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VÉRON & ASSOCIÉS AVOCATS

T R I B U N A L
D E G R A N D E
I N S T A N C E
O F P A R I S

■

3rd chamber 4th section

Docket No. **10/08089**

JUDGMENT
handed down on 30 September 2010

Original copy No.: 13

Summons of:
8 March 2007

CLAIMANT

RATIOPHARM GmbH
Graf-Arco-Strasse 3
D-89070 ULM
GERMANY

represented by Mr Pierre COUSIN-COUSIN MOATTY CHEVALIER, attorney-at-law, member of the Paris Bar – courthouse box #R159

DEFENDANT

H. LUNDBECK A/S
Ottiliavej 9,
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DENMARK

represented by Ms Marina COUSTE-HOWREY LLP, attorney-at-law, member of the Paris Bar, courthouse box L295

COMPOSITION OF THE *TRIBUNAL*

Marie-Claude HERVE, Vice-Presiding Judge
Agnès MARCADE, Judge
Rémy MONCORGE, Judge

assisted by Katia CARDINALE, Court Clerk

Enforceable copies delivered on: 30/09/10

DISCUSSION

At the hearing of 16 June 2010
held publicly

JUDGMENT

Pronounced by handing over the decision to the Court Clerk's office
After due hearing of the parties
in first instance

FACTS AND PROCEEDINGS

H. Lundbeck A/S is the holder of European patent EP 0 347 066 B1 designating France filed on 1 June 1989, claiming priority of a British patent dated 14 June 1988, and granted on 15 March 1995.

The protection of this patent in France was extended by means of the corresponding supplementary protection certificate (SPC) No. 02 C 0050 which is due to expire on 31 May 2014. It mentions that it markets, on the basis of this patent, an antidepressant drug called SEROPLEX (INN – Escitalopram) for which it was granted a marketing authorisation in the European Community on 7 December 2001.

By way of an act dated 8 March 2007, Ratiopharm GmbH served a summons upon H Lundbeck A/S before the *Tribunal de Grande Instance* of Paris for the invalidity of claims 1 to 5 of both the French designation of European patent EP 0 347 066 B1 and the corresponding SPC No. 02 C 0050.

By way of an order dated 11 February 2009, the Judge in charge of the case preparation noted that the MA applications in France on which Ratiopharm GmbH bases its interest in taking an action for invalidity of the French designation of the European patent have been withdrawn and said that there was no reason to note that Ratiopharm GmbH can no longer show "*a process for the filing, with the* Association Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS)[1] *of a marketing authorisation application*". Furthermore, he dismissed H Lundbeck A/S's request pursuant to Article 700 of the French Code of Civil Procedure and referred the case to the hearing of 4 May 2009 only on the issue whether Ratiopharm GmbH's action is admissible.

By way of a judgment dated 16 June 2009, this court held admissible Ratiopharm GmbH's action for invalidity of both the French designation of European patent EP 0 347 066 B1 and the corresponding SPC No. 02 C 0050 and dismissed H Lundbeck A/S's request to stay the proceedings.

By way of a judgment dated 8 December 2009, this court held inadmissible Ratiopharm GmbH's claim for the invalidity of claims 6 and 7 of the French designation of European patent EP 0 347 066 B1 as well as the corresponding SPC No. 02 C 0050 and reserved the requests relating to Article 700 of the French Code of Civil Procedure and to the costs.

[1] Translator's note: the French regulatory body for health products.

In its last pleading dated 12 May 2010, Ratiopharm GmbH requests that the *Tribunal*:
hold invalid claims 1 to 5 of the French designation of European patent EP 0 347 066 B1 for lack of novelty or at least for lack of inventive step pursuant to Articles 138-1a), 52-1, 52-4 and 56 of the European Patent Convention,
hold the invalidity of the supplementary protection certificate No. 02 C 0050 pursuant to the provisions of Articles 15c), 15a), 3c) and 3d) of EC Regulation No. 1768/92,
3c) on the ground that Escitalopram has already been the subject of a SPC No. 95C0009 and
3d) on the ground that since the presence of the MA for Citalopram only has Escitalopram as an active principle, the MA relating to Escitalopram cannot be considered as the first MA pursuant to EC Regulation No. 1768/92,
order that the judgment to be handed down be communicated to the INPI[2] in order to be registered in the French Patent Register;
grant the sum of €100,000 pursuant to Article 700 of the French Code of Civil Procedure.

Concerning the admissibility of its requests, it puts forward the judgment of 16 June 2009, considers that the interest in the action should be appraised at the date of the summons and specifies that its MA applications for Escitalopram were withdrawn in France subsequently to the serving of the summons.

It adds that as a current or potential competitor, it has an interest in lodging an action for the invalidity of the French designation of the European patent at issue because it is already marketing a generic drug of Citalopram and that, as it is already present on the market of antidepressant drugs belonging to the family of serotonin reuptake inhibitors, it naturally has an interest and wants to develop its drug range with a product containing Escitalopram, and wants to do so before 2014.

Concerning the validity, it explains that Citalopram is a racemic compound containing the (+)enantiomer and the (-)enantiomer in equal quantities and that it is a selective serotonin reuptake inhibitor that is used as an active ingredient in the drug Seropram marketed by Lundbeck for major depressive episodes and for the prevention of panic attacks with or without agoraphobia.

It considers that the subject-matter of the patent is a particular enantiomer of Citalopram, namely its (+)enantiomer whose formula is (+)-1-(3-dimethylaminopropyl)-1-(4'fluorophenyl)-1.3-dyhydroiso-benzofuranne-5-carbonitrile and whose INN is Escitalopram.

[2] Translator's note: French Industrial Property Institute

According to Ratiopharm GmbH, the patent description states that almost the entire therapeutic activity with regard to depression in particular is achieved by the (+)enantiomer, since the (-)enantiomer is deprived of all activity.

It infers therefrom that when the racemic (Citalopram) is administered, half the quantity administered is inefficient for the treatment of depression and that, for the same quantity of product, the (+)enantiomer is twice as active as the racemic mixture containing the two enantiomers in equal quantities.

It considers that in the presence of a racemic, the skilled person, within the framework of the common practice of his routine operations, would necessarily consider that one of the enantiomers would have a different activity, *i.e.* in particular the hypothesis that the entire activity would reside in one of the enantiomers and he would verify this hypothesis by performing tests on the activity of each enantiomer in the mixture. It specifies that in order to verify this hypothesis, he necessarily had to separate each of the enantiomers contained in the racemic mixture and perform tests on them. It adds that the separation operations that thus allow one to test each enantiomer are still part of the routine operations. It then considers that by performing all these routine operations, the skilled person could not be surprised to note that the Citalopram activity actually exclusively came from its (+)enantiomer, *i.e.* Escitalopram, and that Lundbeck alleges in vain that it reports the higher efficiency of Escitalopram.

In order to dispute the validity of claim 1 of the European patent at issue, the claimant contends that this claim is invalid for lack of novelty over the prior art documents, namely patents KEFALAS FR No. 2 338 271 filed on 14 January 1997 or LUNDBECK EP 0 171 943 filed on 19 July 1985 or, in the alternative, for lack of inventive step considering the separation of the enantiomers using HPLC chiral chromatography.

According to the claimant, these prior art documents disclosed to the skilled person the (+)enantiomer as well as the means for the isolation thereof and for testing its antidepressant activity in order to verify some technical knowledge that identifies with claim 1 of the LUNDBECK patent EP 0 171 943. It specifies that, should the *Tribunal* consider that the cited prior art documents did not make the Citalopram (+)enantiometre[3] available to the public before the priority date of the patent at issue, this enantiomer obviously results from these documents for the skilled person who knew that the therapeutic activity

[3] Translator's note: typing error, should read « enantiomer »

of a racemic compound may originate from only one of its enantiomers. It infers therefrom that this skilled person could only be anxious not to administer, in a pharmaceutical composition, a non-active compound that could even turn out to be toxic and that he was therefore immediately prompted to separate the Citalopram enantiomers described in the KEFALAS or LUNDBECK prior art documents. It adds that the skilled person, aware of chiral columns that may be used or of other prior methods, would have separated the two enantiomers without performing the slightest inventive step.

Ratiopharm also contends the lack of inventive step of claim 1 considering that the skilled person could obtain the Citalopram enantiomers using other methods. It then puts forward the resolution of a racemic mixture through the formation of Citalopram diastereoisomers and the stereospecific synthesis of the desired enantiomer. It bases this assertion on a report by Professor ROSSET.

Concerning the validity of claims 2 and 3, Ratiopharm puts forward the KEFALAS French patent FR 2 338 271 for lack of novelty or at least for lack of inventive step.

Concerning claims 4 and 5, the claimant puts forward, with regard to the novelty and the inventive step, patents KEFALAS FR 2 338 271 and LUNDBECK EP 0 171 943.

Concerning the SPC, it considers that claims 1 to 5 whose invalidity was demonstrated are claims that relate to the active principle and to the pharmaceutical composition containing it and these are the claims that confer protection on the product which is the subject of the MA for the drug referred to in the SPC. It infers therefrom that the SPC is invalid pursuant to Article 15 of EC Regulation 1768/92.

It adds that the SPC at issue is also invalid pursuant to the above-cited provisions on the ground that the MA on which basis the SPC was granted is not the first MA of this product, *i.e.* the active principle of the drug, contrary to the provisions of Article 3-2 of the above-cited regulation.

It also considers that a SPC was granted on the basis of the KEFALAS patent FR 2 338 271. It infers therefrom that since the product has already been the subject of a certificate, the SPC at issue is invalid pursuant to Article 3 b) of the above-cited regulation.

In its recapitulative pleading notified on 27 May 2010, H Lundbeck A/S wishes:
that it be noted that Ratiopharm GmbH acknowledged and admitted in its summons and in its subsequent pleadings that the "10-year period of data protection granted for the specialty "Escitalopram" will expire in December 2011";
That the Court,
As a main request,
hold inadmissible Ratiopharm GmbH's action for invalidity on the ground of a lack of interest in the action;
stay the proceedings, at least until Ratiopharm GmbH is able to prove the grant of MAs in France that will show its "will to market";
In the alternative,
dismiss all of Ratiopharm GmbH's requests;
hold that claims 1 to 5 of the French designation of European patent EP 0 347 066 B1 are valid;
hold that SPC No. 02 C 0050 is valid;
hold that SPC No. 02 C 0050 will expire on 31 May 2014;
In the very alternative,
appoint an expert to investigate the inventive nature of the European patent at issue at the priority date thereof;
hold that the expert's mission will relate to the resolution by diastereoisomers and to the stereospecific synthesis of the Citalopram enantiomers at the priority date of the European patent and that it shall not exceed four months;
As a main claim, in the alternative and in the very alternative,
order Ratiopharm GmbH to reimburse it, upon presentation of the supporting documents, for all the expenses incurred in its defence;
order Ratiopharm GmbH to pay to it the sum of €600,000 pursuant to Article 700 of the French Code of Civil Procedure;
order the provisional enforcement of the decision;
order Ratiopharm GmbH to pay the entire costs.

It argues in substance that:
the claimant's action is inadmissible for lack of interest, considering that the MA applications filed in France have been withdrawn and that there is no claim currently pending; moreover, the MA applications filed in the other States of the Union have been suspended;
if the action is held admissible, the proceedings should be stayed until the claimant has proven that it fulfilled the administrative obligations laid down in the applicable texts,
the European patent at issue covers an antidepressant drug (Escitalopram) that is more efficient than Citalopram and has a distinct pharmacological mechanism of action, the chemical entities concerned are distinct entities;

claims 1 to 5 are necessarily new over the KEFALAS French patent and the LUNDBECK European patent, which is confirmed by the numerous legal decisions in which the validity of this patent has already been dealt with;
the problem faced by the skilled person was the preparation of an antidepressant drug that is more efficient than Citalopram;
in the absence of all information likely to direct the skilled team towards the separation of the Citalopram enantiomers in order to obtain an antidepressant drug that is more efficient than Citalopram, and considering the common knowledge and the routine tests in 1988 (the patent priority date and a period when Citalopram was enjoying huge success), the preparation of Escitalopram necessarily involved an inventive step;
it was not obvious in 1988 to search for a more efficient antidepressant drug by separating its enantiomers using the HPLC chiral chromatography;
the invalidity request for lack of inventive step based on the stereospecific synthesis of the "desired" enantiomer, a process covered by claim 6 of the European patent, is inadmissible because it repeats word for word the arguments put forward in support of the invalidity of this claim 6 considered as inadmissible in the judgment dated 8 December 2009;
the SPC cannot be held invalid since the patent is valid;
the MA for Citalopram and that of Escitalopram are distinct and the one granted for Citalopram cannot be considered as the first MA for an Escitalopram-based speciality, which is a new active substance, because it would not have authorised the marketing thereof;
Escitalopram has not already been the subject of the SPC which extended the protection of Citalopram.

The end of the proceedings was ordered on 2 June 2010.

GROUNDS FOR THE DECISION

On the plea of inadmissibility

Article 31 of the French Code of Civil Procedure provides that the right of action is available to all those who have a legitimate interest in the success or dismissal of a claim, without prejudice to the cases where the law confers the right of action solely upon persons whom it authorises to raise or oppose a claim, or to defend a particular interest.

H Lundbeck asserts that Ratiopharm based the admissibility of its action for invalidity on marketing authorisation applications for generic drugs of the reference drug Seroplex that have now been withdrawn

in France or suspended in the other European countries and that the action is therefore inadmissible for lack of interest as it can no longer be considered as a direct or potential competitor because it cannot prove that it meets the administrative obligations forbidding all marketing in the absence of a MA[4].

It is established that the interest in the success or the dismissal of a claim is appraised on the day when legal proceedings are instituted.

Moreover, there is no text specifying the persons who are authorised to lodge an action for patent invalidity and, in particular, for a patent relating to a medicinal product. Therefore, it should be considered that every interested person, *i.e.* every current or potential competitor, has an interest in taking an action for the invalidity of a patent.

In this case, as the *Tribunal* already pointed out in its judgment dated 16 June 2009, at the date when the summons was served, *i.e.* 8 March 2007, Ratiopharm's will to market generic drugs of the reference drug Seroplex had been demonstrated. Indeed, the MA applications in France for this specialty were pending before the AFSSAPS and MAs for Escitalopram had been granted in other European countries. Moreover, Ratiopharm is marketing a generic drug of Citalopram whose therapeutic indications are very close to Escitalopram.

Therefore, the existence of the patent at issue and of the SPC relating to it could hinder the development of its activity in the field of antidepressant drugs belonging to the family of serotonin reuptake inhibitors.

The fact that Ratiopharm's MA applications in France have been withdrawn and those in the other European countries suspended is irrelevant. Indeed, there is no text brought to the attention of the *Tribunal* that required the existence of a marketing authorisation application to justify the admissibility of an action for invalidity of the claims of a patent relating to a medicinal product.

Therefore, Ratiopharm proves it has a legitimate interest in taking an action for the invalidity of claims 1 to 5 of the French designation of European patent EP 0 347 066 B1.

H Lundbeck's plea of inadmissibility should be dismissed.

[4] Translator's note: the wording is unclear in this passage, this sentence has the following meaning: because it cannot prove that it meets the administrative **rules** that **subordinate** all marketing to the **grant** of an MA.

On the request to stay the proceedings

H Lundbeck requests that the proceedings be stayed until the claimant has proven the grant of a MA characterizing its "*will to market*" on the ground that it would be absolutely unfair, or even discriminating, not to take into account the administrative constraints relating to the marketing of generic products.

Nevertheless, since Ratiopharm's interest in taking an action for the invalidity of the patent at issue is not related to the existence of a MA pending on the French territory, it does not appear to be a proper administration of justice to stay the proceedings until the claimant has been granted such authorisation.

H Lundbeck's request to stay the proceedings should also be dismissed.

On the validity of the European patent

It should be noted at this stage that European patent EP 0 347 066 filed on 1 June 1989 is no longer in force and that it is considered as the patent that served as a basis for the grant of a supplementary protection certificate No. 02 C 0050 expiring on 31 May 2014 in the proceedings seeking the invalidity of claims 1 to 5 of the French designation of this European patent.

According to Article L 614-12 of the French Intellectual Property Code, a European patent may be revoked with effect for France by court decision on any one of the grounds set out in Article 138(1) of the Munich Convention. If the grounds for revocation affect the patent in part only, revocation shall be pronounced in the form of a limitation of the claims, the description or the drawings.

Article 138, paragraph 1 of the Munich Convention provides that a European patent may be revoked under the laws of a Contracting State, and with effect on the territory of this state only on the grounds that:
- the subject-matter of the European patent is not patentable under Articles 52 to 57;
- the European patent does not disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art;
- the subject-matter of the European patent extends beyond the content of the application as filed or if the patent was granted on a divisional application or on a new application filed under Article 61,

beyond the content of the earlier application as filed;
- the protection conferred by the European patent has been extended;
- the proprietor of the European patent is not entitled under Article 60, paragraph 1.

- *Field of the invention*

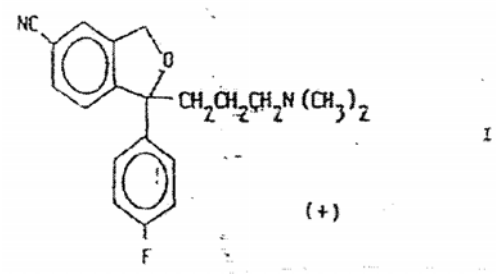
The patent at issue is entitled "enantiomers and their isolation". The invention relates to the two new enantiomers of the antidepressant drug Citalopram and the use of these enantiomers as antidepressant compounds as well as their possible use in geriatrics or in the treatment of obesity and alcoholism.

The patentee explains that the known compound, Citalopram, which has been disclosed in e.g. US patent No. 4,136,193 has proven to be an efficient compound in man and that the work in the development of this compound has been made with the racemate. He adds that Citalopram has been shown pharmaceutically to be a very selective inhibitor of 5-HT (or serotonin) re-uptake but that previous attempts to crystallize diastereomeric salts of Citalopram enantiomers have failed.
He then mentions that surprisingly, it has proven possible to resolve the intermediate product II (diol) into its enantiomers and, finally, in a stereoselective way, to convert these enantiomers into the corresponding Citalopram enantiomers.
He mentions that (page 3 of the description, lines 15 to 17) "*furthermore, it was shown to our surprise that almost the entire 5-HT uptake inhibition resided in the (+)-citalopram enantiomer*".

The patent comprises 7 claims, claims 2 to 5 being dependant claims.

In this case, the dispute only relates to the validity of claims 1, 2, 3, 4, 5 of this European patent.

They read as follows:
1 - (+)–1–(3-dimethylaminopropy1)–1–(4'-fluoropheny1)–1, 3–dihydroisobenzofuran–5–carbonitrile of the following general formula:



and nontoxic acid addition salts thereof.
2 - The pamoic acid addition salt of the compound in claim 1.
3 - A pharmaceutical composition in unit dosage form comprising, as an active ingredient, a compound as defined in claim 1.
4 - A pharmaceutical composition in unit dosage form comprising, as an active ingredient, the compound of claim 2.
5 - A pharmaceutical composition in unit dosage form, according to claim 3 or 4, wherein the active ingredient is present in an amount from 0.1 to 100 milligram per unit dose.

- *On the lack of novelty*

According to the claimant, claim 1 of the patent at issue that aims to cover the Citalopram (+)enantiomer is invalid for lack of novelty.

It puts forward two prior arts documents, namely the following patents:
- French patent No. 2 338 271 filed on 14 January 1977 by KEFALAS (hereinafter referred to as "the KEFALAS patent") describing Citalopram,
- European patent No. 0 171 943 filed on 19 July 1985 by Lundbeck (hereinafter referred to as "the LUNDBECK patent") describing an intermediate for the synthesis of Citalopram and a route for the synthesis of Citalopram.

Ratiopharm first puts forward example 3 of the KEFALAS patent describing Citalopram and the acid addition salts thereof. It also puts forward example 2 of the LUNDBECK patent describing Citalopram and an addition salt thereof: the bromohydrate.

According to the claimant, it appears from these two examples that they describe Citalopram, a racemic compound, *i.e.* comprising in a proportion of 50% the (+)enantiomer in its pure form as well as the means to isolate it and to test its antidepressant activity in order to verify some technical knowledge that identifies with claim 1 of the allegedly invalid patent.

It is not disputed that the Citalopram molecule, disclosed in the form of a racemate by the KEFALAS patent, has an asymmetric carbon and therefore presents two different non-superimposable mirror images, *i.e.* an (+)enantiomer and an (-)enantiomer.

However, the skilled person cannot infer from the two examples cited above that the invention subject-matter of claim 1, *i.e.* the Citalopram (+)enantiomer, can be found in its entirety, with the same elements composing it in the same form, the same arrangement, the same functioning with a view to achieve the same technical result.

Although these two examples describe Citalopram, a racemic compound that contains the (+)enantiomer, it cannot be inferred from these examples that they taught the skilled person, at the priority date of the allegedly invalid patent, the existence of this enantiomer and above all the possibility to isolate it.

Indeed, none of these examples refers to the stereochemistry or to a method for obtaining the separated enantiomers.

Consequently, the invalidity argument drawn from the lack of novelty is not founded, it being recalled that claims 2 to 5 depend on claim 1.

- *On the lack of inventive step*

According to the defendant, claims 1 to 5 of the French designation of the European patent are invalid for lack of inventive step because the skilled person who knew that the therapeutic activity of a racemic compound may reside in only one of its enantiomers and that he could only be anxious not to administer in a pharmaceutical composition a non-active compound that could even turn out to be toxic, was immediately prompted to separate the Citalopram enantiomers described in the KEFALAS or LUNDBECK patents.

It defines the skilled person as being part of a team composed of an organic chemist or a pharmacist specialising in organic molecules for therapeutic purposes and the synthesis thereof, a

pharmacist specialising in the study of organic molecules and also, as Citalopram is a chiral molecule, an analytical chemist specialising in the analysis and the separation of the organic molecules for therapeutic purposes.

It adds that as the skilled person, on the basis of his common knowledge, knew that the "liquid chromatography was a method of choice to separate the enantiomers" and was aware of chiral columns that could be used, he would have separated the two enantiomers without performing the slightest inventive step. According to it, upon reading the KEFALAS patent, he knew how to test the antidepressant activity of each of these enantiomers and he would obviously have isolated, in particular, the (+)enantiomer in its pure form. It infers therefrom that the skilled person would have been able to achieve, by simply carrying out operations deprived of inventive step, the product subject-matter of claim 1 of the patent at issue.

At the priority date of the allegedly invalid patent, *i.e.* 14 June 1988, the skilled person had at his disposal Citalopram disclosed in the KEFALAS and LUNDBECK patents, which is not disputed.

Although this is not clearly mentioned in the description of the invention at issue, it appears from the explanations provided by the patentee and recalled above that the problem faced by the skilled person was to suggest an alternative to the known compound, Citalopram, which has turned out to be an efficient antidepressant compound for man.

Therefore, the skilled person must be defined as a team composed of a medicinal chemist, a pharmacologist and a biochemist, all of them being clinicians, working in the pharmaceutical industry.

There is no element submitted to the discussion that demonstrates that the problem raised was the separation of the enantiomers composing Citalopram, unless one starts from the solution retained in the invention. Therefore, there is no reason to add to this team an analytic chemist specialising in the analysis and the separation of organic molecules for therapeutic purposes.

To solve this problem, the skilled person, in the presence of a chiral therapeutic molecule, could certainly be prompted to separate the enantiomers composing it, in particular by the regulation of the Food and Drug Administration in 1987 which recommended a complete description of the physical and chemical characteristics of the new drugs,

or even by a similar recommendation of the Japanese authority in 1985.

Moreover, it emerges from the elements submitted to the discussion and in particular from Mr Robert ROSSET's reports that the first separation of enantiomers dates back to the end of 19th century and was the work of Louis Pasteur and that, at the priority date of the patent at issue, several chiral drugs were already being marketed in the form of one of the two enantiomers (the one having the highest pharmaceutical activity) and that, consequently, the possibility to separate the two enantiomers from the chiral drugs was known, the said separation not being very easy.

However, unless one confirms the premise that all the other solutions were a priori dismissed, which would therefore lead to reason backwards *i.e.* starting from the invention in dispute, it is not demonstrated that the skilled person chose at all costs to separate the Citalopram enantiomers among those available to him to solve the problem he was faced with.

Indeed, as the defendant points out, nothing forced the skilled person to obtain the enantiomers separately from a regulatory point of view, despite the recommendations of some national authorities such as the FDA. Moreover, while the preparation of a racemic compound enantiomers was uncertain and expensive, Robert ROSSERT pointing out himself that this separation was not very easy, there was no element available to the person skilled in the art that could allow him to predict that one of the Citalopram enantiomers, namely the (+)enantiomer, would be more efficient, since Citalopram was a satisfying molecule in the treatment of depression. In addition, this molecule presented no toxicity requiring the separation of the enantiomers in order not to administer a non-active compound that could turn out to be toxic.

Finally, it does not emerge from the elements submitted to the discussion, as the claimant contends, that at the priority date of the patent "liquid chromatography was a method of choice to separate the enantiomers" and that, since the skilled person was aware of chiral columns that could be used, he would have separated the two enantiomers without performing the slightest inventive step.

Indeed, although it emerges from the articles submitted to the discussion by the claimant that at the priority date of the patent, the high performance liquid chromatography method (HPLC) suitable for a separation was know as such, this method appeared to be at an experimental stage in 1988.

Moreover, the availability on the market of the CHIRALCEL OD column that made the implementation of this method possible is not established because it emerges from the affidavit of Dr Nishimura, the President of DAICEL, submitted to the proceedings by the defendant that the CHIRALCEL OD column manufactured by this company was launched on the market in 1989 only. This statement is supported by Professor Clark who worked in relation with Mr Okamoto and who specifies that he was not able to obtain a CHIRALCEL OD column until 1989.

Therefore, it is not demonstrated that for the skilled person, the separation of the Citalopram enantiomers using the high performance liquid chromatography method (HPLC) was obvious at the priority date of the patent.

Ratiopharm also contends that claim 1 lacks an inventive step considering that the skilled person could obtain Citalopram enantiomers using other methods.

It then puts forward the resolution of a racemic mixture through the formation of Citalopram diastereomers and the stereospecific synthesis of the desired enantiomer.

Firstly, it considers that the skilled person, by implementing the well-known method consisting in the separation of the isomers by diastereomeric resolution and by using, as the starting product, intermediates or derivatives of Citalopram as those which the inventor of the patent in dispute, Dr Bogeso, mentions having implemented in an affidavit dated 8 September 2008, would have obtained Citalopram by simply carrying out operations devoid of inventive step, of which the claims of the European patent in dispute are also devoid.

However, it emerges from the very description of the patent in dispute on page 2 lines 26 to 28 that the previous attempts to crystallize diastereomeric salts of Citalopram enantiomers have failed. It also appears from the extensive literature submitted to the discussion that this method was known at the priority date of the patent for the difficulties it caused and the uncertain results it provided. Therefore, the skilled person, should he have considered this method, would rapidly have rejected it. Besides, Mr Rosset, the claimant's expert, considers in particular that the crystallization of diastereomeric salts, the asymmetric synthesis and the multi-stage synthesis were part of an approach that seemed to be very time-consuming.

Dr Bogeso also mentions in point 49 of his affidavit of 8 September 2008 that concerning his attempts to directly resolve Citalopram, he implemented several standard techniques aiming at crystallization, hoping that this would finally lead to the formation of crystals. However, he was unable to produce any crystal from these Citalopram derivatives.

Moreover, unless one conducts here again a reasoning backwards, *i.e.* starting from the invention, the *Tribunal* cannot follow the claimant's demonstration according to which the skilled person makes choices without any element from the state of the art suggesting him to do so.

Concerning the stereospecific synthesis of the desired enantiomer, Ratiopharm considers that the skilled person starts from the LUNDBECK patent EP 943 and that, to solve the problem consisting in modifying the synthesis route described in this patent in order to obtain not a racemic mixture but an optically pure enantiomer, there is reason to start from a precursor in the form of a single enantiomer: the diol. It then applies itself to demonstrate that the skilled person, in order to solve the technical problem he was faced with in view of the closest state of the art, had to use a pure diol enantiomer in (S), then to form a leaving group on the primary alcohol by forming a sulfonic ester and then to apply basic Sn2 reaction conditions in order to obtain a pure enantiomer of Citalopram.

This argument was developed in support of the invalidity of claims 1 to 5 of the French designation of the European patent in dispute in a pleading notified on 31 July 2009 and it cannot be considered as unfair for the party claiming the invalidity of a patent to develop a new reasoning in support of the argument drawn from the lack of inventive step raised since the beginning of these proceedings.

Moreover, there is reason to differentiate a new request that can be considered inadmissible, pursuant to Article 70 of the French Code of Civil Procedure, if it is not related to the main proceedings by a sufficient bond, and the new arguments developed by a party in support of a request that has already been lodged before the court. Therefore, the details provided by the claimant concerning the stereospecific synthesis of the desired enantiomer aim at supporting the lack of inventive step and therefore the invalidity of main claim 1 and cannot be considered as a new request.

Therefore, it does not collide with the *res judicata* of the judgment dated 8 December 2009 holding inadmissible Ratiopharm's request that claims 6 and 7 be held invalid.

Therefore, the inadmissibility raised by the defendant should be set aside.

On the other hand, as the defendant rightly puts forward, the stereospecific synthesis route for obtaining the desired enantiomer can only be explored by the skilled person in an attempt to isolate an enantiomer whose properties were necessarily known by the latter, before all implementation of a process allowing one to obtain it.

However, as was demonstrated above, it is not established by the claimant, unless one conducts a reasoning backwards, *i.e.* starting from the invention in dispute, that the skilled person chose at all costs the separation of the Citalopram enantiomers among the methods available to him for solving the problem he was faced with.

Therefore, in the absence of a prior art document that could prove such choice, the stereospecific synthesis of the desired enantiomer could not be obviously followed by the skilled person at the priority date of the patent.

Ratiopharm therefore fails in demonstrating the lack of inventive step of claim 1 of the French designation of European patent EP 0 347 066.

Consequently, the invalidity argument drawn from the lack of inventive step is not founded, it being recalled that claims 2 to 5 depend on claim 1.

Therefore, claims 1 to 5 of European patent EP 0 347 066 are valid.

<u>On the validity of supplementary protection certificate (SPC) No. 02 C 0050</u>

Ratiopharm's request that the SPC at issue be held invalid on the basis of the provisions of article 15 1° c) of EC Regulation No. 1768/92, now 469/2009 can only be dismissed, as claims 1 to 5 of the French designation of European patent EP 0 347 066, which represents the basic patent, have been considered valid.

Ratiopharm then contends that this SPC is invalid pursuant to the provisions of Article 15 1° a) and Article 3 b)

and d) of the above-cited regulation on the ground that MA NL 27 538 mentioned in the application for the grant of the SPC at issue is not the first marketing authorisation for the product, *i.e.* the drug active principle.

It puts forward that a previous MA NL 16 222 dated 26 December 1994 on which SPC 95 C 0009 was based had already been granted for the said product on the ground that the S-Citalopram is the active principle both when it is the only one present in the drug and when it is present with its enantiomer R, *i.e.* when Citalopram is present in the form of a racemate.

It emerges from the elements submitted to the discussion that on 23 August 1995, H Lundbeck was granted SCP No. 95 C 0009, based on patent FR 2 338 271 referred to as the KEFALAS patent and referring to MA NL 16 222 of 26 December 1994 as well as the product denomination "Citalopram bromhydrate".

SCP No. 02 C 0050 which is based on European patent EP 0 347 066 refers, as a first MA with effect in France, to MA NL 27538 granted on 21 August 2002 and to the product denomination "Escitalopram". Pursuant to the provisions of Article 13 of the above-cited regulation, it will expire on 31 May 2014, which is not disputed by the claimant.

According to the provisions of Article 3 b) and d) of the above-cited community regulation, a certificate is delivered if the product, as a medicinal product, was granted a marketing authorisation which is still valid pursuant to directive 2001/83/CE or directive 2001/82/CE depending on the case and that this authorisation is the first marketing authorisation of the product, as a medicinal product. The product is defined in Article 1 b) of the same text as the active principle or the combination active principles of a medicinal product.

The claimant considers that Escitalopram is not a new active substance and that the MA for Escitalopram is part of the global MA granted for Citalopram, which is confirmed according to the claimant by the decision of the Dutch Medicines Evaluation Board (MEB) which considered that the MA for Escitalopram could be applied for on the basis of Article 10 (1) of directive 2001/83/CE.

It is established that H Lundbeck was granted two distinct MAs to market Citalopram-based drugs and the Escitalopram-based ones.

However, the grant of two distinct MAs does not mean that these are different products as defined by the community regulation.

Although, as the defendant contends, the *Tribunal* cannot go against decisions of the European Commission as regards the duration of the protection concerning the preclinical and clinical data of, in particular, Escitalopram as a new active substance, it is up to the *Tribunal* to appraise whether the conditions relating to the validity of the SPC at issue are duly fulfilled with regard to the provisions of the above-cited community regulation and in particular to make sure that the MA referred to in the application really is the first marketing authorisation of the product, as a medicinal product.

However, it cannot be contended, as the defendant does, that Escitalopram must be considered as a simple variant of Citalopram on the ground that the (-)enantiomer only has little effect in the said product and must be compared to an impurity or to an inert compound.

H Lundbeck's statements during proceedings for the grant of an MA before the Swedish authority cannot be considered as showing that Citalopram and Escitalopram are one and the same product.

Indeed, in addition to the fact that these statements, which were made in the context of the grant of an authorisation is of no consequence in the appraisal of the validity of a SPC, the (-)enantiomer composing 50% of the Citalopram racemate cannot be reduced to a simple impurity even if its efficiency is less important than the (+)enantiomer. As a matter of fact, it appears from the elements provided that the (-)enantiomer, regardless of its activity, is a substance that contributes to the pharmaceutical activity of the Citalopram racemate. Moreover, according to the Vidal dictionary, for a common therapeutic indication, the Escitalopram dosage (20 mg) does not correspond to half the Citalopram dosage (60 mg).

Moreover, it emerges from the elements submitted to the discussion that the subject of MA NL 16 222 is a drug having the racemic form of Citalopram and not a mixture of its enantiomers, and that the subject of MA NL 27 538 is a drug having the form of an Escitalopram enantiomer.

Therefore, the product subject of the SPC at issue is another product than Citalopram as the racemic form and an individual enantiomer are distinct active principles presenting specific and distinct mechanisms of pharmacologic action.

Finally, it should be specified that Escitalopram, which is the subject-matter of claim 1 of European patent EP 0 347 066, cannot be considered as a simple Citalopram derivative, as it is a new product pursuant to patent law.

It results from the above that MA NL 27 538 mentioned in the application for the grant of the SPC at issue is the first marketing authorisation of the product Escitalopram.

The claimant finally puts forward the provisions of article 3 c) of the community regulation providing that a SPC can only be granted if the product has not already been the subject of a certificate. Therefore, it considers that the KEFALAS patent covers the racemate as well as each of the enantiomers and that the product Escitalopram protected by the KEFALAS patent has already been the subject of SPC 95 C 0009.

However, as was previously set out, the product subject of the MA referred to in SCP 90 C 0009 is a drug having the racemic form of Citalopram and not, as the claimant contends, the enantiomers.

Moreover, although the Court of Justice considered that Article 3 b) had to be interpreted as meaning that a product in the form mentioned in the MA is protected by a basic patent still in force, the certificate is likely to cover the product, as a medicinal product, in all the forms falling within the protection of the basic patent, it is not clearly established that the scope of the KEFALAS French patent covers not only the racemate but also each of the enantiomers and in particular an enantiomer in a pure form, as Citalopram and Escitalopram are different products pursuant to patent law.

Therefore, the request for invalidity of SPC No. 02 C 0050 is dismissed.

<u>On the other requests</u>

There is no reason to accede to H Lundbeck's assertion that Ratiopharm acknowledged and admitted in its summons and its subsequent pleadings that "the 10-year period of data protection granted for the specialty "Escitalopram" will expire in December 2011" as this request does not create any right.

There is reason to order Ratiopharm, the losing party, to pay the costs which shall be recovered pursuant to the provisions of Article 699 of the French Code of Civil Procedure.

Pursuant to Article 700 of the French Code of Civil Procedure, it must be ordered to pay to H Lundbeck a sum that can be fairly set at €150,000 in compensation for the irrecoverable costs paid by the latter for the assertion of its rights.

This sum appears sufficient and there is no reason to accede to H Lundbeck's request that the claimant be ordered to reimburse it, upon presentation of the supporting documents, for all the expenses incurred in its defence;

The circumstances of this case do not justify ordering a provisional enforcement.

ON THESE GROUNDS

The *Tribunal*, ruling by handing over the decision to the Court Clerk's office, after due hearing of the parties and in first instance,

Dismisses H Lundbeck's plea of inadmissibility;

Dismisses H Lundbeck's request to stay the proceedings;

Holds valid claims 1 to 5 of the French designation of European patent EP 0 347 066 B1 held by H Lundbeck;

Holds valid the supplementary protection certificate No. 02 C 0050 expiring on 31 May 2014 and held by H Lundbeck;

Consequently,

Dismisses all of Ratiopharm GmbH's requests;

Dismisses H Lundbeck's request that Ratiopharm GmbH be ordered to reimburse it, upon presentation of the supporting documents, for all the expenses incurred in its defence;

Holds that there is no reason to accede to H Lundbeck's assertion that Ratiopharm acknowledged and admitted in its summons and its subsequent pleadings that "the 10-year period of data protection granted for the specialty "Escitalopram" will expire in December 2011;

Orders Ratiopharm GmbH to pay to H Lundbeck the sum of €150,000 pursuant to Article 700 of the French Code of Civil Procedure;

Orders Ratiopharm GmbH to pay the legal costs which should be recovered pursuant to the provisions of Article 699 of the French Code of Civil Procedure;

Holds that there is no reason to pronounce the provisional enforcement.

Ordered and adjudged in PARIS on the THIRTIETH OF SEPTEMBER TWO THOUSAND AND TEN

The Clerk **The Presiding Judge**

signature *signature*