the filing date, it can be understood that types I to IV were derived as crystalline forms (excluding solvates) of tylosin, among which type I crystal form of claim 1 of the present case is thermodynamically stable than amorphous form or types II, III and IV crystal forms of tylosin, and has lower hygroscopicity than types II and III crystal forms.
- B. The prior art invention discloses a pale yellow solid compound of tylosin, but does not disclose whether its form is a crystal form or an amorphous form, and there is no material on which to view that it is well-known that tylosin has various crystalline forms (crystal polymorphism), etc. at the time of filing of claim 1 of the present case. The tylosin pale yellow solid compound disclosed in the prior art invention and type I crystal form claimed by claim 1 of the present case are different not only in terms of starting material to derive their respective forms, but also in terms of specific crystallization process variables including solvent, temperature and

time, etc. In this regard, solely based on the data regarding the common polymorph screening method at the time of filing submitted by the respondent, it is unclear whether a skilled person in the art can properly adjust crystallization process variables or easily derive type I crystal form having the aforementioned characteristics from the prior art invention via the common polymorph screening.

- C. The specification of the present case discloses detailed experimental data relating to thermodynamic stability and hygroscopicity, etc. of tylosin types I to IV crystal forms, and it can be understood that type I crystal form, which is claim 1 of the present case, has quantitatively superior thermodynamic stability compared to type II crystal form, and exerts lower hygroscopicity than type II crystal form and type III crystal form, while the prior art invention does not even disclose a crystal form of tylosin that has the same level of thermodynamic stability as type II crystal form or exerts the same level of hygroscopicity as types II and III crystal forms. Given the foregoing, with the data submitted by the respondent alone, it is hard to conclude that the effect of type I crystal form, which has superior thermodynamic stability compared to type II crystal form and lower hygroscopicity compared to types II and III crystal forms, is predictable from the prior art invention.
- D. In conclusion, it is hard to conclude that claim 1 of the present case can be easily invented by a skilled person in the art from the prior art invention, based on the data submitted by the respondent alone, without hindsight analysis premising that a skilled person in the art has already learned the content of the invention disclosed in the specification of the present case.

4. Our opinion

In previous Decision No. 2010Hu2865 relating to crystalline inventions, it was held, 'It is general to check the presence of polymorph for the formulation design of a pharmaceutical compound. Accordingly, in the field of pharmaceutical compound, so-called 'crystalline invention' which claims a compound of a specific crystalline form that differs only in crystalline form from a known compound cannot be denied inventive step as long as there is a qualitatively different effect from the effect of the known compound or there is a quantitatively remarkable difference, if no qualitatively different effect, unless there are special circumstances,' which can be understood to mean that inventive step of crystalline inventions can be determined based on determination of remarkability in effect alone, without determination of difficulty of constitution.

In this regard, the original decision used Decision No. 2010Hu2865 as related legal reasoning, and denied difficulty in constitution of the crystalline invention on the

ground that a skilled person in the art can sufficiently recognize the possibility that tylosin disclosed in the prior art invention may present in various crystal forms even if the prior art invention does not suggest or imply the presence of the crystal form of tylosin, based on the common technical knowledge that a compound may have various crystalline forms and that pharmaceutical properties may differ.

However, Decision No. 2018Hu10923 held that difficulty in constitution of the crystalline invention can be acknowledged depending on the level of disclosure of the prior art invention, pointing out that the fact that polymorph screening is a commonly conducted experiment and whether a specific crystalline form of a crystalline invention can be easily reached through the experiment are separate issues, thereby specifically suggesting criteria for determining difficulty in constitution of the crystalline invention.

The above decision shares the common purport with Supreme Court Decision No. 2019Hu10609 dated April 8, 2021 holding that difficulty in constitution should be also considered in determining inventive step of a selection invention, and it is expected that crystal form inventions with acknowledged inventive step will be increased by the influence of the decision.