c) *Other Secondary Considerations*

Apart from unexpected results, scepticism of experts, long felt need, failures of others, copying, licensing, commercial success, and others are recognised in the U.S. as secondary considerations for nonobviousness.[220] The Federal Circuit exploited these considerations explicitly in the *Olanzapine* decision. Commercial success of selection inventions, however, is less likely to play a role as a secondary consideration.[221]

3. Considerations

a) *Person Skilled in the Art in the Olanzapine Decision*

As discussed in III.B, the Courts provide special criteria for the novelty assessment of chemical inventions, especially enantiomer inventions, based on the "unpredictability" of chemical inventions. Since their effect is difficult to predict, a reasonable expectation of success plays an important role.

Picking up on the facts of the *Olanzapine* decision, the structural difference of olanzapine (-ethyl) from the closest compound (-methyl) is only one-carbon-shorter alkyl, and a prior art reference disclosed that this shorter alkyl substitution in position 2 of the thiophene ring appeared to increase the activity.[222] The German Federal Court of Justice held that this finding did not change the result since only very few substituents having a methyl group at the 2-position had been prepared because of the bad activity.[223] In this regard, this paper would like to argue that it might not have been easily judged whether the prior art sufficiently encouraged a person skilled in the art to substitute ethyl group for the methyl. This is because the level of skill of the person skilled in the art would be regarded differently from the Court's finding, especially today.

Jacob LJ rejected defendant Dr. Reddy's Labs' argument that one skilled in the art would not bother with SAR(Structure-Activity Relationship) but press on with the actual Chakrabarti compounds because the skilled person was an academic who

220 *See generally,* Martin J. Adelman, et al., Cases and Materials on Patent Law 343-347, (3d ed, 2009); *See also* Forest Labs *supra* note 79, at 1267.
221 *See supra* III.B.1.a)(1).
222 *See* Olanzapine, BGH, *supra* 112, at para 55.
223 *Id.* (noting that only 10 out of 48 compounds have no substituents at all (*Cf.* preferred group of compounds in prior art was one of compounds having halogen atom) and 8 out of above 10 have 'ethyl' group in position 2 of the thiophene ring.).

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did not work in the industry.[224] This again can be interpreted such that if the person skilled in the art had worked in the industry, he would have pressed on with the actual Chakrabarti compounds. In fact, the daily practice of laboratories in the pharmaceutical industry is that they do not only pursue so-called 'lead-compounds' but in addition to that always pursue so-called 'fall-back positions', in preparation for the more than frequent failures of 'lead-compound' projects.[225] This could have been even more so in *Olanzapine* case, because the prior art in this case disclosed that a shorter alkyl substitution appeared to increase the activity. As the Courts properly noted, it is hard to predict the activity of chemicals until a test is performed. Thus, if the skilled person was a person in the pharmaceutical industry, he would have tried to confirm for every possibility whether it works, because of the very unpredictability.

It is acknowledged that the corresponding patent of the *Olanzapine* case was filed more than a decade ago, and the chemical synthesis has tremendously developed ever since.[226] It is expected, therefore, that courts will perceive the person skilled in the pharmaceutical art more properly in the future.

b) Reasonable Expectation of Success: Escitalopram Decision

As Judge Rader stated in the Pfizer decision, the reasonable expectation of success analysis should be wisely employed.[227] However, one can easily see that there is a difference with respect to unpredictability of success between selecting one out of two and selecting one out of hundreds or even out of millions. In addition, the possible advantages of enantiomers over racemates are well acknowledged,[228] and therefore the person skilled in the art would be motivated to explore the enantiomers. Considering that obviousness does not require absolute predictability of success,[229] the fact that some of the motivated trials would turn out to be failures does not necessarily negate a reasonable expectation of success.[230]

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224 Dr Reddy's Labs, The Court of Appeal, *supra* note 91, at para 69.

225 *See also,* Vincent L. Capuano, *Obviousness of Chemical Compounds: The "Lead Compound" Concept*, Intell. Prop. Today 33, 35 (2007).

226 *See e.g.,* John S. Lazo, *Combinatorial Chemistry and Contemporary Pharmacology*, 293 J. Pharmacol. Exp. Ther. 705, 705 (2000) (explaining "Combinatorial Chemistry", which is a method of preparing a large number of chemical compounds, and which enables a company to routinely produce over 100,000 new and unique compounds per year.).

227 *See* Pfizer, *supra* note196, at 1384.

228 *See supra* note 124.

229 *See generally supra IV.B.1.c)*.

230 *See* Darrow, *supra* note 124, at para 58.

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It can be understood that the decisions discussed here are possibly based on the policy reason that we need at least these incremental innovations. However, it is time to reconsider whether this policy may lead to innovative companies concentrating their research on these fields rather than on drug discovery which is entirely new, and therefore preventing the development of innovative medications in the future.

4. Conclusion

The determination of nonobviousness is a rather complicated and difficult task. In addition, the test for nonobviousness depends more on the difference between the facts of the cases than the test for novelty. Regarding the nonobviousness of enantiomer patents in particular, it was argued that the decisions of the Federal Circuit on this issue have been mixed although they may not be regarded as necessarily inconsistent with each other, considering different evidentiary records to determine the existence of a motivation for the person skilled in the art to separate enantiomers with a reasonable expectation of success, the teaching in the prior art, the existence of superior properties of isolated enantiomers, and so on.[231, 232] As Eisenberg said, it is not easy to find a meaningful guideline for the question of obviousness[233] in this regard. In line with these issues, the particularity of the pharmaceutical industry in terms of low predictability and the level of skill of a person skilled in the art also need to be considered.

C. Impact of Lowering the Bar for the Patentability of Selection Inventions

Based on the enablement issue in anticipation, novelty at least is not a tough hurdle for a selected species from a disclosed broad Markush type claim or an enantiomer from a disclosed mixture of two enantiomers. This may increase the number of newly granted selection patents. The possible impact of patentability of selection inventions after grant is discussed below.

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231 *See* Rebecca S. Eisenberg, *Pharma's Nonobvious Problem,* 12 Lewis & Clark L. Rev. 375, 424-427 (2008).

232 *See also* Rochelle Cooper Dreyfuss, *Nonobviousness: A Comment on Three Learned Papers,* 12 Lewis & Clark L. Rev. 431, 441 (2008) (noting that the Federal Circuit's view on nonobviousness of enantiomer patents seems to be remarkably flexible).

233 Eisenberg, *supra* note 231, at 427.

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