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Patentability of Chemical Selection Inventions: The Olanzapine and Escitalopram Decisions

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Table of Contents

I. Introduction

Innovations are mostly derived from already existing technologies that may or may not have been patented.

Selection inventions have been an important issue in the area of patent law from various aspects including novelty, inventive step, sufficiency of disclosure, and the like. Among these issues, novelty is one of the most fundamental issues in patentability and/or validity assessment, to have been hotly discussed in the field of chemical, biotechnological, or pharmaceutical inventions.

It is hard to find statutory definitions of what a selection invention is. However, the expression "selection invention" might be generally understood as an invention that has a specific concept selected from a prior broader or larger generic concept of invention, and that pertains superior or advantageous properties to the broader concept which have not been disclosed in the prior art. Selection can be generally categorized as two types,[1] but, in fact, has various forms, such as selection of (a member of) compound(s), processes, dimensions, a range of values, parameters, crystal forms, nanoscales and so on from the class, the broader range, or the various forms of previously disclosed inventions.[2] Thus a selection invention is an invention which falls under the scope of prior art disclosure, but has not been individually disclosed in the prior art.[3]

On the one hand, patent laws require a claimed invention to be new, to involve an inventive step (non-obviousness), to be susceptible of industrial application (utility)[4] and to be sufficiently supported by description (sufficiency of disclosure).[5] Although the requirement of novelty varies slightly from jurisdiction to jurisdiction, an invention generally is considered to be new if it does not form part of the

1 Guidelines for Examination in EPO C-IV. 1.C.4. ((a) chemical substances and group of substances in respect or general formulae (Markush formulae) under which they fall (b) products or processes defined by parameter ranges as against known products or processes characterized by wider or overlapping parameter ranges).

2 *See generally* Chris P. Miller ET AL., The Chemist's Companion Guide to Patent Law 15 (2010). *See also* Richard T. Jackson, *A Lockean Approach to the Compulsory Patent Licensing Controversy,* 9 J. Tech. L. & Pol'y, 116, 119 (2004) (discussing similar concept, namely, the concept of an improvement patent or dependent patent, which can be defined as one that cannot be used without infringing an earlier, existing patent.).

3 *See, e.g.,* Israel Agranat et al., *Intellectual property and chirality of drugs.* 4 Drug Discov. Today 313, 313-314 (1999).

4 *See, e.g.,* European Patent Convention (hereinafter 'EPC') Art. 52 (1).

5 *See, e.g.,* EPC Art. 84; 35 United States Code (hereinafter 'U.S.C.') § 112.

state of the art.[6] Novelty is a prerequisite for patentability for preventing something which already existed in the public domain being monopolized. On the other hand, a selection invention, by nature, is selected from the broader concept of a "previously known" invention; therefore construction of the concept of novelty in selection inventions has been debated.

Patents play different roles in different fields of technology. There is no dispute that the pharmaceutical industry as one of the most technology-based industries is one of the industries that depends most on the patent system,[7].[8] Thus, barring of patentability of selection inventions has an especially heavy impact in the pharmaceutical industry in several of the above aspects as follows, although the selection issue is not limited to pharmaceutical or chemical inventions.[9]

Innovative pharmaceutical companies have suffered loss of revenues due to expirations of patents on so-called blockbuster products. The numbers of these expirations are expected to reach their peak around 2011. They have not managed to compensate the loss with new follow-up innovations.[10] This may also explain the active merger and acquisition activities in pharmaceutical sectors[11] worldwide. Low productivity of R&D can be observed when looking at recorded statistics from 1998 to 2008. The cost of R&D over the past decade has increased by about 80%, but the number of NMEs (new molecular entities) has decreased by around 40% (see Fig. 1) .[12] This result becomes even more surprising considering the fact that i) the average cost to bring an NME to market is estimated to be up to around $1.8 billion,[13] ii) this has happened during the most technological and scientific period

6 *See, e.g.,* EPC 54 (1); 35 U.S.C. § 102.

7 *See also* Wesley M. Cohen et al., *Protecting Their Intellectual Assets: Appropriability Conditions and Why Manufacturing Firms Patent (or Not)* 23-24, Nat'l Bureau of Econ. Res., working Paper No. 7752, (2000) (reporting that the pharmaceutical industry, whose product is a discrete product like medication is the most efficient industry to exploit patents to create revenues from them either by commercializing the invention by the patent owner itself or by licensing them).

8 *See also* Benjamin N. Roin, *Unpatentable Drugs and the Standards of Patentability,* 87 Tex. L. Rev. 503, 513 (2009) (indicating that "[i]t is well known that pharmaceutical companies generally refuse to develop new drugs unless they have strong patent protection over them.").

9 *See also* Mark J. Davison et al., Australian Intellectual Property Law, 434 (2008) (providing exemplary cases of selection issues in mechanical and electrical inventions.).

10 *See, e.g.,* Steven M. Paul et al., *How to improve R&D productivity: the pharmaceutical industry's grand challenge*. 9 Nat. Rev. Drug Discov. 203, 203 (2010).

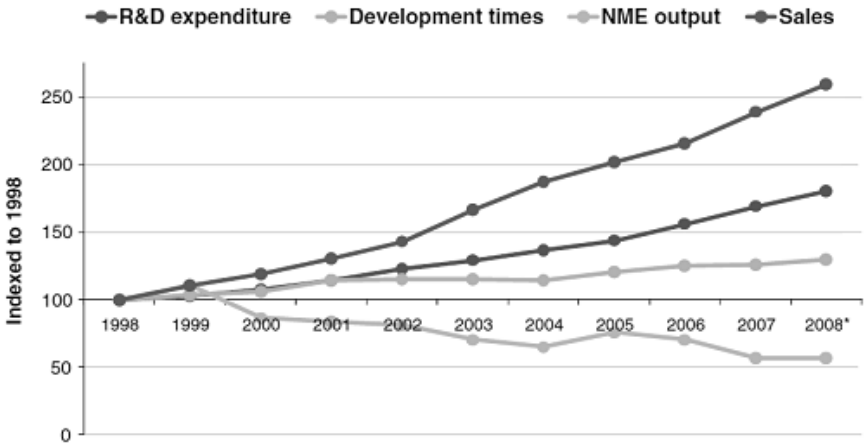
11 Among several reasons for this activity in the global pharmaceutical industry, the absence of proper R&D activities, expiry of patents and recalls of high-profile blockbusters can be counted.

12 Article in Press: H.-J Federsel, *Process R&D under the magnifying glass: Organization, business model, challenges, and scientific context*. Bioorg. Med. Chem. Doi:20.1016/j.bmc.2010.06.029.

13 Paul et al., *supra* note 10, at 204; *see also* Peter Landers, *Cost of Developing a New Drug Increases to About $1.7 Billion*, Wall St. J., Dec. 8, 2003, at B4 (2003).

of development ever, and iii) there is an urgent unmet need for new medications especially in the field of oncology and CNS (central nervous system) diseases.

Figure 1:
Global R&D expenditure, development times, global pharmaceutical sales and new molecular entity output 1998-2008.



Source: CMR International (2009 FactBook) & IMS Health.

It is much more difficult to bring a new medication to market because of several reasons including increased regulatory requests for study data relating not only to efficacy but also to safety, higher failure rate of targeting novel mechanisms, and advances in science and technology.

Over the last decade, observed market withdrawals for safety based reasons have brought the regulatory bodies' attention to the safety of drugs, which was intensified after the withdrawal of Vioxx® in 2004. The withdrawal of Vioxx from the market cast serious doubts on the reliability of clinical data and on the regulatory bodies' approval process, which created demands for higher transparency of data and resulted in lower approval rates of NMEs. This situation made innovative companies more cautious, and did hardly encourage them to conduct new research because the potential for more frequent failure to obtain regulatory approval for new medications may mean a zero return on the investment in R&D.[14] In addition, even after launching a new drug, innovative companies can never just celebrate and relax. This is because litigations related to safety-based withdrawals and the costs asso-

14 For instance, Vioxx's successor Arcoxia has been denied for its approval in April 2007, which meant a return of zero dollars to Merck.

ciated with it have undeniably and sharply soared. For instance, Merck spent around one billion dollar for the defense in 27,000 cases regarding product liability for Vioxx and related class actions within two years after the withdrawal thereof.[15]

It was shown that an R&D process based on unprecedented (novel) targets has a lower success rate (3 to 5%) than one based on precedented (traditional) targets (8%),[16,17] This means that an innovative pharmaceutical company should investigate several hundred more novel targets to be able to launch a single new product, which partly explains the negative net present value in regards to NCE (New chemical entity) developments.[18]

The lower success rate in new drug development than before might also be attributed to the fast development of technology. In fact, there is a higher proportion of pipeline dropouts because of undesired toxicity.[19] More technologies are involved and employed to predict toxicity and safety,[20] however, this developments may provide higher specificity and lower detection limit of trace elements and in turn leads to possible candidates or even targets dropping out in their early stages than before.

The above reasons may contribute to the trend that pharmaceutical companies focus research more on improving the characteristics of medications with which they have extensive experience in the market after approval by the regulatory body, than on developing entirely new medications. The recent report of the European Commission on the pharmaceutical sector,[21] for example, shows the following trend with innovative companies: i) a markedly sharp increase of the number of patent applications in pharmaceutical inventions was observed during the period of 2000 to 2007;[22] ii) 93% of the pending applications were classified as selection inven-

15 *See* Thomas N. Tiedt, *The Drug Safety System Conundrum,* 62 Food & Drug L.J. 547, 548 (2007).

16 Philip Ma et al., *Value of novelty?,* 1 Nat. Rev. Drug Discov. 571, 581-572 (2002). The precedented targets normally mean that those that has been successful in development of human medication.

17 Article in Press: David A. Fryburg, *Do technical and commercial biases contribute to the pharmaceutical industry's productivity problems? An analysis of how reordering priorities can improve productivity.* Drug Discov. Today. doi:10.1016/j.drudis.2010.06.010 (2010.).

18 *Id.*

19 *See* Gary W. Caldwell, *Compound Optimization in Early- and Late-phase Drug Discovery: Acceptable PharmacokineticProperties Utilizing Combined Physicochemical, in vitro and in vivo Screens,* 3 Curr. Opin. Drug Discov. Dev. 30, 30-31 (2000).

20 *See e.g.,* Dale E. Johnson, *Predicting Human Safety: Screening and Computational Approaches,* 5 Drug Discov. Today, 445, 445 (2000).

21 *See* European Commission's pharmaceutical sector inquiry report, available at http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/communication_en.pdf.

22 This statistics was based on the IPC (International Patent Classification) A61K with some exceptions (e.g.: preparations for dentistry(A61K6) and so on), which can be regarded as the closest proxy for pharmaceutical applications.

tions;[23] and iii) 84% of the granted patents were categorized as selection inventions as well. Examples of these efforts which may be categorized as selection inventions are salts, polymorphs, esters, isomers, metabolites, prodrugs, pharmacokinetic profiles, and combinations of innovative medications.[24]

This trend, together with ferocious attacks from generic drug makers, resulted in rich jurisprudence on the patentability of selection inventions with quite diverging decisions. This was true in European jurisdictions e.g., as far as Germany is concerned, until the "*Olanzapine*[25]" decision of the German Federal Court of Justice related to a chemical selection invention, with which the German approach became to be in line with the EPO case law by deviating from the "Fluoran" decision[26] . The ruler pronounced in this decision is confirmed by the later "*Escitalopram*" decision[27] directed to another important class of medications known as chiral drugs, which brought the German Federal Court of Justice case law into conformity with corresponding decisions in the U.K. and U.S.A. as well.

This thesis will start by giving some background information on Markush type claims, and chemistry of enantiomers. Then the jurisprudence on the patentability requirements for selection inventions will be given, first in terms of novelty, then followed by the nonobviousness requirement. Then discussions about the anticipation and obviousness issues in view of the *Olanzapine* and the *Escitalopram* decisions will be provided. This paper will then turn to the issues raised after granting of selection inventions. Lastly some different views in other jurisdictions will be provided as well.

23 The terminology in the pharmaceutical Sector Inquiry is "secondary patent (application)" which is an application not related to the first the patent (application) for the active molecules. for which the contrary category of 'primary patent (application)' is used.

24 So-called 'life cycle management' or 'evergreening' of pharmaceutical patents; *See also* IV.C.1.

25 A blockbuster marketed by Eli Lilly, called Zyprexa®.

26 Bundesgerichtshof[BGH] [Federal Court of Justice] (hereinafter, 'Fluoran') Jan. 26, 1988 International Review of Intellectual Property and Competition Law [IIC, hereinafter 'IIC'] IIC 736, 1989 (Ger.). Since official translations of materials in language other than English are not always available, the author did it by consulting other's translation or by herself. For accuracy, please check its original version.

27 Bundesgerichtshof [BGH] [Federal Court of Justice] (hereinafter, 'Escitalopram, Federal Court of Justice') Sept. 10, 2009, Gewerblicher Rechtsschutz und Urheberrecht [GRUR, hereinafter 'GRUR'] 123, 2010 (Ger.).

II. Background

A. Markush type claim

There are several special claim formats, such as Jepson type claims, product-by-process claims, means-plus-function claims, step-plus-function claims, Markush type claims, and so on. Markush type claims can be used where no generic term exists which describes the desired individual species and includes claim members selected from a group.[28] For example, "a metal selected from the group comprising nickel, palladium, and platinum". The purpose of a Markush type claim is to describe a group of individual elements which have common features or similar properties, or which have an equivalent basis for categorization in the same group.[29]

The downsides of broad Markush type claims are that they can be difficult to search, increase the prosecution time and examination errors, undermine their status as the prior arts, and be unclear in their scope of protection.[30] Advantages of Markush type claims include that they can offer broader protection for the patentee, be easier to file as one multinational patent application rather than several separate patent applications, and provide the licensor with a better basis for cross-licensing agreements with licensees who own improvement (selection) patents used the licensor's invention.[31] Almost all pharmaceutical patents are basically drafted with Markush type claims. Since selection patent claims, by nature, are directed to a specific species or a subgroup thereof which falls within the prior wider genus, it has been considered whether the disclosure in Markush type claims invalidates a later selection patent.

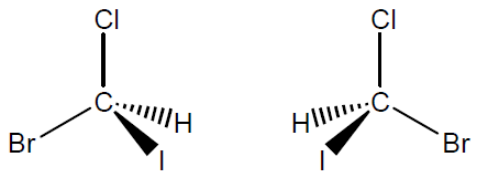
B. Enantiomers and Related Patents

Enantiomers are compounds which have the same molecular formulas but the special structure of one compound is the nonsuperimposable mirror image of the other,

28 *See, e.g.*, Alan L. Durham, Patent Law Essentials: A Concise Guide 61 (2nd ed. 2004).
29 *See, e.g.*, Edward H. Valance, *Understanding the Markush Claim in Chemical Patents*, 1 J. Chem. Doc. 87, 87-88 (1961).
30 *See* Lucille J. Brown, *The Markush Challenge*, 31 J. Chem. Inf. Comput. Sci. 2, 3-4 (1991).
31 *Id.* at 2-3.

thereby being called "chiral" which is a Greek term meaning "handedness".[32] The enantiomers are not identical to each other, but have at least one "stereocenter" which is a carbon atom with four different groups attached.[33] A "racemic mixture" or a "racemate" refers to a mixture of the R and S enantiomers which is normally produced through a chemical reaction which prepares a chiral compound from an achiral compound in normal conditions.

Figure 2:
Example of enantiomer-bromochloroiodomethane



Enantiomer patents can be defined as patents which claim selected individual enantiomers of a chiral drug which was previously disclosed as racemates in the prior art, e.g. in a basic patent. For this reason, an enantiomer patent can be categorized as claiming a selection invention.[34] Enantiomer patents are normally filed later than the filing date of basic patents, therefore the expiry dates of enantiomer patents are later than that of the corresponding basic patent. The top three best-selling global drugs from 2007 to 2009 are drugs of single enantiomers which are claimed in enantiomer patents, namely, Lipitor (Atorvastatin calcium), Plavix (Clopidogrel bisulfate), and Nexium (esomeprazole magnesium).[35] The importance of enantiomer patents is reflected in the upcoming 'patent cliff[36]' threat by the expiry of enantiomer patents of blockbuster chiral drugs.[37]

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32 *See generally* Johnson. A. William, Invitation to Organic Chemistry 612-613 (1999).

33 For example, two different mirror-imaged forms are a „right handed form" and a „left-handed form" In Figure 2, the carbon atom in the center is a stereocenter to which four different groups has been attached, namely Br, Cl, I, and H. Some compounds having more than two chiral centers result in multiple possible three-dimensional arrangements which are known as diastereomers.

34 A basic patent can also be referred as a broader patent or an earlier patent.

35 IMS Health, Top 15 Global Products 2009, available at http://www.imshealth.com/deployedfiles/imshealth/Global/Content/StaticFile/Top_Line_Data/Global_Top_15_Products.pdf.

36 *See* Peter Mansell, *Who is afraid of the patent cliff?* 1 SCRIP Executive Briefing 1, 1–16, (2008) (explaining that "patent cliff" is a term for the loss of revenue which occurs when the monopoly granted by patents is lost and the generic versions of drugs enter into the market. It is expected that the patent cliff reaches its peak in 2010-2011 as patents of many blockbusters including SanofiAventis' Clopidogrel, Pfizer's Atorvastatin, and others expire.).

37 *See* Israel Agranat et al., *The Strategy of Enantiomer Patents of Drugs* 15 Drug Discov. Today 163, 169 (1999).

The validity of enantiomer patents has often been challenged by generic pharmaceutical companies on the grounds of lack of novelty, lack of inventive step, lack of utility, double patenting, and insufficiency of disclosure.[38]

38 *Id.* at163.

III. Jurisprudence on the patentability requirements for selection inventions

Under this title, it will be discussed what the courts in three major jurisdictions have decided about the patentability requirements of selection inventions, with a view to the recent *Olanzapine* and *Escitalopram* decisions.

A. Facts of the Cases

1. Facts in Olanzapine

The patent in suit was Eli Lilly's patent (EP 0,454,436, US 5,229,382) on a single chemical compound olanzapine, which is a widely prescribed anti-psychotic agent used for the treatment of schizophrenia. The most pertinent prior art reference disclosed a general formula covering theoretically many millions of individual compounds; identified around 100 compounds by name and 15 compounds prepared; but did not disclose olanzapine specifically. Another prior art document disclosed Structure-Activity-Relationship observations of a group of compounds and several closely neighboring compounds to olanzapine, but neither enabled nor even disclosed olanzapine.

The questions at issue were the effect of a particular kind of disclosure, namely, a "Markush" formula which could cover many millions of compounds, the consideration of structural similarity of compounds, and whether a person skilled in the art can modify or supplement the prior art reference's teaching to determine the disclosure of prior art. In the UK, the law of novelty in the context of selection patents was particularly debated in relation to its *IG Rule*.[39]

2. Facts in Escitalopram

The challenged patent was EP 0,347,006 (U.S. RE34,712) belonging to Lundbeck on the (S)-enantiomer of citalopram (Escitalopram), a selective serotonin reuptake inhibitor anti-depressant. The most relevant prior art reference was a patent disclosing a general formula of the racemate mixture of (S)- and (R)- enantiomers.

39 *See infra* III.B.3.

The main issues for debate were whether the prior disclosure of racemate allowing a person skilled in the art clearly to recognize two enantiomers was enough to destroy the novelty of an enantiomer, and it should have been enabled in the prior art. In the UK, whether or to what extent a claim directed to more than one product or process should have been enabled by the description, known as "Biogen insufficiency" was argued as well.

B. Novelty Requirement

1. From the German Perspective: "Parting from Fluoran"

Selection patents have been granted in Germany from the nineteenth century on.[40] After the introduction of claims directed to chemical compounds *per se* on January 1, 1968, however, there has been much discussion about whether the general principles of German Patent Law can be directly applied to chemical compound patents.[41] Before the *Olanzapine* decision of the Federal Court of Justice, chemical selection inventions from the genus had not been considered as novel, since the general formula was regarded as disclosing the individual species according to the *Fluoran* decision.[42] Before the *Olanzapine* decision, this approach regarding the generic disclosure[43] was opposite to the position of the EPO Boards of Appeal. The Federal Court of Justice confirmed its new position on this issue in the *Escitalopram* decision, the first decision on the patentability of an enantiomer.[44]

40 *See* Volker Vossius, *Selection Inventions in Chemistry According to German Patent Law – A problem of Novelty*, 59 J. Pat. Off. Soc'y 180, 180-181 (1977).

41 *Id.*

42 Fluoran, *supra* note 26.

43 *See e.g.,* T 651/91, available at http://legal.european-patent-office.org/dg3/biblio/t910651du1.htm (confirming that a generic disclosure does not normally take away the novelty of any specific example falling within that disclosure. The board further added that a disclosure could be generic even where it only left open the choice between two alternatives).

44 Wolrad Prinz zu Waldeck und Pyrmont, *BGH: Enantiomer eines bekannten Razemats kann patentiert warden- „Escitalopram "(BGH : enantiomer of a known racemate can be patented – " Escitalopram "),* (Gewerblicher Rechtsschutz und Urheberrecht, Praxis im Immaterial- und Wettbewerbsrecht) [GRUR-Prax], 13 (2010) (stating that the Escitalopram decision seems to show that the Court continues its new line regarding the concept of disclosure stated in its Olanzapine decision.).

a) Markush Claim – Olanzapine Decision[45]

(1) Federal Patent Court Decision[46]

The *Olanzapine* patent was held invalid mainly based on anticipation by a prior art reference[47] (hereinafter 'Chakrabarti') that disclosed a genus of compounds as a general formula[48] covering olanzapine and 45 individual compounds. However, Chakrabarti disclosed explicitly neither the olanzapine itself nor indication thereof. The Federal Patent Court referred to the "electric plug-in connection" decision of the Federal Court of Justice :[49]

> "According to the decision "*Elektrische Steckverbindung*" (electric plug-in connection), the disclosure of a previously published document is not limited to a literal description, but also comprises modifications that are obvious to the skilled person from the whole context of the document, in such a manner that they will become evident to him when carefully studying them and focussing more on their obvious meaning than on the words, i.e. when "*reading between the lines*", *even if he is not aware of that*.[50]"

Applying this rule, the Court stated that the "novelty of a chemical compound is to be regarded as anticipated if the skilled person can derive from the prior publication a clear indication to this specific compound, i.e. if he will read this compound between the lines without difficulty, and if due to this indication he will be capable of obtaining said substance without difficulty".[51] In addition, the court explicitly mentioned that it was not required that this substance had *de facto* already been produced in line with the *α-Aminobenzylpenicillin* case[52] and the *Fluoran* case.

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45 In a nut shell, the Federal Patent Court revoked the Olanzapine patent. The patentee appealed to the Federal Court of Justice. While this appeal was pending, the patentee applied to the Düsseldorf District Court for preliminary injunction for infringement of the Olanzapine patent by a competitor, which was denied. The patentee filed an appeal also against this decision, whereupon surprisingly enough and for the first time in history, the Düsseldorf Court of Appeal granted the injunction, although the patent had been revoked in the first instance, and the first instance decision had not yet been reversed by the Federal Court of Justice. The Federal Court of Justice finally held that the Olanzapine patent was valid.

46 Bundespatentgericht (BPatG) [Federal Patent Court] Jun. 4, 2007, *Neuheitsschädliche Vorwegnahme einer chemischen Verbindung zur Herstellung eines Arzneimittels (Novelty-destroying anticipation of a chemical compound for the preparation of a medication)*, Neue Juristische Online Zeitschrift [NJOZ], 4786, 2007 (Ger.); Case number 3 Ni 21/04 combined with case number 3 Ni 41/06. (hereinafter, "*Olanzapine, Federal Patent Court*")..

47 This prior art is the scientific article: Chakrabarti et al., *4-Piperazinyl-10H-thieno[2,3-b][1,5]benzodiazepines as Potential Neuroleptics*, 23 J. Med. Chem. 878, 878-884 (1980).

48 See Olanzapine, Federal Patent Court, *supra* note 46, at 4796-97 (the defendant argued Chakrabarti does not disclose the general formula of the Markush formula type, but the court disagreed.).

49 Bundesgerichtshof [BGH] [Federal Court of Justice] Jan. 17, 1995, GRUR, 330, 1995 (Ger.).

50 *See* Olanzapine, Federal Patent Court, *supra* note 46, at 4792.

51 *Id.*

52 Bundesgerichtshof [BGH] [Federal Court of Justice] May 30, 1978, GRUR, 696, 698, 1978 (Ger.).

According to *Fluoran*, it is decisive when determining novelty, whether a person skilled in the art will be capable of implementing the invention relating to this compound and of preparing the compound without difficulty, on the basis of the indications given with regard to the contested compound of the prior publication.[53]

The Court noted that in this case, a skilled person would be able to obtain all necessary information[54] to manufacture olanzapine from Chakrabarti, and therefore it is a novelty-destroying disclosure of olanzapine.[55] The Court stated that based on the further disclosures of Chakrabarti such as structure and activity relationship, three directly neighboring compounds, and manufacturing procedure, olanzapine was anticipated by Chakrabarti.[56]

(2) Federal Court of Justice Decision[57]

In contrast to the holding of the Federal Patent Court, the Federal Court of Justice held in the appeals decision that it was not necessary to determine in what form a person skilled in the art can perform a certain general teaching, *using his technical knowledge, or how he can modify this teaching*, if necessary.[58] The important point is *exclusively what a person skilled in the art derives from the prior publication as the content of the specific (general) teaching*.[59] The court went on that the deciding factor was rather what can be "*directly and unambiguously" derived from a document*, from the point of view of a person skilled in the art, which is in line with the jurisprudence of the Boards of Appeal of the European Patent Office.[60]

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53 See Olanzapine, Federal Patent Court*, supra* note 46, at 4798.

54 The court illustrated this information as follows: lead structure of formula I, a group of only 12 compounds, 3 specific compounds immediately "neighboring" olanzapine, neuroleptic activity of compounds which is useful for treating diseases such as schizophrenia.

55 *See* Gerhard Barth, et al., *The Olanzapine Patent Dispute: German Court Grants a Preliminary Injunction on a Patent Invalidated by the First-Instance Federal Patent Court*, 27 Biotech. L. Rep. 532, 532-533 (2008).

56 *See* Olanzapine, Federal Patent Court, *supra* note 46, at 4795-96 (e.g.: … between these three directly adjacent compounds, there is one gap which is to be filled by olanzapine...).

57 Bundesgerichtshof [BGH] [Federal Court of Justice] (hereinafter, "Olanzapine, Federal Court of Justice") Dec.16, 2008, IIC 596, 2009 (Ger.).

58 *Id.*, at 599.

59 *Id.*

60 *Id.*; The Federal Court of Justice cited the relevant BoA decision as follows: 1982 OJ 296 – Diastereomers/ BAYER; 1984 OJ 401 – Spiro compounds/CIBA GEIGY; 1988 OJ 381 – Xanthines/DRACO; 1990 OJ 195 – Enantiomers/HOECHST; decision dated 19 February 2003, T 94-/98 – Diastereomers of 3-cephem-4-carboxylic acid-1-(isopropoxycarbonyloxy) ethyl ester/HOECHST; *See also* Peter Meier-Beck, Die *Rechtsprechung des Bundesgerichtshofs zum Patent und Gebrauchsmusterrecht im Jahr 2008[The jurisprudence of Federal Court of Justice for patent and utility model law in 2008]*, GRUR 893, 895 (2009) (Ger.).

The Court stated that the determination of what was not explicitly mentioned in the characteristics of the claim and in the text of the specification but was obvious for a person skilled in the art to implement the teaching being protected and therefore did not require any special disclosure is, not aimed at supplementing the disclosure with the technical knowledge. The purpose is not different from the determination of the meaning of a claim, i.e. that technical information which a person skilled in the art derives from the source with the background of his technical knowledge.[61] Citing the *Elektrische Steckverbindung* decision, the Court held that modifications would only be allowable, if the modifications were so obvious to the person skilled in the art, in the overall context of the document, that they were easily evident to him when reading the document attentively, paying attention less to the words than to their meaning, so that he essentially 'reads them along' in his thoughts.[62]

The Court, then, applied this principle to the chemical compound invention as follows: "The *decisive factor is whether the concrete compound is disclosed* or not, and for this purpose, information that easily enables the person skilled in the art to specifically implement the invention relating to this chemical compound, i.e. to obtain the specific substance, is required".[63] The Court clarified its position against the *Fluoran* decision by explaining that the *Fluoran* case was held under the Patent Act of 1968 and that the Court did not adhere to this decision for the current law. The Court held further that a not explicitly disclosed individual compound could only be considered to have been disclosed *if a person skilled in the art "reads it along"* in the sense of the *Elektrische Steckverbindung* decision, for example because it was familiar to him as the usual implementation of the stated general formula, and therefore occurred to him as also having been meant when he read the general formula.[64] Otherwise, the disclosure of the individual compound was necessary to destroy novelty.[65]

61 *Id*.
62 *Id.*
63 *Id.*, at 600.
64 *Id.*
65 *Id.*

b) Enantiomer Invention – Escitalopram Decision

(1) Federal Patent Court Decision[66]

The Federal Patent Court stated that the patent was invalid for lack of novelty. A chemical compound having one chiral atom was no longer novel where claimed in the form of an enantiomer, if specific indication of the enantiomer in a prior publication had been given, and if the skilled person was able to produce the compound on the basis of this indication and his general knowledge.[67] The court found that the person skilled in the art would easily have been able to separate the Escitalopram from the racemic mixture disclosed in the prior art patent specification in a way which was commonly used before the priority date of the *Escitalopram* patent.[68]

(2) Federal Court of Justice Decision

While admitting that the person skilled in the art on the basis of his general knowledge had been able to recognize that citalopram having a chiral carbon had two different structures, the Federal Court of Justice stated that this fact does not lead to a disclosure which is detrimental to novelty.[69] Citing the *Olanzapine* decision, the Court said that, in order to *'make them* [the individual enantiomers] *available' to the skilled person for the purpose of novelty examination,* further information was as a rule required, in particular with regard to their *individualisation*.[70] The Court concluded that since the prior document did not directly and unambiguously disclose the individual enantiomers to the person skilled in the art and since he had to find a way to resolve the racemate, the prior patent was not detrimental to novelty.[71]

66 Bundespatentgericht (BPatG) [Federal Patent Court] Apr. 24, 2007, Beck-Rechtsprechung [BeckRS], 14624, (2007) (Ger.).
67 *Id.,* at para II, especially II b).
68 *Id.*
69 Escitalopram, Federal Court of Justice, *supra* note 27, at para 30.
70 *Id.,* para 33.
71 *Id.*, para 35.

2. From the U.S. Perspective

The terminology 'selection invention' has not been frequently referred to in U.S. Courts,[72] which instead use the expression 'genus/species'. However, Federal Circuit has also decided on this matter.

a) Markush Claim – Olanzapine Decision[73]

In its *Olanzapine* decision, the Federal Circuit restated that "anticipation is a question of fact, including whether or not an element is inherent in the prior art and the prior art reference must disclose each and every feature of the claimed invention, either explicitly or inherently".[74] The defendants argued that 'Chakrabarti' anticipated the patent in view of *In re* Petering[75] and *In re* Schaumann.[76] In *In re* Petering the Court held that a prior art reference disclosing a limited genus of twenty compounds rendered every species within the genus unpatentable. In *In re* Schaumann, the Court held that when a small genus places a claimed species in the possession of the public, the species was obvious even if the genus were not small enough to reject. However, in his opinion Judge Rader distinguished the *Olanzapine* case, where Chakrabarti disclosed millions of compounds, from the above two cases, where limited numbers of specific preferences, namely 'some 20 compounds', or '14 compounds' were disclosed, respectively. He noted that Chakrabarti in the *Olanzapine* case had not "expressly spelled out a definite and limited class of compounds that enabled a person of ordinary skill in the art to at once envisage each member of this limited class".[77] Judge Rader also stated that "one would have to depart from the teaching of the article and recombine the components of the specific illustrative compounds *with hindsight"* to make the olanzapine starting from the Chakrabarti disclosure[78]

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72 But see Eli Lilly and Company v Zenith Goldline Pharmaceuticals. Inc., 364 F.Supp 2d 820, 897 (S.D. Ind. 2005) (stating that selection inventions, also referred to as "improvement patents," are a normal consequence of technological progress and are expressly provided for by statute. 35 U.S.C. § 101 ("Whoever invents . . . any new and useful . . . composition of matter, or any . . . *improvement thereof* . . . may obtain a patent therefor . . .") (emphasis added).

73 Eli Lilly and Company v Zenith Goldline Pharmaceuticals. Inc., 471 F.3d 1369 (Fed. Cir. 2006) (hereinafter, 'Eli Lilly'). In fact, this was the first decision among three jurisdictions which upheld the validity of Olanzapine patent.

74 *Id.*, at 1375.

75 *In re* Petering, 301 F.2d 681 (C.C.P.A. 1962).

76 *In re* Schaumann, 572 F.2d 312 (C.C.P.A.1987).

77 Eli Lilly, *supra* note73, at 1376.

78 *Id.*, at 1377.

b) Enantiomer Invention – Escitalopram Decision[79]

The District Court found that the alleged prior art did not disclose 'substantially pure' Escitalopram and did not enable the person skilled in the art to obtain the product since the separation technique at the time of the invention was relatively new and unpredictable, and that the inventor himself failed to separate the enantiomer several times.[80]

Stating that it did not find errors in the District Court's conclusion, the Federal Circuit reconfirmed that since the prior art, which in effect even *did state* Escitalopram, *did not enable* the person skilled in the art to obtain the enantiomer, it *did not anticipate* the claimed invention.[81]

3. From the UK Perspective: "Parting from IG Rule"

A specific rule for selection inventions was developed from the early twentieth century on in the UK as established by Maugham J in *I.G. Farbenindustrie's A.G.'s Patent* case[82] (hereinafter "*IG Rule*"). This *IG Rule* stated three traditional requirements for the selection invention in the UK as follows: i) a selection patent to be valid must be based *on some substantial advantage* to be secured by the use of the selected members (the phrase will be understood to include the case of a substantial disadvantage to be thereby avoided); ii) *the whole of the selected members* must *possess the advantage* in question; iii) the selection must be in respect of *a quality of a special character* which can fairly be said to *be peculiar to the selected group*.[83] It had been well established, without distinguishing between novelty and non-obviousness,[84] until the *Olanzapine* decision, where the Court declared the end of the rule's life. As a result, when the invention can be found novel in the first place, it does not have to be considered any longer whether it is a valid selection invention according to the *IG Rule*.[85]

79 Forest Labs., Inc. v. Ivax Pharms., Inc., (hereinafter, 'Forest Labs.') 501 F.3d 1263 (Fed. Cir. 2007).
80 *Id.,* at 1265.
81 *Id.,* at 1268-69.
82 I.G. Farbenindustrie's AG's Patent 47 R.P.C. 289, 322-3 (1930).
83 *Id.*
84 *See Infra* note 96 and accompanying text.
85 *See e.g.,* Robert Fitt, *Selection Patents and Markush Claims in Europe,* 20 Biotech. L. Rep. 17, 18 (2010).

a) Markush Claim – Olanzapine Decision

(1) Patent Court Decision[86]

Floyd J noted that the Markush formula in the *Olanzapine* case was capable of encompassing many millions of compounds, and that the effect of this disclosure was at issue.[87] While citing the relevant EPO Boards of Appeal decisions, Floyd J confirmed that a prior disclosure did not take away the novelty of a claim to a specific compound unless the compound was disclosed in "individualized form" and attention would have focused on compounds actually described.[88] Floyd J further referred to the three general propositions of the *IG Rule* for selection inventions. However, he rejected this three steps test,[89] applied the standard approach to testing novelty, and held that the patent was novel.[90]

(2) Court of Appeal Decision[91]

Jacob LJ in his opinion firmly rejected the argument that "every chemical class disclosure discloses each and every member of the class" for two reasons: i) being an *a priori* consideration and ii) not being consistent with the jurisprudence of the Boards of Appeal of the European Patent Office, particularly the *Hoechst Enantiomers* decision.[92] With respect to the *a priori* consideration, he argued as follows:

> "An old question and answer runs as a follows: "Where does a wise man hide a leaf? In a forest." It is, at least faintly, ridiculous to say that a particular leaf has been made available to you by telling you that it is in Sherwood Forest. Once identified, you can of course see it. But if not identified you know only the generality: that Sherwood Forest has millions of leaves" .[93]

This argument was in line with the separate judgement of Lord Neuberger.[94] While citing the EPO's Board of Appeal decision, Jacob LJ reiterated that "an anticipation

86 Dr Reddy's Laboratories Ltd v Eli Lilly & Company Ltd(hereinafter, 'Dr Reddy's Lab, Patent Court'),R.P.C. 19 (2008) (U.K.).
87 *Id.,* at para 79.
88 *Id.,* at paras 91-94; *See also supra* note 57, at 600 (In the Olanzapine*, Federal Court of Justice,* the court clearly stated that its position is in line with the EPO and UK jurisprudence, and referred to this part of the UK decision).
89 *See supra* note 82 and accompanying text.
90 Dr Reddy's Lab, Patent Court, *supra* note 86, at paras 109, 139; *See also* Brian Cordery et al., *Patent cases in 2008-Review of Patent Cases in English Courts in 2008,* 38 C.I.P.A. J. 110, 112 (2009).
91 Dr Reddy's Laboratories Ltd v Eli Lilly & Company Ltd (hereinafter, 'Dr Reddy's Lab, Court of Appeal'), EWCA Civ 1362 (2009), available at http://www.bailii.org/ew/cases/EWCA/Civ/2009/1362.html.
92 T 0296/87, O.J.EPO 195, 1990.
93 Dr Reddy's Lab, Court of Appeal, *supra* note 90*,* at paras 25-30.
94 *Id.,* at para 108.

is an 'individualised description' of the later claimed compound or class of compounds".[95]

Jacob LJ said that the "selection invention" rule of *I.G. Farbenindustrie's Patent* was developed to avoid a finding of anticipation, did not draw a distinction between lack of novelty and obviousness, and was too strict because it is difficult to show that a group (compound) has a 'substantial advantage' over the whole prior class without an enormous amount of experiments.[96] Jacob LJ determined that the IG rule was just 'a part of legal history', but not part of the living law (post-1977 law).[97] Lord Neuberger noted that this issue was "not dissimilar from the enantiomer/racemate issue"[98] and recognized the difficulty in the application of the I.G. rule where the prior class of compounds was very large.[99]

b) Enantiomer Invention – Escitalopram Decision

While citing *Synthon BV v Smithkline Beecham Plc*[100] , Lord Hoffmann restated that to anticipate a patent, the prior art must disclose the claimed invention and enable the ordinary skilled person to perform it, and that it is settled jurisprudence in the EPO[101] that disclosure of a racemate does not in itself amount to disclosure of each of its enantiomers.[102] Regarding the plaintiff's argument that claim 1 is not only directed to the isolated enantiomer, Lord Hoffmann said that the claim did not include an unresolved part of the racemate, based on the title of the patent ('new enantiomers and their isolation') and the knowledge of a person skilled in the art.[103] Jacob LJ stated further that this was a pure question of construction, and that how much more than 50% of the (+) enantiomer must have been present for a product in order to fall within the claim was, simply a moot point in the validity court.[104] The Patent Court already had held that the claims were novel, and there was no further discussion in the upper court. Since the challenge based on lack of

95 *Id.,* at para 30.
96 *Id.*, at paras 36-39; This issue also may be discussed at *infra III.C.3.a)(2.)*.
97 *Id.*, at para 37; *See also* Mannual of Patent Practice – UK Patents Act 1977, paragraph 3.89-3.90 (July 2010).
98 Generics v Lundbeck, the House of Lords, (hereinafter, 'Generics, the House of the Lords') R.P.C.13 (2009) (U.K.).
99 *Id.*, at paras 103-104.
100 Synthon BV v Smithkline Beecham Plc, the House of Lords, Oct. 20, 2005, R.P.C. 10, (2006)(U.K.).
101 Generics v Lundbeck (hereinafter, 'Generics, Court of appeal'), R.P.C. 19 (2008) (U.K.); Lord Hoffmann also cited the decisions T 296/87 (OJ 1990, 19, point 6.2), T 1048/92 and T 1046/97.
102 *Id.,* at para 9.
103 *Id.*, at paras 10-13.
104 *Id.,* at para 50.

novelty had failed in both courts below, it was not renewed before the House of Lords.[105]

4. Summary

Whereas a specific prior art disclosure can take away the novelty of a generic claim, making it unpatentable, the reverse situation is more complicated.[106] In Germany, it seems that the Federal Court of Justice parts from the Fluoran decision, where a Markush claim disclosure in the prior art would be enough to be a novelty-destroying prior reference, and even selection of one out of two would be novel, unless the selected compound was enabled in the prior art. In the U.K., while the court declared its own old I.G. Rule on selection inventions as a part of history, a selection invention no longer has to satisfy this Rule, making it easier to meet the novelty requirement. In the U.S., the novelty requirement for an enantiomer was reconfirmed as having to be enabled by the invention, and for an invention claimed as Markush type it seems to depend on the finite number of class or compounds, which shifts the discussion to whether the non-obviousness requirement is met. Overall, thanks to the much lowered bar of novelty in major jurisdictions, challenging novelty of a selected class (compound, enantiomer) out of a Markush type disclosure, or even out of two genus (racemate) has become more difficult than ever.

C. Nonobviousness Requirement

1. From the German Perspective

a) Markush Claim – Olanzapine Decision[107]

The Federal Court of Justice held that olanzapine was not obvious to the person skilled in the art over neither 'Chakrabarti' document nor other prior art in any other manner.[108]

Interestingly enough, while doing so, the Federal Court of Justice confirmed that its position was not in line with the EPO's to determine obviousness, in "only"

105 Generics, the House of the Lords, *supra* note 98, at paras 11, 43, 65 (also noting that the patentee would not have intended to cover racemate.).
106 1 Donald S. Chisum, Chisum on Patents § 3.02[2][a]- [b] (2010).
107 Since the Federal Patent Court did not excessively discussed about the inventive step of the invention, the Federal Court of Justice decision would only be addressed under this section; *See also* Olanzapine, Federal Patent court, *supra* note46, at 4811.
108 *See* Olanzapine, Federal Court of Justice, *supra* note 57, at 601.

applying the so-called "problem-solution approach[109]" which started from its fundamental step to identify the 'closest prior art'. While disagreeing with the Federal Patent Court's assumption that a person skilled in the art would have chosen Chakrabarti first, the Court stated that there was no such higher ranking of the "closest prior art"; and only from a retrospective view it became clear what prior publication came closest to the invention and how an inventor could have approached the problem, in order to arrive at the solution according to the invention.[110] It seems that the court is concerned about the risk of hindsight if as a starting point for the determination of an inventive step, one selects the closet prior art. The Court also stated that the selection of the starting point therefore required the justification that generally lay in the efforts of a person skilled in the art to find a better solution for a specific purpose than the known state of the art makes available.[111] While elaborating the structure and activity relationship of the disclosed compounds, the Court held that since 'Chakrabarti' taught away or provided information which was out of the scope to make skilled person be interesting or promising to reach the olanzapine, it was not obvious.[112]

The Court also stated that obviousness could only be confirmed if an ordinary person skilled in the art *could* not only have had obtained the invention by combining e.g. two citations, but also, that a suggestion/motivation ("hint") to do that combination would be necessary to come to the conclusion of obviousness. The Court confirmed its position, as already expressed earlier, that this "hint", however, would not have to be in the to be combined citations of prior art themselves, but also could be found in the general mindset and knowledge of the ordinary person skilled in the art. Insofar, the Court's position is, and always has been, in line what KSR vs. Teleflex in U.S. has taught, different from the EPO's position according to which the "hint" has to be in the citations themselves.

109 Guidelines for Examination in EPO C-IV. 11.5 *"Problem-and-solution approach"* (stating that in order to assess inventive step in an objective and predictable manner, the so-called "problem-and-solution approach" should be applied. Thus deviation from this approach should be exceptional. In the problem-and-solution approach, there are three main stages: (i) determining the "closest prior art", (ii) establishing the "objective technical problem" to be solved, and (iii) considering whether or not the claimed invention, starting from the closest prior art and the objective technical problem, would have been obvious to the skilled person.).

110 Olanzapine, Federal Court of Justice, *supra* note 57, at 601.

111 *Id.,* at 601-602.

112 Bundesgerichtshof [BGH] [Federal Court of Justice] (hereinafter 'Olanzapine, BGH') Dec. 16, 2008, BeckRS 05422, paras 52-57, 2009 (Ger.).

b) Enantiomer Invention – Escitalopram Decision

The Federal Patent Court held that it was obvious to resort to the method of chiral chromatography to separate the enantiomers.

The Federal Court of Justice agreed that a person skilled in the art had reason at the date of priority to attempt to produce or isolate the citalopram's enantiomers since it was known that one enantiomer can have a better effect and other might have the opposite or side effect.[113] However, based on the fact that there was no obvious way to obtain the escitalopram at the date of priority; that it was not certain which way would provide industrially useful scale production; that there was not enough motivation to choose the method; that there was uncertain expectation of success; and that there were many failures to separate it, the Court held that the invention is not obvious.[114]

2. From the U.S. Perspective

Nonobviousness has been a much more difficult requirement to meet than the novelty requirement,[115] and in the U.S., after the KSR decision, it has been hotly discussed whether this Supreme Court decision has changed the law of obviousness.[116]

a) Markush Claim – Olanzapine Decision

The U.S. Federal Circuit held that several prior art references, in fact, *taught away* from exploring the compounds which did not possess an electron-withdrawing group in one benzene ring, where olanzapine exactly has a hydrogen atom.[117] On the one hand, he recognized the *structural similarity* with a compound which has an ethyl group('ethyl-olanzapine') instead of a methyl group of olanzapine; on the other hand, Judge Rader addressed that patentability for a chemical compound did not depend only on structural similarity, but also accounted for the unexpected

113 Escitalopram, Federal Court of Justice, *supra* note 24, at paras 37-38; *But see also Id.*, paras 39-41 (noting that there was no overwhelming need to separate the enantiomer.).
114 *Id.*, paras at 42-65.
115 *See e.g.,* Miles J. Sweet, *The Patentability of Chiral Drugs Post-KSR: The More Things Change, the More They Stay the Same*, 24 Berkeley Tech. L.J. 129, 136 (2009).
116 *See e.g.,* Jonathan M. Spenner, *Obvious-to Try Obviousness of Chemical Enantiomers in View of Pre-and Post-KSR Analysis*, 90 J. Pat. & Trademark Off. Soc'y, 477, 478-479 (2008).
117 Eli Lilly, *supra* note 73, at para 40.

beneficial significant properties which might render the invention to be nonobvious.[118] After he noted the similarity with the case of *Yamanouchi Pharm. Co., Ltd. V. Danbury Pharmacal*,[119] Inc., he also stated that the defendants did not sufficiently show the motivation for a person skilled in the art to select the above 'ethyl-olanzapine' as a lead which did not contain an electron-withdrawing group.[120] This analogy is interesting, since in *Yamanouchi* an entire complex combination was required; selecting and combining separate parts of two embodiments followed by further chemical reactions to produce the patented compound; however, there was only a single difference between the compounds in the prior art (ethyl group) and that in the patent at issue (methyl group). While citing *Yamanouchi* again, the Judge stated that to make the combination as a whole be obvious is not the mere identification in the prior art of each component, but rather a motivation to select the reference and to combine them in the particular claimed manner to reach the claimed invention.[121] One may consider this was even so because it was held before *KSR v. Teleflex* in 2007.[122] The court held that it was not obvious based on the above 'teaching away' and extensive 'secondary considerations of nonobviousness' such as; (i) a long-felt and unmet need; (ii) failure of others; (iii) industry acclaim; and (iv) unexpected results.

b) Enantiomer Invention – Escitalopram Decision

The District Court found that the alleged prior art did not provide a reasonable expectation of success to obtain the enantiomer for similar reasons to those of enablement regarding the same prior art.[123] The Court also found that one of ordinary skill in the art at the time of the invention would generally have been motivated to develop new compounds rather than undertake the difficult and unpredictable task of resolving a known racemate.[124]

118 *Id.,* at paras 42-44.
119 Yamanouchi Pharm. Co., Ltd. v. Danbury Pharmacal, Inc., 231 F.3d 1339, 1344 (Fed. Cir. 2000) (holding that [The ANDA filer] did not show sufficient motivation for person skilled in the art at the time of invention to take any necessary steps to reach the patented invention from the prior arts).
120 Eli Lilly, *supra* note 73*,* at para 45.
121 *Id*., at para 47.
122 KSR Int'l Co. v. Teleflex Inc., (hereinafter, 'KSR') Apr. 30, 2007, 127 U.S. 1727 (2007) (holding that TSM(teaching, suggestion, and motivation test) test provides helpful insights, unless it is applied too rigidly).
123 Forest Labs., *supra* note 79, at 1267.
124 *Id; Contra* German Federal Court of Justice's position at III.C.1.b); *Contra* Jonathan J. Darrow, *The Patentability of Enantiomers: Implications for the Pharmaceutical Industry,* 2 STAN. TECH. L. REV. paras 21 and 39 (2007).

The Federal Circuit addressed that Ivax only emphasized the evidence that was favourable to their desired outcome without addressing the evidence favourable to Forest, such as the failure of the inventors to resolve citalopram without undue experiments, and so on.[125] Judge Lourie concluded that it was not obvious to the person skilled in the art. Considering this decision was given several months after KSR, this decision is interesting because the Federal Circuit did not address more than the ordinary view regarding obviousness while relying on the District Court's finding based on Graham v. John Deere Co..[126]

3. From the UK Perspective

a) Markush Claim – Olanzapine Decision

(1) Patent Court Decision

Floyd J employed the structure approach of the obviousness test in *Windsurfing v. Tabur Marine* case,[127] found the 'skilled addressee' as a team of scientists with a particular interest in finding anti-psychotics, led by a medicinal chemist having access to other disciplines such as pharmacology and toxicology,[128] found 'common general knowledge' as medicinal chemistry including structure-activity-relationships, psychological disorders and associated side effects,[129] and held the patent was not obvious over all prior arts argued.[130] Considering determination of what a person skilled in the art perceived at the filing date was crucial to determine obviousness,[131] this court seems to start from the very basic element. In addition, he found that 'commercial success' is not helpful in deciding obviousness, since the fact alone did not support obviousness if olanzapine was technically obvious.[132] He emphasised that the commercial success was not because the third parties had

125 *Id.,* at 1268.
126 Graham v. John Deere Co., 383 U.S. 684 (1966).
127 Windsurfing International Inc. v Tabur Marine (GB) Ltd. R.P.C. 59 (1985) (Gt Brit.). (4 step tests to the obviousness: (1) (a) Identify the notional "person skilled in the art" (b) Identify the relevant common general knowledge of that person; (2) Identify the inventive concept of the claim in question or if that cannot readily be done, construe it; (3) Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed; (4) Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?").
128 Dr Reddy's Lab, Patent Court, *supra* note 86, para 140.
129 *Id.*, paras 141-148.
130 *Id.*, paras 149-184.
131 *See also* Spenner, *supra* note116, at 477.
132 Dr Reddy's Lab, Patent Court, *supra* note86, para 185.

not appreciated the advantages of olanzapine, but because the basic patent covering olanzapine had prevented the manufacture and sale of olanzapine.[133]

(2) Court of Appeal Decision

Jacob LJ stated that the objection of obviousness could be made where there was *'no real technical advance'* in the art, since the patent monopoly could be justified by the technical contribution to the art.[134] While endorsing Jacob LJ's position on this issue, Lord Neuberger noted that whether the selection was arbitrary, or whether the teaching of prior art established that the selection achieved 'a particular technical result', should be asked.[135] If there was not technical advance, it was just an arbitrary selection which was obvious. However, since olanzapine provided its superior therapeutic effect to the prior arts, and selection from almost millions of compounds could not be regarded as random,[136] it was nonobvious over the prior arts.

b) Enantiomer Invention – Escitalopram Decision

(1) Court of Appeal Decision

Before this Court, whether the so-called amino diol route for resolving the racemate would have been obvious was an issue.[137] Lord Hoffmann stated that the appeal court might reverse the trial judge's finding when the error of principle occurred that the judge failed to consider whether it was obvious for the skilled person to try the reaction to see if it worked, like in the *Biogen*[138] case.[139] While stating Kitchin J applied the state of law correctly to the facts of this case, Lord Hoffmann shortly rejected the nonobviousness argument. Regarding the plaintiff's argument that a person skilled in the art could have come to the invention by doing a short and simple experiment, Jacob LJ rejected this argument stating that by itself is not enough ; as one could say that 'with hindsight' of many inventions; and as it was

133 *Id*., para 186.
134 Dr Reddy's Lab, Court of Appeal, *supra* note91, at paras 40-52.
135 *Id.*, at para 109.
136 *Id.,* at paras 54-57, 98-101, 109-115.
137 Generics, Court of appeal*, supra* note 101, at para 14.
138 Biogen Inc v. Medeva Plc (hereinafter "Biogen"), Oct. 31, 1996, UKHL 18, 1996; R.P.C. 1, 1997.
139 Generics, Court of appeal, *supra* note 101, at para 23.

not enough motivation for a skilled person to carry it out. Therefore, the invention was not obvious.

(2) The House of Lords Decision

Since attack based on obviousness failed in both courts below, it was not a big issue before the House of Lords. On the other hand, Lord Neuberger summarized basic knowledge about enantiomers which had long been known as follows: i) two enantiomers could have different properties from each other; ii) a racemate's therapeutic effect might be mainly dependent on one enantiomer; iii) the other enantiomer might have toxic or side-effects; iv) the only way to tell which one had which effect was to separate one from another and to compare; iv) however, above was not possible to predict yet.[140] He continued that the notion to obtain a pure therapeutic form from a racemate is obvious, but to obtain a pure form is not obvious, and it was particularly difficult to separate (S)-citalopram from the racemate.[141] Thus it seems that Lord Neuberger weighted the difficulty of separation of racemates to determine obviousness.

4. Summary

These decisions show that the courts share and consider various factors to determine obviousness, such as level of knowledge of persons skilled in the art, structural similarity, motivation to carry it out, unexpected beneficial properties (a real technical advance), teach-away, previous failures, hindsight issue, reasonable expectation of success (arbitrariness), and so on. For example, similar to the 'obvious-to-try' doctrine, Jacob LJ stated that enough motivation and a simple statement that the experiment would have been short and simple was not sufficient. Also as Jacob LJ tried to warned against the hindsight bias, the German Federal Court of Justice stated that only from a retrospective view, one could be sure what was the closest prior art. However, regarding whether there was enough motivation to separate the enantiomer, the U.S. Federal Circuit seemed to have a different view from the German Federal Court of Justice, and this issue will be discussed further at IV.B.

140 Generics, the House of Lords, *supra* note 98, at para 61.
141 *Id.,* paras 61-65.

D. Summary and Conclusion

In Germany, a broad genus claim or even a genus with two species disclosure in prior art cannot prevent the species be patented per se., which could be regarded as what applies in other jurisdictions. In the U.K., there is no longer a need to prove the selection has a substantial advantage over the wider group where the selection was made[142] and even a known product can be patented as a product per se depending how difficult it is to make it available. In the U.S., the much-disputed KSR decision does not seem to influence enough at least on *Escitalopram* decision. As a brief conclusion, it would be fair to say that it gets to be more difficult to challenge the selection inventions, and easier to get patents on them. These series of changes on patentability will be further analysed in the following section.

142 Fitt, *supra* note 85, at 20.

IV. Discussion

Patents claiming basic inventions like new medical entities are generally very broad, and thus are difficult to be circumvented. During the term of a basic patent, it is not possible to launch a product in the market that relies on dependent patents, unless the dependent patent holder infringes or licenses-in the basic patent. However, even after expiration of the patent, it is still not easy to freely bring a product to the market, especially in the pharmaceutical fields. This is because innovative companies try to extend their exclusivities in the market and to recoup their investments through seeking patents for selected or improved inventions, based on their basic and fundamental patents. Furthermore, the same activities could be conducted by third parties, either competitors of innovative companies or generic companies. Therefore, the existence and number of selection patents has an impact on the freedom of generic companies.

As the European Commission reported in its pharmaceutical sector inquiry, 80~90% of pending claims or granted patents during the period of 2000 to 2007 were categorized as selection inventions.[143] Patentability requirements for selection inventions may play an important role in the pharmaceutical market. The higher or stricter the patentability requirements for selection inventions, the lower is the likelihood that patents are granted for them, and the easier the market entries of generics. In this section, the implications of laws of patentability on selection inventions will be discussed.

A. Anticipation

1. Relativity[144] of Novelty

The novelty requirement for inventions is not controversial.[145] It is 'a separate examination' step for patentability, as the German Federal Court of Justice stated

143 *See supra* notes 21-23 and accompanying texts.

144 One may distinguish "relative novelty" from "absolute novelty" in terms of degree of disclosure. The former may mean that a particular prior disclosure or use of the invention is not regarded as prior art which takes away the novelty of the invention. The latter may mean that the invention must not have been previously disclosed anywhere in the world in any way before the filing date. *See also* Lewis Anten, *What's new with novelty – Section 102 of S. 643*, 54 J. Pat. Off. Soc'y 75, 75-76 (1972). The latter may also be understood as

in its *Olanzapine* decision,[146] and has a different purpose and function from obviousness.[147] The Federal Court of Justice noted its purpose of avoiding double patenting, and it is acknowledged that novelty as a basic patentability requirement is mandated to ascertain that no exclusive right is given to an invention that is already in the public domain.[148]

If every element of a claimed invention is identically disclosed, either explicitly or inherently,[149] in a single prior art document, the document deprives the invention of novelty,[150,151] The document 'anticipates' the claimed invention when it enables the whole claimed invention on top of disclosing each and every element of the invention.[152] In case the prior art fails to disclose one or more elements of the

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the novelty requirement under EPC Art. 54 and Art. 55. *See also* Patents and Technological Progress in a Globalized World 4-5 (Wolrad Prinz zu Waldeck und Pyrmont et al. eds., 2009) (indicating that all disclosures of the invention are considered as prior art without any restriction with respect to time, place, or manner.). However, "relativity" of novelty in this paper is different from these concepts, and will be discussed in this section.

145 *See* John F. Duffy, *Rethinking the Prospect Theory of Patents,* 71 U. Chi. L. Rev. 439, 502-503 (2004).

146 Olanzapine, the Federal Court of Justice, *supra* note 57, at 599.

147 *See also* Winfried Tilmann, *Validity of Selective Product Claims – Venice Conferences III and V, Lundbeck and Olanzapine,* IIC 149, 151-152 (2010); *See also* Diastereomers/BAYER, Feb. 09, 1982, 8 O.J.E.P.O. 296, 301 (1982) (holding that the purpose of Art. 54(1) EPC is to prevent the state of the art being patented again.).

148 Sean B. Seymore, *Rethinking Novelty in Patent Law*, 60 Duke L. J. 1, 2 (forthcoming 2011); *See also* Tilmann *supra* note147*,* at 151-152 ("According to the outdated view, the purpose of novelty requirement was interpreted as 'avoiding double patenting', however, the prior art must not necessarily be a patent document, it is well acknowledged that the purpose is to avoid patenting an information which already has been given to the public by a first disclosure.").

149 *See* Schering corp. v. Geneva Pharms., Inc., 339 F.3d 1373, 1377 (Fed. Cir. 2003) "A prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference." (citing Continental Can Co. v. Monsanto Co., 948 F.2d 1264, 1268 (Fed.Cir.1991).

150 EPC Art. 54; 35. U.S.C. § 102(a) and (b); *See* Lindemann Maschinenfabrik GmbH v. Am. Hoist & Derrick Co., 730 F.2d 1452, 1458 (Fed. Cir. 1984) (holding that the trier of fact must identify the elements of the claims, determine their meaning in light of the specification and prosecution history, and identify corresponding elements disclosed in the allegedly anticipating reference); *See also* Glaxo Inc. v. Novopharm Ltd., 52 F.3d 1043, 1047 (Fed. Cir. 1995) (holding that a prior art reference must disclose each and every feature of the claimed invention, either explicitly or inherently.

151 *See also* Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347-49 (Fed. Cir. 1999) (holding that anticipation requires that the four corners of a single prior art document describe every element of the claimed invention, either expressly or inherently, such that a person of ordinary skill in the art could practice the invention without undue experimentation).

152 *Id.*, at 1347-1349; *See also* F. Scott Kieff et al., Principle of Patent Law 525 (4th ed. 2008); *See also* Elan Pharms., Inc. v. Mayo Found., 346 F.3d 1051, 1054 (Fed. Cir. 2003) (holding a reference is enabled when its disclosures are sufficient to allow one of skill in the art to make and use the claimed invention, quoting Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc., 246 F.3d 1368, 1374 (Fed. Cir. 2001)).

claimed invention or to enable the claimed invention, an obviousness rejection may still be raised with respect to the prior art.

At first glance, the assessment of novelty seems to be relatively straightforward and simple.[153] The only test for novelty would be to compare the claimed invention and the entire knowledge of the prior art, and to determine that the claimed invention is novel when there is a difference from what is already known, regardless of the degree or extent of the difference.[154] However, it is not as easy as it sounds. Firstly, the determination of novelty involves many factors. It is, in fact, dominated by standards which need judgement based on various elements, just as other patentability determinations.[155] For example, in order to decide inherent anticipation – "it is inherently disclosed only if it is the natural result flowing from the explicit disclosure of the prior art" –, it should be judged what is regarded as a "natural result".[156] To determine whether the invention is either explicitly or inherently anticipated in an enabling manner, we should judge the level of ordinary skill of "the person of ordinary skill in the art" and the degree of experiments which would be regarded as "undue".[157] Secondly, the complexity of determining novelty varies according to technology. It is more straightforward in relatively predictable fields like electrical or mechanical engineering; however, it is more difficult for chemical, biotechnological, or pharmaceutical inventions which lie in unpredictable fields.[158] Thirdly, it also depends on the developmental status of inventions. The novelty requirement is easier to achieve for fundamental inventions (e.g. basic patents) than for improvement inventions[159]considering the increasing

153 *See e.g.*, F Scott Kieff, *The Case for Registering Patents and the Law and Economics of Present Patent-Obtaining Rules*, 45 B. C. L. Rev., 55, 86-87 (2003).

154 *See* François Dessemontet, The Legal Protection of Know-how in the United States of America 194 (H.W. Clarke trans., 2d ed. 1976).

155 John F. Duffy, *Rules and Standards on the Forefront of Patentability,* 51 Wm. & Mary L. Rev. 609, 638-639 (2009).

156 *Id.*, at 638; *See also Schering*, *supra* note 149, at 1379 (holding an invention to be inherently disclosed only "if it is the natural result flowing from the explicit disclosure of the prior art.".).

157 Id.; *see also* Advanced Display Sys., Inc. v. Kent State Univ., 212 F.3d 1272, 1282 (Fed. Cir. 2000) (holding that anticipation requires describing every element of the claimed invention, either expressly or inherently, such that a person of ordinary skill in the art could practice the invention without undue experimentation); exemplary multifactors to determine "undue" experiments are given in U.S. Patent & Trademark Office, Manual of Patent Examining Procedure, § 2164.01 (8th ed. 8th rev. 2010) [hereinafter MPEP] (citing *In re* Wands, 858 F.2d 731, 737 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.).

158 Seymore, *supra* note 148, at 9-10, 14-16.

159 *See also* Theon van Dijk, *Patent Height and Competition in Product Improvements,* 44 J. Indus. Econom. 151, 152-153 (1996).

amount of prior arts over time. Fourthly, the novelty requirement is treated more strictly in the pharmaceutical field than in other technical fields, since novelty is judged based on whether the idea of the invention is new, not on whether the product has been accessible to the public.[160] Put differently, the mere earlier disclosure of an idea, not the accessibility of a product can keep the invention from being patented, thereby possibly disincentivizing pharmaceutical companies to launch a product, wherein the launch can take longer than in other industries. Lastly but most importantly, the novelty requirement including the level of enablement depends on the jurisdiction and on the developmental status of law. Therefore, the assessment of novelty seems to be rather relative. In the next section, the last mentioned aspect of novelty, i.e. the enablement requirement is further discussed.

2. Enablement as a Requirement for Anticipation

What is the relationship between anticipation and enablement? An enabling disclosure is required for anticipation of the invention in main jurisdictions. The German Federal Court of Justice held in the *Olanzapine* decision that the concept of disclosure was exclusively what a person skilled in the art directly and unambiguously derives from the prior art as the content of teaching, thereby enabling him to specifically carry out the invention.[161] Under US practice, too, in order to anticipate the claimed invention, a prior art disclosure must enable it either explicitly or inherently, such that the skilled artisan could practice the invention without undue experimentation.[162] Tilmann interpreted this requirement in accordance with the narrow purpose of the novelty requirement, namely, to avoid double-patenting.[163] He said that it was correct to require that the information in a prior art document discloses 'directly and unambiguously' the subject matter of a claim to avoid double-patenting, and also noted that this came close to the wordings of EPC Arts. 83 and 84.[164] Enablement has played a key role in the context of anticipation; however, it has rarely been discussed.[165]

The main differences between enablement as a requirement for anticipation and enablement as a requirement for sufficiency of disclosure can be summarised as

160 Roin, *supra* note 8, at 517-518.
161 *Id.,* at 599-600.
162 *See* Kieff, *supra* note 152; *see also* Smithkline Beecham Corporation v. Apotex Corp., 403 F.3d 1328, 1342 (Fed. Cir. 2005); *see* also *In re* Brown, 329 F.2d 1006 (C.C.P.A. 1964).
163 See Tilmann, *supra* note 147, at 152.
164 *Id.*
165 *See* Seymore, *supra* note 148, at 6; *see also, e.g.,* Chester v. Miller, 906 F.2d 1574, 1576 n. 2 (Fed. Cir. 1990) (noting that for being prior art under section 102(b), the reference must place the anticipating subject matter at issue into the possession of the public through an enabling disclosure).

follows: The first distinction hinges on whether the requirement is introduced by legislative or by judicial bodies. The enablement requirement (sufficiency of disclosure) for obtaining a patent is clearly stated in the statutes, e.g. EPC Art 83 or 35 U.S.C. § 112.[166] However, the enablement requirement for anticipation is specified neither in EPC Art 54, nor 35 U.S.C. § 102, nor anywhere else in the patent statutes. This requirement for anticipation was established by the courts.[167]

The second difference depends on whether the utility of the invention is to be enabled as well. The Federal Circuit in *Novo. Nordisk Pharms., Inc. v. Bio-Tech. Gen. Corp*.[168] confirmed that the standard for enablement of a prior art reference for purposes of anticipation under § 102 differed from the enablement standard under 35 U.S.C. § 112, namely, the specification should enable a person skilled in the art to 'use' the invention to meet the requirement under § 112, but the specification did not need to do so to meet the requirement under § 102.[169]

The third difference is whether the scope of the invention has to be enabled when the prior art reference is a patent (application) itself. In order to meet the enablement requirement for the 'patent-obtaining purpose' under EPC Art 83 or 35 U.S.C. § 112, the specification must enable the whole scope of the claimed invention, but to meet it for 'patent-defeating purpose', it would be enough to enable the scope of the invention at issue.[170] Thus, the description of a single embodiment for a broad claim in an earlier patent (application) can enable the invention for anticipation purposes, but the same embodiment alone may not be enough to provide a sufficient description for the earlier patent (application) itself.[171] However, even in this case,

166 EPC Art. 83 (2007) (stating that the European patent application shall disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art); 35 U.S.C. § 112 ¶1 (2006) (stating that the specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same).

167 Janice M. Mueller et al., *Enabling Patent Law's Inherent Anticipation Doctrine*, 45 Hous. L. Rev. 1101, 1137-38 (2008); *see also In re* LeGrice, 301 F.2d 929, 939 (C.C.P.A. 1962) (holding that anticipation under § 102(b) "requires that the description of the invention in the printed publication must be an 'enabling' description").

168 Novo. Nordisk Pharms., Inc. v. Bio-Tech. Gen. Corp., 424 F.3d 1347, 1359 (Fed. Cir. 2005) (citing Rasmusson v. SmithKline Beecham Corp., 413 F.3d 1318, 1325 (Fed.Cir.2005).

169 *Id.* (citing *In re* Hafner, 410 F.2d 1403, 1405 (C.C.P.A.1969)); *see also* in re Schoenwald, 964 F.2d 1122, 1124 (citing *In re* Donohue, 632 F.2d 123, 126 (C.C.P.A. 1980) ("proof of utility is not a prerequisite to availability of a prior art reference under 35 U.S.C. § 102(b)"); *see also Bristol-Myers Squibb, supra* note152, at 1379 (holding that anticipation does not require actual performance of suggestions in a disclosure. Rather, anticipation only requires that those suggestions be enabled to one of skill in the art.). This can be viewed differently in different jurisdictions.

170 Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1562 (Fed. Cir. 1991); *see also* Kieff et al., *supra* note 152, at 207-211.

171 *In re* Lukach, 442 F.2d 967, 969 (C.C.P.A. 1971) (noting the difference of the enablement requirement for the patent obtaining purposes from that for the patent defeating purposes).

the single embodiment of the prior art reference (earlier patent) could have enabled a narrower claim scope in the earlier patent, covering at least the embodiment itself.

In the *Olanzapine* case, the issue went further, as is discussed in this paper.[172] That is, in case the earlier patent did not enable the later claimed invention because there was no single embodiment to do so in the earlier patent even with consideration of the common knowledge of a person skilled in the art, one may say that the whole claim of the earlier patent can not have been fully enabled. The implication of this will be discussed in detail in section IV.A.3.b).

There are several differences of enablement[173] between the patent-defeating context and the patent-obtaining context. Among them, the difference in the scope of enablement has several implications, and thus the impact of this requirement is further discussed below.

3. Implications of Enablement Requirement in Anticipation

The enablement requirement held by the *Olanzapine* decision and confirmed by the *Escitalopram* decision, brought us not only some clear guidelines to the novelty test, but also several impacts on the law of patentability on selection inventions. These impacts are further discussed.

a) The Test of Anticipation: Precedent Test of Obviousness?

As the German Federal Court of Justice said, novelty examination is a separate test to determine patentability[174] and is not a 'first step of examining obviousness'. However, by way of lowering the bar for novelty, the Courts seem not to sufficiently differentiate the test of novelty from that of obviousness.

In particular, the *Escitalopram* court made significant efforts to evaluate the difficulty of the resolution of citalopram *in order to assess novelty,* after admitting that it was apparent that a racemate of a chemical compound like citalopram had equal amounts of two enantiomers. In the end, the Court found that this did not lead to Escitalopram being anticipated. This could be interpreted as novelty being dependent on the difficulty of obtaining a claimed compound, based on the common

172 *See generally supra* III.A.1.
173 *See also* Mueller *supra* note 167 (asserting that different standards of enablement should be applied in each context.).
174 Olanzapine, the Federal Court of Justice, *supra* note 57, at 599.

knowledge of a person skilled in the art. The level of enablement of the prior art reference is determined in order to assess novelty.

Since the enablement requirement is considered when assessing novelty,[175] the determination of novelty has became more relative and, to some extent, similar to the test of obviousness. In the U.S., *prima facie* obviousness established based on the prior art disclosure of racemates and *de facto* disclosure of the enantiomer itself was rebutted based on no reasonable expectation of success and the difficulty of separation.[176] It may be difficult to differentiate between a skilled person not being able to obtain the claimed invention within the context of anticipation from there being no expectation of success to separate within the context of nonobviousness. This in turn tells us that the courts possibly do not clearly distinguish between the novelty and the nonobviousness requirements, which is contrary to what the German Federal Court of Justice has postulated.[177] It seems at least that the same test is repeated in both steps, or that both steps are determined by a single test for the assessment of patentability. Can it therefore be said that the test for novelty is placed in the broader context of the test for "inventive step"[178]?

b) A Possible Ground for Challenging the Basic Patent

Again, as the German Federal Court of Justice held, a prior art reference does not directly and unambiguously reveal an invention unless the publication makes it easily possible for the person skilled in the art to obtain it. Since the prior art reference in the *Olanzapine* case did not enable the claimed invention, it did not anticipate the invention (i.e. the single compound, olanzapine).[179] At this point, it is necessary to recall the definition of a selection invention. Since a selection invention (e.g. a compound) is an invention selected from the broader concept of an earlier invention (e.g. a Markush type claim), the scope of this invention, by definition, should fall into the scope of the earlier patent,[180] which is the case in the *Olanzapine* decision. Thus, both the selection patent claiming olanzapine and the earlier patent claiming the broader scope of invention cover the compound, olanzapine. This leads to the conclusion that the fact the earlier patent document cannot enable the selection invention in the anticipatory context would inevitably mean that the earlier patent application did not enable its own claimed invention at least

175 *See Infra* IV.A.2.
176 *See* Sweet, *supra* note 115, at 142; *See also* Forest Lab *supra* note 79, at 1268; *See also infra* IV.B.1.c).
177 Olanzapine, the Federal Court of Justice, *supra* note 57, at 599.
178 *See e.g.,* Tilmann *supra* note147, at 158-159.
179 *See supra* III.B.1.
180 *See e.g.*, Agranat et al., *supra* note 3.

in part (e.g. covering that compound). In other words, when the earlier patent fails to enable the later selection invention, in the patent-defeating enablement context, it fails to enable its own claims in part, in the patent-supporting enablement context. Given that the selection invention has been patented over the basic prior patent, the prior patent would be invalid at least with respect to a part of its claim scope, for insufficiency of its disclosure.[181] The selection invention then is not a dependent invention any more, and the owner of the selection invention does not need to license the basic patent. Other relevant issues will be further discussed in the next section.

c) Other Implications of the Rules for Disclosure in the Olanzapine Case

In the *Olanzapine* decision, the rules for 'disclosure' were explained in relation to anticipation. Further areas where the rules for disclosure play a role are: i) validity of priority claiming (priority application(s) v. application claiming the priority); ii) sufficiency of the disclosure (content of the application v. claim scope); iii) support for amendments (content of the application v. amended claim); and iv) limitation or validity of patent (content of the application v. patent).[182]

Let's have a look at these "concept of disclosure" issues while applying the *Olanzapine* case. Take a patent application, which has one independent Markush type claim theoretically covering several thousands of compounds and several dependent claims, and discloses 10 embodiments. For example, under the examination of sufficiency of disclosure, an examiner may object to other claims except those claiming 10 embodiments on the basis that they are not 'directly and unambiguously' disclosed, unless those claims are so obvious to the person skilled in the art, in the overall context of the document, that they are easily evident to him when reading the document attentively. In turn, when the applicant would try to overcome

181 *See e.g.,* Dr Reddy's Lab, Court of Appeal, *supra* note 91, at para 116 (Lord Neuberger partly noted that if there had been a challenge to the validity of the 235 patent on appropriate grounds (e.g. under section 72(1)(c) of the UK Patent Act: ground for the revocation: the specification of the patent does not disclose the invention clearly enough and completely enough for it to be performed by a person skilled in the art), it would have been revoked); *But see* Examination Guidelines for Patent and Utility Model in Japan (June 2010) 1.5.3. (3)(2) (hereinafter "Japanese Examination Guidelines") (noting that to acknowledge that the chemical substance is not disclosed in the prior art disclosing the chemical formula, does not mean "that the claim violates the enablement requirement under Art. 36(4) of Japanese Patent Act where the publication is a patent application claiming the chemical substance as one of alternatives of a Markush-type formula".).

182 *See e.g.* Tilmann *supra* note147, at 159; *See also e.g.,*Wolfgang Bublak et. al., *Offenbarungsgehalt der Vorveröffentlichung einer chemischen Strukturformel (Disclosure in the Prior Publication of a Chemical Structural Formula)*, GRUR 382, 389 (2009).

this rejection ground through the amendment of claims,[183] he may only obtain his exclusivity for the claims directed to 10 individual embodiments out of at most 100 times compounds in the extreme, because of the same reason as above. Assume that there were only 3 individual embodiments in the priority application – it is a very typical case in which the applicant prepares more embodiments during a 12 month period -, can even 10 individual embodiments enjoy the claiming of priority?

It would be interesting to see whether the Federal Court of Justice will uniformly apply this concept of disclosure in terms of novelty to other areas of disclosure, and if not, to what extent it would do so.

4. Conclusion

It is acknowledged that determination of the patentability of selection inventions is a more difficult issue,[184] and is considered case by case, specifically different from other inventions.[185]

The *Olanzapine* and the *Escitalopram* decisions lowered the bar for patentability, especially for the novelty requirement with respect to selection inventions. On the one hand, it is understood that society wants to motivate companies to research these areas, and thus more selection inventions become available. However, on the other hand, it is hard to find a justification for the fact that selection inventions are treated differently from basic inventions.

Floyd J said in the *Olanzapine* decision that the above discussed extension of the exclusivity term could not alter the principles to be applied when deciding whether the patent's teaching was novel or non-obvious over the basic patent.[186] In his opinion, this situation should not be treated differently from when the basic patent is owned by a party other than the patentee, or when the prior part is not a patent document.[187] It may be difficult to understand why the same reasoning should not be applied to the treatment of selection inventions and basic inventions. The possible impact of this enablement requirement, i.e. a possible extension of exclusivity, will be considered in further depth in IV.C.

183 *See e.g.,* Heiko Sendrowski, *"Olanzapine" – eine Offenbarung? (Olanzapine – a disclosure?)* GRUR 797, 801 (2009).
184 Chisum, *supra* note 106, at § 3.02[2][b].
185 *See also* MPEP *supra* note 157, § 2131.03 (When the prior art discloses a range which touches, overlaps or is within the claimed range, but no specific examples falling within the claimed range are disclosed, a case by case determination must be made as to anticipation).
186 *See* Dr Reddy's Lab, Patent Court*, supra* note 86.
187 *Id.*

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

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]

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.).

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.).

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.

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.

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.

1. Easier Extension of Exclusive Right: "Evergreening" or "Life-Cycle Management"

This impact is increased if a selection invention is filed by the patentee of the basic patent, which is frequent because the basic patent holder has more and better knowledge and experience regarding the substance. This is because after exploiting his exclusive right and keeping third parties from using the basic patent, the exclusivity would be prolonged based on the grant of selection patents. This issue is even more important in relation to enantiomer patents because the grant of such patents would result in the issuance of a supplementary protection certificate which provides further market exclusivity[234] in addition to the patent monopoly. This phenomenon in the pharmaceutical field is called an "evergreening" strategy (normally by generic companies) or a "life-cycle management" strategy (generally by innovative companies), which is used by innovative companies to prolong the market exclusivity of their products to the extent the law allows.[235]

With regard to this issue, Floyd J stated in the *Olanzapine* decision that the basic patent prevented a third party from bringing olanzapine to the market[236] until the expiry of the basic patent. Lord Neuberger in the same case stated that it was unfair and inappropriate that Lilly should be able, in effect, to re-monopolise olanzapine in 1990 given that they had already done so in 1978 with the grant of its basic patent. Therefore, the impact of lowered bar for patentability of selection inventions would provide a much easier *de facto* extension of the exclusive right to the compound, given that the selection invention is held by the basic patent holder.

2. More Limitations to Exploiting Selection Patents

a) Scope of a Selection Invention over a Basic Patent

Before discussing the matter of exploitation of selection patents, the scope of selection patents and basic patents in force is clarified herein. The decisive factor for defining the scope of a patent is not what was invented, but what was claimed and granted.[237] In other words, the scope of a patent is determined by the claim lan-

234 Escitalopram, Federal Court of the Justice, *supra* note 27, paras 66-77.
235 Michael Enzo Furrow, *Pharmaceutical Patent Life-Cycle Management After KSR v. Teleflex*, 63 Food & Drug L.J. 275, 276-277 (2008).
236 *See* Dr Reddy's Lab, Patent Court, *supra* note86.
237 Oberster Gerichtshof [OGH] [Supreme Court] Apr. 22, 1986, docket No. 4 Ob 319/86, IIC 80 (1989) (Austria)(holding that the deciding factor is not what was invented, but what was claimed and granted).

guage,[238] regardless of what was really invented. This notion is especially important for selection inventions. Even though the inventor of a basic invention did not perceive the later improvement invention as his invention at the filing date, the later selection invention might be found to infringe the claim of a basic patent whose language is broad enough to cover the later invention.[239]

In his article, Lemley categorized and addressed three kinds of improvement inventions[240] based on the level of social contribution, namely, a minor improvement, a significant improvement, and a radical improvement.[241] According to Lemley, a minor improvement cannot be patented but is covered by the basic patent. A significant improvement could be patented but still falls within the scope of the basic patent, and therefore the basic patentee cannot capture the value of the improvement patent but can prevent the significant improver from using his basic invention, because an improvement patent is covered by the basic patent's claim. A radical improvement, of course, can be patented; while it literally infringes the basic patent claim, it may be protected under the 'reverse doctrine of equivalents', which will be discussed later.[242] In this regard, a decision of the German Federal Court of Justice holds that an embodiment which is the subject matter of a younger patent does not exclude infringement of an older patent which may, for instance, cover the younger patent's embodiment in general terms.[243] Considering that improvement/dependent patents infringe the basic patent in any way at least literally,[244] it seems worthwhile to discuss strategies for not discouraging improvement inventions while at the same time securing the reward of basic inventions.

Let us return to the *Olanzapine* case, as an example. After *Olanzapine*, less selection patents should be rejected at least on the ground of anticipation, i.e. for the basic patent disclosing the selected species.[245] *Under this setting, the more selection*

238 *See e.g.,* EPC Art. 69.
239 *See* Mark A. Lemley, *The Economics of Improvement in Intellectual Property Law* 75 Tex. L. Rev. 989, 991, 1000-1009 (1996-1997).
240 Improvement patent generally refers to a patent that is issued on an application filed later in time than a prior application and tends to build up the previously disclosed or patented invention . Thus, it does not have the same meaning as 'selection invention', however, it would be helpful to use this term to find the relationship between the selection invention and basic invention. The same goes to the 'dependent patents'.
241 Lemley *supra* note 256, at 1007-1013.
242 *Id*.
243 Hans-Rainer Jaenischen, *The Grant of a Compulsory License for Recombinant γ-IFN in Germany*, 11 Biotech. L. Rep. 369, 375 (1992); See also Bundesgerichtshof [BGH] [Federal Court of Justice] Jul.12, 1990, GRUR, 436 1991 (Ger.); *See also* Merges *supra* note 297, at 873-878.
244 *See also* Irina Haracoglou, Competition Law and Patents: a follow-on innovation perspective in the biopharmaceutical industry 60 (2008) (noting that it is broadly referred to as the "dependent patent", as it cannot be worked without infringing the earlier issued patent).
245 *See generally supra* III.B.

patents are granted, the more issues with respect to the exploitation of selection inventions arise, especially when the basic patent holder denies granting of a license. Where can we find remedies for these problems?

b) Possible Solutions

Improvement patents held by the patentee of the basic patent do not pose a problem in this respect, except for the "evergreening" issue.[246] Therefore, only those patents which are held by a third party who cannot exploit its invention without licensing the basic patent will be discussed.

(1) Reverse Doctrine of Equivalence

"The reverse doctrine of equivalence" is a doctrine that exists only in the US. This doctrine can only be applied where an improvement patent literally infringes the scope of a basic patent. If the degree of its improvement is sufficiently radical it can be found non-infringing even though it may literally and clearly infringe the scope of the basic patent.[247] This doctrine was named so because it is the opposite concept of the doctrine of equivalence, where something can be found infringing despite the fact that it is not literally covered by the claim.[248] Although the first reverse doctrine case cited is a case from 1898[249] and the U.S. Federal Circuit recognized its potential significance for the biotechnology industry,[250] this doctrine has rarely been applied in practice.[251] This is because a sufficient level of radicalness is not certain and there is concern that it might reduce the basic patentees' incentives in the first place. Accordingly, this doctrine is better used restrictively .[252]

246 *See generally supra IV.C.1.*
247 *Id.,* at 1011.
248 *See* Robert Merges, *Intellectual Property Rights and Bargaining Breakdown: The Case of Blocking Patents* 62 Tenn. L. Rev. 75, 91 (1994-1995).
249 Westinghouse v. Boyden Power Brake Co., 170 U.S. 537 (1898).
250 *See* Scripps Clinic & Research Foundation v. Genentech, Inc., 927 F.2d 1565 (Fed. Cir. 1991) (holding Genentech's recombinant version of the Factor VIII:C does not infringe Scripps' version of Factor VIII:C, which is isolated from the human blood, based on Genentech's version's far most commercial significance).
251 *See* Merges, *supra* note 248, at 75, 91, and 93-94.
252 *See* Merges, *supra* note 297, at 867-868.

(2) Patent Act Consideration – Compulsory License

A compulsory license as an exceptional measure, i.e., a license authorised by a governmental body to a third party, for using the patent without the patentee's consent, for various reasons,[253] can be granted either on a significant improvement or on a radical improvement.[254] Art. 31(1) of the Agreement on Trade-Related Aspects of Intellectual Property Rights [hereinafter "TRIPs Agreement"[255]] provides several grounds for the granting of a compulsory license, which is determined by the member states, but is not binding. For example, the Japanese,[256] German,[257] and Korean[258] Patent Acts have provisions for compulsory licenses for reasons of public interest and for dependent patents. The UK Patents Act[259] and the Swiss Patent Act[260] provide a compulsory license provision for a dependent patent. In Europe, the authorities may be more willing to grant compulsory licenses. However, relatively few such licenses have actually been granted.[261] Since these provisions are rarely used, a German case concerning gamma-interferon will be reviewed to explore the possibility of granting a compulsory license for a dependent patent.

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253 Jerome H. Reichman et al., *Non-Voluntary Licensing of Patented Inventions: Historical Perspective, Legal Frame-work under TRIPS, and an Overview of the Practice in Canada and the USA*1-2, (June 2003), available at http:// www.ictsd.org/pubs/ictsd_series/iprs/CS_reichman_hasenzahl.pdf.; *See also* Haracoglou, *supra* note 244, at 50.

254 This is according to Lemley's definition. The more general term would be a 'dependent patent'.

255 Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, Legal Instruments – Results of the Uruguay Round vol. 31, 33 I.L.M. 81 (1994).

256 Tokkyohō [Japanese Patent Act] Art. 93, para. 1 (Japan) (Award granting non-exclusive license for public interest) and Art. 92, para. 1 (Award granting non-exclusive license to work own patented invention).

257 Patentgesetz [German Patent Act, hereinafter GPA] Art 24(1) and 24(2) (Ger.); *translated* in World Intellectual Property Organization, Patent Law, http://www.wipo.int/clea/docs_new/pdf/en/de/de081en.pdf
Art. 24(1) : "A non-exclusive authorization to commercially exploit an invention shall be granted by the Patent Court in individual cases in accordance with the following provisions (compulsory license) if
1. the applicant for a license has unsuccessfully endeavored during a reasonable period of time to obtain from the patentee consent to exploit the invention under reasonable conditions usual in trade; and
2. *public interest* commands the grant of a compulsory license."
Art. 24(2): *see infra* note 268 and accompanied text.

258 Teukheo boeb [Korean Patent Act] Art 107, para. 1, no. 3 (S. Kor) (Award for the Grant of a Non-exclusive License and Art 138, para. 1 (Trial for Granting a Non-exclusive License).

259 Patents Act of 1977, §§ 48, 48A(1)(b)(i), (4), (c) (2004)(U.K.); For the U.S. Practice, *See generally also* David A. Balto & Andrew W. Wolman, *Intellectual Property and Antitrust: General Principles* 43 IDEA 395, 409-410, (2003) (addressing general trend in the United States with regards to compulsory licensing of which is not in the favor).

260 Switzerland Patent Act Art. 36; *See also supra* note 244, at 60.

261 Jerome H. Reichman, *Intellectual Property in the Twenty-first Century: Will the Developing Countries Lead or Follow?* 46 Hous L. Rev. 1115, 1139, (2009).

Since the introduction of the compulsory licensing provision into the German Patent Act in 1911, 12 applications for compulsory licenses have been filed before the German Federal Patent Court.[262] From these, only one compulsory license has been granted under section 24(1) of a GPA, on June 7, 1991.[263] This grant allowed the German company Bioferon to produce, to offer, and to market 'Polyferon' containing recombinant human gamma-Interferon *for a new medical indication* (chronic polyarthritis, which was widespread in Germany) which was developed by Bioferon itself. It was interpreted that the German Federal Patent Court stimulated the development of new medical uses of known products and enhanced the medical care through granting compulsory licenses.[264] It was further interpreted that the acknowledgeable necessary public interest under GPA § 24(1) could be i) a drug at issue showing characteristics which were not shown by an already marketed drug or ii) a drug avoiding undesired side effects of a marketed drug.[265] However, the German Federal Court of Justice revoked this license in December 5, 1995,[266] mainly based on lack of sufficient 'public interest" to justify granting a compulsory license.[267]

In the *Olanzapine* case, if the two patentees were different, one might have had recourse to GPA § 24(2),[268] which corresponds to Article 31(1) TRIPs Agreement and allows the grant of a compulsory license for a dependent patent, which cannot be exploited without using another invention protected by a previous patent and belonging to a different owner.[269] Section 24(2) of the GPA provides for compulsory licensing for dependent patents as follows:

> "If the applicant for a license is unable to exploit an invention for which he holds protection under a patent of later date without infringing a patent of earlier date, he shall be entitled within the framework of subsection (1) to request the grant of a compulsory license with respect to the owner of the patent of earlier date *if his own invention comprises*, in comparison with that under the patent of earlier date, *an important technical advance of considerable commercial significance*. The patentee may require the applicant for a license to grant him a counter license under reasonable conditions for the exploitation of the patented invention of later date."

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262 Astrid Buhrow et al., *Grenzen Ausschließlicher Rechte Geistigen Eigentums durch Kartellrecht (Q187) [Limitations on Exclusive Intellectual Property Rights by Competition Law (Q187)],* Gewerblicher Rechtsschutz und Urheberrecht Internationaler Teil. [GRUR Int.], 407, 409 (2005) (Ger.).

263 Bundespatentgericht (BPatG) [Federal Patent Court] Jun. 7, 1991, GRUR Int., 98 (1994) (Ger.).

264 *See* Jaenischen, *supra* note 243, at 375.

265 *Id.*

266 Bundesgerichtshof [BGH] [Federal Court of Justice] Dec. 5, 1995, GRUR, 190, 1996 (Ger.).

267 *See* Kimberly M. Thomas, *Protecting Academic and Non-Profit Research: Creating a Compulsory Licensing Provision in the Absence of an Experimental Use Exception*, 23 Santa Clara Computer & High Tech. L. J. 347, 364-365 (2007).

268 *See supra* note257, Section 24(2).

269 *See* IPR Helpdesk, *Some Basic Issues Surrounding Improvements Made to Patented Invention and to Dependent Patents,* available at *http://www.ipr-helpdesk.org/.*

This provision provides the opportunity to obtain a compulsory license under the condition that the improvement patent contains an important technical advance of considerable economic significance, in comparison with those of the basic patent, and plays a role in preventing the huddling of innovation by blocking patents[270] and in improving the technological development.

In the U.S., it was suggested that the U.S. courts should grant compulsory licenses as a remedy for antitrust violations and/or that compulsory license provisions should be incorporated into the U.S. Patent Act.[271] The more preferable solution would be enacting (or implementing) compulsory licensing provisions, for the public's interest[272] and for the dependent patent.[273]

(3) Competition Law Consideration – the Orange Book Standard Decision

One may try to find remedies against the blocking effect of basic patents in the competition law area, namely, by way of claiming a so-called "compulsory license objection" or "Euro-defence"[274] against the action for patent infringement. In this regard, the German Federal Court of Justice recently pronounced its decision on the *Orange Book Standard* case (KZR 39/06).[275]

The patent at issue was a patent on a standard known as the "Orange Book Standard" related to the manufacture of writable CDs. The Court provided some guidelines for this defence in that the defendant had to act like a "true licensee", by i) determining a reasonable license fee objectively (presumably based on common practice in the relevant industry or market intelligence); ii) regularly rendering accounts; iii) paying or depositing (e.g. into an escrow account) the hypothetical license fees.

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270 Joseph Straus, *Patent Application: Obstacle for Innovation and Abuse of Dominant Position under Article 102 TFEU?* J. Eur. & Compet. Prac., 1, 12-13 (forthcoming 2010) doi: 10.1093/jeclap/lpq011.

271 *See* Jackson, *supra* note 2, at 119, 142-143.

272 *See* Thomas, *supra* note 267, at 365.

273 *See also* Jerome H. Reichman, *Harmonization without Consensus: Critical Reflections on Drafting a Substantive Patent Law Treaty* 57 Duke L. J. 85, 116 (2007) (addressing when necessary, compulsory licenses to unblock dependent patents and enable improvers to reach the market could also be enacted, a solution that remains fully consistent with the TRIPs Agreement.).

274 *See* Thomas Hays, *An application of the European Rules on Trademark Exhaustion to Extra-market Goods* 91 Trademark Rep. 675, 679 (2001) (addressing the "Euro Defense" as follows: "Euro Defense" is a legal tactic akin to alleging "unclean hands". A defendant asserts that, while it may have infringed upon an intellectual property right under other circumstances, enforcement of that right would be a violation of the EC's competition laws, particularly of EC Treaty Articles 81 and 82 (now EFTU Articles 101 and 102)).

275 Bundesgerichtshof [BGH] [Federal Court of Justice] May 6, 2009, [GRUR], 694, 2009 (Ger.).

However, before an analogy to the situation of dependent patents can be drawn, to solve the above problem, a number of open questions should be answered by the Federal Court of Justice, like what is a reasonable amount of royalty, whether the defendant still can raise a non-infringement argument, and others.

c) Conclusion

The holdings in the *Olanzapine* and *Escitalopram* cases have heightened the level of disclosure in the prior art necessary to anticipate selection inventions. In addition to the discussion about the justification for allowing more selection patents, the limited exploitation thereof is another issue, once they are granted. In other words, the change in the patentability requirements could possibly just bring more but almost useless patents in so far as the basic patent is in force. This is even more so because a most adequate solution, the compulsory license, has hardly been used.

However, this issue may not be a real problem in jurisdictions whose laws allow the grant of compulsory licenses for dependent patents and try to use this legal instrument to a greater extent and as necessary.

D. Different view in other jurisdictions

1. Selection Inventions in Korea

Recently the Korean Supreme Court rendered its decisions on the patentability of enantiomer patents on the world's top blockbusters, namely Plavix and Lipitor.

a) Clopidogrel Decision[276]

Sanofi-Aventis' Korean Patent No. 103094 on dextro-rotatory[277] enantiomer of clopidogrel was challenged over the earlier patent claiming clopidogrel as racemate.[278]

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276 Supreme Court Decision [S. Ct.],(hereinafter 'Sanofi-Aventis') 2008Hu736, 2008Hu743, Oct. 15, 2009 (S. Kor.).

277 "Dextro-rotatory" and "levo-rotatory" is another way of indicating the chirality of each enantiomer. However, there is no fixed relation to the (R)- or (S)- enantiomer. For example, an (*R)* isomer can be either dextro-rotatory or levo-rotatory.

278 The prior patent disclosed especially ".. is an asymmetric carbon atom. In fact, this formula represents both the dextro-rotatory molecule claimed as well as its levo-rotatory enantiomer.".

Based on the facts that the prior patent explicitly disclosed the compound having one chiral centre and two enantiomers, the Supreme Court held that in order to deny the novelty of selection invention, the prior patent should disclose the specific concept specifically, or a person skilled in the art can learn the existence of the selection invention directly from the prior patent based on the disclosure thereof and common knowledge at the time of application[279] . Further, the Court stated that "since clopidogrel was specifically disclosed and the person skilled in the art acknowledged the racemate, its dextro-rotatory enantiomer, and levo-rotatory enantiomers as separate compounds, it is *not necessary* that the method of separation or possibility of separation of enantiomers from racemates to obtain enantiomers are disclosed *unless the invention is directed to the method to separate dextro-rotatory enantiomer…"*[280]

With regards to obviousness, the Court held that in order for inventive step not to be denied, all specific concepts in the selection invention must show *qualitatively different or qualitatively same but quantitatively superior effects* to that of the prior invention,[281] the effect should be clearly disclosed in the specification of the selection invention by either a description of qualitative differences or data supporting any quantitative advantages.[282] The Court also said that a two-fold superiority in platelet aggregation inhibition or around 1.6-fold superiority in acute toxicity to a prior art racemate could not be regarded as superior considering that the administration of one enantiomer gave around 2-fold better effects than that of a racemate which is a 50:50 mixture of enantiomers.[283]

b) Atorvastatin Decision[284]

The patent in issue was Warner Lambert's Korean Patent No. 167101 claiming one enantiomer of atorvastatin, an anti-cholesterol drug sold under the brand name Lipitor[285] by Pfizer Inc.. The prior art disclosed atorvastatin as a racemate having two chiral centers as a common scenario.

279 Sanofi-Aventis, *supra* note 276, at Headnote 1.
280 *Id.*, at para 1.Na..
281 This requirement seems to be similar to those of I.G. Rule in U.K.
282 *Id.*, at Headnote 2.
283 *Id*., at para 2.Na..
284 Supreme Court Decision [S. Ct.],(hereinafter 'Warner Lambert') 2008Hu3469, Mar. 25, 2010 (S. Kor.)..
285 See also *supra* note 35 and accompanying text (Atorvastatin (Lipitor ®) is the top-selling global drug from 2007 and 2009 with sales of over $ 12.5 billion in 2009).

While citing the *Sanofi-Aventis*[286] case, the Supreme Court held that even though only the racemate of R-trans-heptanoic acid and S-trans-heptanoic acid was disclosed, considering that a carboxamide compound of formula I was acknowledged as separate 4 enantiomers and not as a mixture, a person skilled in the art could have acknowledged formula I's open-ring form, namely, R-trans-heptanoic acid and S-trans-heptanoic acid, as separate enantiomers, too, and thus that the prior art disclosed the R-trans-heptanoic acid .[287] The Court restated that the selection invention was recognized as separate enantiomers, not as a mixture, and it was not necessary to disclose the method of separation or the possibility of separation of the enantiomer from racemates unless the invention was directed to the method of separating the dextrorotatory enantiomer.

The Court also found it obvious since even under the consideration of hygroscopicity or solubility, which were argued by the patentee, there was no special disclosure in the specification which could show any qualitatively different or qualitatively same but quantitatively superior effects.[288]

2. Selection Inventions in Japan

It is rather clearly defined in Japan what a selection invention is; namely, where an invention with a generic concept is expressed in a cited reference, an invention with a more specific concept selected from the generic concept is called a "selection invention".[289] The Japanese Examination guidelines show how to determine the novelty of a selection invention as follows:

> "… if a chemical substance is expressed merely by its name or its chemical formula in a publication, and if it is not clear that a person skilled in the art can produce the chemical substance on the basis of the description in the publication, *even in the light of the common general knowledge as of the filing*, the chemical substance does not fall under "an invention described in a publication" under Article 29(1)(iii)." [290]

The guidelines further state that the prior art disclosure of a generic concept neither implies nor suggests an invention unless the specific concept can be directly derived from the generic invention *considering the common general knowledge*.[291]

It is not certain whether the above 'common general knowledge' corresponds to the 'disclosure' requirement or 'enablement' requirement when determining an-

286 Sanofi-Aventis, *supra* note276.
287 Warner Lambert, *supra* note 284, at para 1.Na..
288 *Id.*, at para 2. Na..
289 See Japanese Examination Guidelines, *supra* note 181, at 2.5.3.(3)(1).
290 *Id.,* at 1.5.3.(3)(2).
291 *Id.,* at 1.5.3.(4)(2).

ticipation. If a person skilled in the art can produce the chemical substance *based on the common general knowledge* at the time of application, however, a publication disclosing a chemical formula could be a novelty-destroying prior art reference.

Regarding the assessment of obviousness of selection inventions, the court held that it may be regarded as nonobvious when it provides an advantageous effect which is not disclosed in the prior art, *qualitatively different or qualitatively same but quantitatively prominent* compared to an invention with a generic concept, neither of the effect being foreseeable with the eye of a person skilled in the art.[292]

3. Summary and Conclusion

According to the Korean Supreme Court, a document which discloses clearly all elements of an invention can certainly be an anticipating prior art reference. In addition, in case that expressions regarding the invention are not sufficient or there is a deficiency of disclosure, a document can be an anticipating prior art reference if a person skilled in the art can easily acknowledge the content of the invention based on the common knowledge or rule of thumb.[293] Different from U.S. or European practice, it does not seem that the disclosure and enablement requirements are clearly distinguished in determining anticipation.[294] Although it seems as if insufficiency of disclosure can be augmented by the knowledge of a person skilled in the art under Korean practice, it would be desirable that the Supreme Court would clarify its view on this issue. Further it would also be interesting to see how the Japanese High Court rules on this issue.

292 Tōkyō Kōtō Saibansho [Tokyo High Ct.] Oct. 31, 1963, Sho 34 (Gyo Na) No. 13 (Japan); Tōkyō Kōtō Saibansho [Tokyo High Ct.] Mar. 30 1978, Sho 51 (Gyo Ke) No. 19 (Japan); Tōkyō Kōtō Saibansho [Tokyo High Ct.] Sho 51 (Gyo Ke) 19 (Japan); Tōkyō Kōtō Saibansho [Tokyo High Ct.] Jul. 30, 1983, Sho 53 (Gyo Ke) No. 20 (Japan); Tōkyō Kōtō Saibansho [Tokyo High Ct.] Sept. 8, 1985, Sho 60 (Gyo Ke) No. 51 (Japan).

293 *In re* University of Florida Research Foundation, Inc., Supreme Court Decision [S. Ct.], 2004Hu2307, Mar. 24, 2006 (S. Kor.).

294 Chaho Chung, et al., *Seontaekbalmyoungin Geoulsang Eesungilchae Balmyoungeui Shingyuseoung Pandan [Novelty Determination of Enantiomer Invention as a Selection Invention],* 49 Seoul National University The Law, 355, 399 (2008)(S. Kor.).

V. Conclusion

This series of decisions on patentability of selection inventions in Europe and in the U.S. clarified or confirmed the novelty requirement thereof. Especially in Germany where the highest litigation activities are observed (between 50 and 70% of all patent litigation activities in Europe),[295] the *Olanzapine* decision was expected and welcomed[296] because it finally harmonized the German approach with the EPO's and other member states' case law.

The essence of these decisions in three jurisdictions is the enablement requirement within the context of anticipation on selection inventions. Namely, it was held that the decisive factor regarding this requirement was what could be *directly and unambiguously* derived from a prior art document. For this purpose, the disclosure of information should enable the person skilled in the art to obtain the specific substance. For example, a prior art reference claimed as a Markush type invention should enable a specific claimed compound (*individualized description*), and the prior art reference of a racemate can only enable a racemate when it provides a method of resolving the claimed enantiomer. This heightened requirement of disclosure in the context of patent-defeating purpose may raise several issues, such as the vague distinction between the tests of novelty and obviousness, possible invalidity grounds for basic patents, and other disclosure related issues.

Moreover, this lowered requirement for novelty may increase the number of selection inventions, which in turn may raise other issues after selection patents are granted. In case the selection patent holder is different from the patentee of the basic patent in force, the former cannot exploit his invention without licensing the basic patent (so-called 'blocking effect'). If the selection invention is owned by the patentee of the basic invention, it would increase the possibility of extension of exclusive rights (so-called 'evergreening effect'). Furthermore, it is reported that where incentives for improvement are increased, incentives for innovative inventions are decreased.[297] Thus, it may encourage companies to conduct more researches on selection inventions which become easier to be patented. This position might be viewed as being in line with some U.S. Federal Circuit decisions where

295 Dietmar Harhoff, Economic Cost-Benefit Analysis of a Unified and Integrated European Patent Litigation System, 2009 available at http://ec.europa.eu/internal_market/indprop/docs/patent/studies/litigation _system_en.pdf.

296 *See e.g.,* Bublak *supra* note 182, at 388.

297 Robert P. Merges, et al., *On the Complex Economics of Patent Scope*, 90 Colum. L. Rev. 839, 873-878 (1990).

the Court has applied the inherent anticipation doctrine in a broader fashion to cases which seemed to attempt evergreening of patents[298] and the recent EU Commission's report about the Pharmaceutical Sector Inquiry.[299] However this whole discussion may not apply where compulsory licenses with respect to dependent patents are granted, which has not yet happened to any significant degree.

298 Mueller, *supra* note 167, at 1106; *see e.g., Smithkline, supra* note 162 at 1342-44; *see also e.g.,* McNeil-PPC, Inc. V. L. Perrigo Co., 337 F.3d 1362, 1373 (Fed. Cir. 2003).

299 *See generally,* European Commission's pharmaceutical sector inquiry report, *supra* note 21.

Abstract

Selection inventions can be defined as inventions that have a specific concept selected from a prior broader or larger generic concept of invention, and that have superior or advantageous properties to the broader concept which have not been disclosed in the prior art. Considering innovations are mostly derived from existing technologies, selection inventions are typical examples. As recognized from the *IG Rule* in the U.K. jurisprudence which does not clearly distinguish novelty from obviousness, however, the novelty of selection inventions has been debated from the very beginning of their history. The importance of selection inventions, especially in the pharmaceutical industry is higher than previously, since this industry has seen R&D expenditure soar and the dearth of new medical entities over the last decade. According to the recent report of the European Commission on a pharmaceutical sector inquiry, this trend seems to be proven to some extent.

Selections in *Olanzapine* and *Escitalopram* cases, were directed to a species selection from a broad Markush type disclosure or an enantiomer selection from a racemate containing two enantiomers, respectively. Novelty of selection inventions was the core issue in the courts, since the prior art reference did disclose either the genus of a claimed compound as a broad Markush type claim covering species (Olanzapine) or a racemic mixture of two enantiomers (Escitalopram), but both did not enable the person skilled in the art. Overall, the courts held that the disclosure of a broad genus or a racemate itself is not sufficient to anticipate a claimed invention, and should provide "direct and unambiguous" disclosure or "individualized description" of claimed compound. For this purpose, the claimed compound should be enabled in the prior art reference. In *Olanzapine*, both the highest courts in Germany and U.K. parted from their old case law, namely, *Fluoran* regarding the novelty over genus disclosure and its *IG Rule* on special requirements on patentability of selection inventions. The assessment of disclosure in prior art references was heavily based on the difficulty of preparing the claimed compound.

The next issue before the courts was, of course, the obviousness requirement. Obviousness could be assumed based on the structural similarity of compounds, but this assumption was reverted in all courts again. It was interesting to see that the German Federal Court of Justice did not agree with the EPO's so called 'problem-solution approach' while alerting hindsight bias. But, not surprisingly various elements for determining obviousness were assessed in courts, like insufficient motivation to reach the claimed compound, teach-away, hindsight issues, unex-

pected results and the like. In *Escitalopram*, the previous failures to obtain the claimed compound, i.e., the difficulty of preparation played an important role in determining nonobviousness over the prior art reference.

The novelty requirement has a fundamental function in the patent system, since it is required to prevent from re-monopolizing something that already exists in the public domain. Thus the change in novelty assessment can have a significant impact on patent law. Determining novelty involves several relative elements, and among those, the enablement requirement within the context of anticipation raises the following issues. Firstly, since the difficulty of obtaining a claimed invention is assessed in the novelty test, the same step can be taken again when determining obviousness. Secondly, given that a prior art reference is a basic patent, since both a basic and its selection patent cover the same compound (selected species), this failure of enablement in the context of patent-defeating purposes may also mean the failure thereof in the context of patent-obtaining purpose. Thirdly, this disclosure issue may impact other concepts of disclosures in patent law, such as validity of priority claims, support of amendment over the original disclosure, limitation or validity of patents, and so on.

Since the level of obviousness is judged by a person skilled in the art, the perception of this hypothetical person plays a key role in determining obviousness. It was suggested in this paper that the courts might define a person skilled in the pharmaceutical art differently from they have done. Regarding the obviousness of enantiomers, one may easily compare the difficulty to obtain one compound out of two to that out of millions. It is, of course, not easy to find a meaningful guideline for the question of obviousness.

The scope of selection patents falls within the scope of basic patents. In case both patents belong to the same patentee, this may possibly be an "evergreening" situation. If the patent holder of a selection invention is different, the freedom to exploit the later patentee's exclusive right would be limited (so-called "blocking effect") until the basic patent expires. This is even more so because a satisfactory solution, the compulsory license, has hardly been used. Thus, one may also wonder how much the increased number of selection inventions would be helpful to society.

Lastly, this paper would like to pose i) whether this lowered bar for the patentability of selection inventions would provide more incentives for companies to focus on second-generation inventions rather than first-generation inventions, thereby making less new medical entities available in the future; and ii) whether society is ready to avail of selection inventions by providing proper legal schemes which may allow patentees of selection inventions to make those inventions more available.

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