B. Obviousness

As stated in the statues, the invention should not be obvious to the person skilled in the art. The concept of the person skilled in the art is important to determine obviousness. He is a hypothetical person and has a level of skill which is determined within the art in general but which does not specifically match the level of skill of the inventors.[188]

In determining obviousness, the U.S. patent system uses a special procedural tool called '*prima facie* obviousness'. Namely, once it is established, the burden of proof is shifted to the applicant, and he could overcome this rejection ground by rebutting.[189] Not all other jurisdictions use this concept; however, it is used as a basis to discuss relevant issues of obviousness of selection inventions below.

1. Prima Facie Obviousness

a) Size of the Genus

It is well established that a genus not explicitly disclosing a later species does not anticipate the later species claim.[190] In addition, the mere fact that the claimed compound in the later invention is covered by the prior art generic formula is in itself not yet regarded as rendering the claimed compound obvious over the prior art.[191] However, in general, if the genus or generic formula in the prior art discloses only a small number of substituents, it is more likely that the species from the genus would be found obvious, specifically *prima facie* obvious.[192] The opposite situation is also true.[193] In other words, the chance that a selection of a species is not obvious

188 *See e.g.,* Spenner, *supra* note 116, at 483.
189 *See* Darrow, *supra* note 124, para 44.
190 *See* Chisum, *supra* note 106, at § 3.02[2][b]; *see also* Metabolite Laboratories, Inc. v. Laboratory Corporation of America Holdings, 370 F.3d 1354, 1367-71 (Fed. Cir. 2004) (holding that a prior art reference that discloses a genus still does not inherently disclose all species within that broad category); *See also* Meier-Beck, *supra* note 60, at 985.
191 *See In re* Jones, 958 F.2d 347, 350, (Fed.Cir.1992) (holding that the fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious); *see also, e.g., In re* Baird, 16 F.3d, 383 (holding that three claimed compounds out of a prior art genus containing more than 100 million species would be found as non-obvious).
192 *See* Jerome Rosenstock, The Law of Chemical and Pharmaceutical Invention, Patent and Nonpatent Protection § 8.02[D] (2d ed. Supp. 2008). This would be more the case under the U.S. practice, so-called 'finite obvious-to-try argument'; *but see also* Darrow, *supra* note 124, para 26 (2007) (However, it is not clear how many species must be included in the prior art genus to make the claimed species non-obvious, and the case law has not provided enough data points regarding this issue).
193 *Id.*

increases with the size of the genus, even if this factor itself is not sufficient to support non-obviousness.[194]

The size of the genus has special impacts in the 'finite obvious to try' case. As *Spenner* properly noted, when there is a finite number of possibilities from which to start, a technique that is within the grasp of the POSITA is used to modify the prior art to arrive at the claimed invention, and the results are not unexpected, then the invention is obvious.[195] *Pfizer v. Apotex* is a case in point regarding the "finite obvious-to-try situation".[196] A prior patent claimed amlodipine and its pharmaceutically acceptable salts, disclosed maleate as the best salts, but did not explicitly disclose besylate.[197] A later patent application claiming amlodipine besylate salt was rejected over the above prior patent in combination with the *Berge* reference which disclosed "53 FDA-approved, commercially marketed anions, including benzene sulphonate,[198] which are useful for making pharmaceutically-acceptable salts",[199] on the basis of a reasonable expectation of success. The Court found the fact that there were a limited number of choices to start from, and a reasonable probability of success to make the salt, even prevented the unexpected results that were found in this case from rebutting the *prima facie* obviousness.

The size of the genus is one of the most important elements in determining obviousness, but all of the circumstances should be considered as a whole.[200] Even a genus of only two, i.e. the genus for an enantiomer of a racemic compound having one chiral centre[201] by itself, does not make a prima facie obviousness case.

b) Structural Similarity

A homologous series of chemical compounds can raise a *prima facie* case of obviousness,[202] which could be established when one shows structural similarity and similar utilities between the prior art and the claimed invention, and adequate sup-

194 *See* Darrow, *supra* note 124, at para 28.
195 *See* Spenner, *supra* note 116, at 510 (noting that this is as the 'finite obvious-to-try situation').
196 Pfizer, Inc. v. Apotex, Inc., (hereinafter, 'Pfizer') 480 F.3d 1348 (Fed. Cir. 2007).
197 *Id.*, at 1353.
198 Benzene sulphonate is also referred to as besylate.
199 *See* Pfizer, *supra* note196, at 1355 (This *en banc* decision was not unanimous, i.e., Judges Newman, Lourie, and Rader wrote their own dissent. Regarding the 'obvious to try' analysis, Judge Rader stated that since a salt selection was unpredictable, there would not have been a reasonable expectation of success.).
200 *See also In re* Petering *supra* note 75, at 681 (holding that "it is not the mere number of compounds …which is significant … but, rather, the total circumstances involved…").
201 *See also* Spenner, *supra* note116, at 500-501; *See also In re* Petering, *supra* note 75.
202 *See* Rosenstock, *supra* note 192, at § 8.02[A].

port in the prior art for the change from the prior art.[203] As an extreme again, one can take an enantiomer as an example whose structure is already determined and is only different from its spatial configuration. As Judge Rader stated in the *Olanzapine* decision, however, obviousness of a chemical compound based on structural similarity can be rebutted.

c) Reasonable Expectation of Success

For determining obviousness, it is to be determined whether a person skilled in the art was motivated to reach the claimed invention.[204] To derive the claimed invention from the prior art (or to motivate to reach the claimed invention), the person skilled in the art should have had a "reasonable expectation of success".[205] In addition, the Court in *In re O'Farrell* stated that "[o]bviousness does not require absolute predictability of success and all that is required is a reasonable expectation of success."[206] Considering the unpredictability of pharmaceutical inventions,[207] this element is very important for determining obviousness.

For the racemate, the possibility of its resolution is included in this 'reasonable expectation of success'.[208] As an example, in *In re Adamson*,[209] since the invention was recognized in the prior art as a separate enatiomeric species, the patentability of a normal synthesis of a single chiral centre compound was denied. In *In re* Williams,[210] to the contrary, in consideration of there being no appreciation of a possibility to resolve the enantiomers, the invention was held not obvious. In *Ortho-McNeil*, even though the resolution had proved to be difficult, since the prior art still enabled a person skilled in the art to separate the racemate,[211] the *prima facie* case was established. Therefore, as Spenner noted, "the more difficult and

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203 *See In re* Deuel, 51 F.3d, 1552, 1569-70 (Fed. Cir, 1995); *See also* MPEP § 2144.09.
204 *Id.* (holding that "*prima facie* case of unpatentability requires that the teachings of the prior art suggest the claimed compounds to a person of ordinary skill in the art.").
205 *See e.g., In re* O'Farrell, 853 F.2d, 894, 904 (Fed. Cir. 1988).
206 *Id.*, at 903.
207 *See* Pfizer, *supra* note 196, at 1384 (Rader, J. dissenting).
208 *See* Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc., (hereinafter, 'Ortho-McNeil') 348 F. Supp. 2d 713, 752-53 (N.D.W.Va. 2004).
209 *See In re* Adamson, 275 F.2d 952 (C.C.P.A. 1960) (the prior art did not disclose the racemic nature, but in combination of other references which disclosed the compound's chirality having chiral carbon, and resolution methods used to resolve the claimed compound, the court held that it was obvious).
210 *See In re* Williams, 171 F.2d 319 (C.C.P.A. 1948).
211 *Id.,* at 753.

nonobvious the separation, the more likely the enantiomers are nonobvious over the racemate,[212] which seems to be confirmed in all three jurisdictions.[213]

2. Overcoming Obviousness

a) Teach away

A prior art reference can be said to teach away from the invention when it "is discouraged from following the path set out in the reference, or would be led in a direction divergent from the path taken by the applicant."[214] This is one significant factor to consider when determining obviousness[215] and is a common response to a validity attack on the grounds of obviousness.[216] Teaching away from the prior art reference was one of the main findings in the *Olanzapine* decision in three jurisdictions.[217]

b) Unexpected Results

Showing unexpected substantially improved results can be a way of overcoming a *prima facie* case of obviousness.[218] For instance, an unexpected result would be a superiority of the invention in a characteristic which is shared with the prior art compounds. For a species claim, the superior unexpected activity over the genus can rebut a *prima facie* obviousness rejection against structural similarity. For enantiomer inventions, increased pharmacological activity can be an unexpected result. In addition, the Court in Ortho-McNeil also considered other factors like solubility as unexpected results.[219]

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212 *See* Spenner, *supra* note 116, at 489; *see also* Generics, the House of Lords, *supra* note 98, at para 61-65.
213 *See supra III.C.1.b)*, III.C.2.b), and III.C.3.b).
214 *In re* Gurley, 27 F.3d 551, 553 (Fed. Cir. 1994).
215 *See e.g.,* Durham, *supra* note28, at 111.
216 *See e.g.,* Lance Leonard Barry, *Teaching a Way is not Teaching Away*, 79 J. Pat. & Trademark Off. Soc'y 867, 867 (1997).
217 *See generally supra* III.C.
218 *See In re* Sony, 54 F.3d 746, 750-751 (Fed. Cir. 1995).
219 *See* Ortho-McNeil, *supra* note 208, at 754-55 (holding that it would not have been expected that an enantiomer is "twice as potent, about ten times more soluble, and appreciable less toxic" than its racemate.).