English translation by

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 1st section

Docket No. **07/16296**

JUDGMENT

Original copy No.: 8 **handed down on 28 September 2010**

CLAIMANTS

ACTAVIS GROUP
Dalshraun 1
220 Hafnarfjordur
Iceland

ALFRED E. TIEFENBACHER GMBH
Van-der-Smissen-Strasse 1
D-22767 Hamburg
Germany

represented by Mr Yves Bizollon – Bird & Bird, attorney-at-law,
member of the Paris Bar – courthouse box R255

DEFENDANT

MERCK SHARP & DOHME CORP, formerly known as MERCK & CO. INC
126 East Lincoln Avenue
Rahway, New Jersey 07065
United States of America

represented by Mr Pierre Lenoir – Allen & Overy LLP, attorney-at-law,
member of the Paris Bar, courthouse box J022

COMPOSITION OF THE COURT

Marie-Christine Courboulay, Vice-Presiding Judge
Marie Salord, Vice-Presiding Judge
Cécile Viton, Judge

assisted by Léoncia Bellon, Court Clerk

Enforceable copies delivered on: 5/10/10

DISCUSSION

At the hearing of 5 July 2010, held publicly before Ms Marie-Christine Courboulay and Ms Cécile Viton, reporting judges, who, without opposition on behalf of the attorneys-at-law, held the hearing alone and, after hearing the parties' attorneys-at-law, gave an account of it to the *Tribunal*, pursuant to the provisions of Article 786 of the French Code of Civil Procedure.

JUDGMENT

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

FACTS AND PARTIES' CLAIMS

Actavis is a company governed by the laws of Iceland, specialised in the manufacture and distribution of pharmaceutical products.

Merck & Co. is a company governed by the laws of the United States of America, a global leader in pharmaceutical products. It is the owner of European patent EP 0 724 444.

The patent was filed on 11 October 1994, under the priority of two American patent applications of 15 October 1993 and 17 March 1994. Mention of its grant was published in the European Patent Bulletin on 6 August 1997.

It is kept in force by the regular payment of yearly fees to the French patent office (*INPI*). It was filed and granted in English; a translation into French was handed to the *INPI* and published in the official bulletin of industrial property (*BOPI*) No. 42 dated 17 October 1997.

The patent relates to a "method of treating androgenic alopecia with 5α reductase inhibitors".

On 22 November 2007, Actavis Group and the company Alfred. E. Tefenbacher also known as A.E.T brought proceedings against Merck & Co. requesting that the Judge hold claims 1, 2 and 3 of the French designation of Patent EP 0 724 444 invalid for lack of industrial application, for lack of novelty and for lack of inventive step, in accordance with Articles L. 614-12 of the French Intellectual Property Code and Articles 53(c), 54, 56 and 138 of the European Patent Convention.

In their recapitulative pleading of 28 June 2010, Actavis Group and A.E.T requested that the *Tribunal:*
hold claims 1, 2 and 3 of the French designation of Patent EP 0 724 444 invalid for lack of industrial application, for lack of novelty and for lack of inventive step,
order the registration of the judgment to be handed down in the French patent register (*RNB*) held at the *INPI*, at the request of the Chief Court Clerk of the *Tribunal*,
order Merck & Co. to pay the sum of €100,000 each to Actavis and A.E.T on the basis of Article 700 of the French Code of Civil Procedure;

order Merck & Co. to bear the entire costs of these proceedings, which will be recovered by Mr Bizollon upon his statutory declaration.

The claimants argued that the technical problem which the patent aims at resolving would therefore be to administer, for the treatment of androgenic alopecia, a medicament whose active ingredient, known in its composition and for this application, is finasteride, in "the lowest dosage possible"; they also argued that claim 1 of the patent only relates to an administration dose, with this dose being purely arbitrary, and that the wording of claim 1 includes particular characteristics, relating not to the definition of the active ingredient nor even to the name of the pathology to be treated, but relating to the method of administration and to the dosage: characteristic (c) of claim 1 specifies the amount of active ingredient to be administered.
The claimants add that the choice of the value range from 0.05 to 1 mg of finasteride, the quintessence of the invention, is not explained; that it is only mentioned in column 2, lines 3 to 5 of the patent that the "applicants have surprisingly and unexpectedly discovered that a low daily dosage of finasteride is particularly useful in the treatment of androgenic alopecia"; that the patent does not contain any experimental results to that effect.
They add that claim 1 of the Patent is drafted in the "Swiss-type" format.

They allege that the methods of therapeutic treatment are excluded from patentability by Article 53(c) EPC (formerly Article 52(4) EPC), that a dosage is a method of treatment and as such is excluded from patentability, that the subject-matter of its claims is lacking novelty and does not involve any inventive step over the prior art cited.

In its latest pleading of 16 June 2010, Merck & Co. Ltd requested that the *Tribunal*:
Hold the patent valid.
Consequently,
dismiss all the claims of Actavis and A.E.T.
Order the claimants to pay to Merck & Co. Ltd the sum of €317,785.32 and the exchange value in euros on the day of the payment of $59,439.21 pursuant to Article 700 of the French Code of Civil Procedure.
Order the claimants to pay the entire costs of these proceedings which will be recovered by Mr Pierre Lenoir pursuant to Article 699 of the French Code of Civil Procedure.

Merck argued that parallel proceedings were brought in other European countries, that in its 21 May 2010 decision the High Court of Justice held that the patent was not a non-patentable method of treatment, that it was novel and consequently valid, that the *Bundespatentgericht* considered that the German designation of patent EP 0 724 444 was lacking novelty by relying on the decision issued by the *Bundesgerichtshof* in the Carvedilol II case.

Merck points out that in its decision G2/08 of 19 February 2010, the EPO Enlarged Board of Appeal answered that where it is already known to use a medicament to treat an illness, Article 54(5) EPC does not exclude that this medicament be patented for use in a different therapy treatment of the same illness; that such patenting is also not excluded where a dosage regime is the only feature claimed which is not comprised in the state of the art; and finally that where the subject-matter of a claim is rendered novel only by a new therapeutic use of a medicament, such claim may no longer have the format of a so-called Swiss-type claim as instituted by decision G 5/83; that consequently the subject-matter itself of patent EP 0 724 444 is not excluded from patentability by Article 53(c) EPC.
It also argued that the invention such as protected in patent EP 0 724 444 differs from the prior art owing to a new dosage and therefore satisfies the novelty criterion.
It analysed the different documents asserted as prior art, then defined the technical problem posed [to] the skilled person in order to assess the inventive step of the patent's teaching.

The closing order was pronounced on 30 June 2010.

GROUNDS

Patent EP 0 724 444 relates to a medicament for treating androgenic alopecia.

Alopecia refers to the thinning or permanent loss of hair from the head or body. There are different forms of alopecia (such as acute alopecia caused, for example, by chemotherapy, stress, nutritional deficiencies…, or localised alopecia caused by skin problems such as tumours, burns, radiotherapy, etc…). Among those different categories, androgenic alopecia is the most common and frequent form of hair loss: it involves the lowering of hair density or complete loss of hair, in particular in men. This widely spread phenomenon can be explained by various factors although it is commonly admitted that it is related to the effect of androgen hormones and in particular to the excessive accumulation of testosterone, hence its name "androgenic alopecia".

Main claim 1 of the Patent is worded as follows:
"The use of 17ß-(N-tert-butylcarbamoyl)-4-aza-5-alpha-androst-1-ene-3-one for the preparation of a medicament for oral administration useful for the treatment of androgenic alopecia in a person and wherein the dosage amount is about 0.05 to 1.0 mg."
It sets out three main characteristics:
1- use of finasteride for the preparation of a medicament for oral absorption,
2- useful for treating androgenic alopecia,
3- the (daily) dose of the active ingredient finasteride ranging from 0.05 to 1 mg.

The patent sets out the problem to be resolved which is "to administer the lowest dosage possible of a pharmaceutical compound to a patient and still maintain therapeutic efficacy".

It mentions the possible side effects only at the end of the first paragraph of the preamble in a quite general manner as follows:
"*However, these products, though devoid of hormonal effects, compete with all natural androgens for receptor sites, and hence have a tendency to feminize a male host or the male fetus of a female host and/or initiate feed-back effects which would cause hyperstimulation of the testes.*"

Nowhere is it mentioned in the patent that the invention is intended to prevent those side effects which are neither quantified nor assessed.

On the patentability of the invention covered by patent EP 0 724 444.

The scope of the patent over the state of the art, and therefore its subject-matter, should be defined.

In the preamble of the patent, it is explained that androgenic alopecia is the result of hyperandrogenic stimulation caused by the hormone 5α-DIHYDROTESTOSTERONE (DHT), that this hormone 5α-DIHYDROTESTOSTERONE (DHT) is known to form in the human body by the action of the enzyme TESTOSTERONE-5α-REDUCTASE (commonly identified as 5α-REDUCTASE) acting on the hormone TESTOSTERONE; it is also explained that the enzyme 5α-REDUCTASE is found upstream of the androgenic alopecia process, this enzyme having the effect of producing the 5α-DIHYDROTESTOSTERONE –DHT- which is itself the principal mediator of androgenic activity.

It was also known that androgenic alopecia can be stopped or prevented through the use of an inhibitor of the 5α-REDUCTASE, that the active ingredient known as finasteride (also named 17ß-(N-tert-butylcarbamoyl)-4-aza-5α-androst-1-ene-3-one) was already known as an inhibitor of the 5α-REDUCTASE and that the active ingredient was known to be efficacious for treating hyperandrogenic conditions.

On 20 February 1985, Merck filed a first patent EP 0 155 096 the subject-matter of which was to protect a group of compounds of inhibitors of testosterone 5α-reductase, including finasteride. This first patent covers in particular, in its claim 5, the inhibitor compounds including finasteride "for use in treating one or more of the hyperandrogenic conditions of acne vulgaris, seborrhea, female hirsutism, and benign prostatic hyperplasia by oral, parenteral or topical administration".

Therefore, the use of finasteride as a compound to treat hyperandrogenic conditions by oral, parenteral or topical administration had been disclosed since at least February 1985.

After this patent, Merck & Co. Ltd marketed finasteride under the trade name "Chibro Proscar" as a medicament administered orally (systemically) for the treatment of benign prostatic hyperplasia at a 5 mg dosage.

Merck then filed a second patent EP 0 285 382 on 30 March 1988, claiming the priority of a US patent of 3 April 1987, the subject-matter of which is the recommendation of the use of the inhibitor finasteride for treating androgenic alopecia. The teaching of this patent disclosed a topical application, or external application, of the substance for treating androgenic alopecia.

Consequently, the use of finasteride was known as a medicament to treat androgenic alopecia.

Those patents therefore mention various possible methods of administration of finasteride (topical and systemic) and consider certain specific dosages, these dosages ranging from 5 to 2,000 mg.

Therefore, the use of finasteride as the enzyme 5α-REDUCTASE inhibitor for treating androgenic alopecia had been taught for a long time as shown by the patents filed and exploited by the defendant itself.

This is the reason why claim 1 of the patent was drafted in the Swiss-type format which, before decision G2/08 of the EPO Enlarged Board of Appeal, allowed an already known substance to be patented for a second therapeutic use.

Merck & Co. Ltd adds that two types of 5α-REDUCTASE enzymes called isoenzymes were discovered after patent EP 382. One of these enzymes, called type-1 isoenzyme, can be found in skin tissues and in particular in the scalp, whereas the type-2 isoenzyme would mainly be found in the prostatic tissue.

Yet, if patent EP 0 724 444 does indeed refer to those two forms of isoenzymes in the preamble and specifies that the medicament marketed for the treatment of prostatic hyperplasia under the trade name "PROSCAR" is an enzyme 5α-REDUCTASE inhibitor (lines 42 to 45, column 1 of the patent), it does not make any reference to the particular form of finasteride used in the invention, only naming finasteride under its general form.

Never, at any time, does the patent claim, contrary to the defendant's pleading, a use of finasteride on type-1 enzyme 5α-REDUCTASE for the treatment of androgenic alopecia resulting from a particular discovery according to which finasteride would have a surprising and unexpected effect on the type-1 enzyme 5α-REDUCTASE.

It is only stated on page 3 of the patent and in a general manner that the "applicants have surprisingly and unexpectedly discovered that a low daily dosage of finasteride is particularly useful in the treatment of androgenic alopecia."

Consequently, the use of finasteride for treating androgenic alopecia was already known and therefore only the dosage of about 0.05 to 1.0 mg is claimed as novel and protectable.

It therefore remains to be determined whether Merck & Co. Ltd could patent the invention for a specific dosage, namely a daily dose of the active ingredient finasteride varying from 0.05 to 1 mg.

The defendant relies mainly on the EPO case law and particularly on decision G2/08.

As rightly pointed out by the claimants, the French courts are not bound by the decisions of the EPO which is not a court (as opposed to the European Union courts' decisions which are binding to national courts) so that these decisions even issued by the Enlarged Board of Appeal are merely indications of the analysis made by the EPO to grant European patents.

The same is true of the decisions of the courts of the European Union Member States which contribute to the legal debate by explaining the reasoning of each national court on the point of law referred to them, but which are not binding on national case law.

Article 53 (c) EPC provides that:
"European patents shall not be granted in respect of:
(…)
(c) methods for treatment of the human (…) body by surgery or therapy and diagnostic methods (…); this provision shall not apply to products, in particular substances or compositions, for use in any of these methods."

It is evident from the last sentence of this provision that it is possible to patent a substance or a composition (new and inventive) for the use of a therapeutic treatment, that is, within a medical treatment.

As to Article 54(4) EPC 2000, it provides that:
"…shall not exclude the patentability of any substance or composition, comprised in the state of the art, for use in a method referred to in Article 53(c), [therapeutic method] provided that its use for any such method is not comprised in the state of the art."

Article L. 611-16 of the French Intellectual Property Code excludes from patentability methods of treatment of the human or animal body by surgery or therapy and of diagnosis practised on the human or animal body considered to be capable of industrial application.

The same prohibition as that included in the EPC 2000 is therefore incorporated into national legislation.

The Enlarged Board of Appeal logically drew the legal conclusion from this new article which allows a same substance to be patented for a second therapeutic application, by stating that the Swiss-type format of the claims was no longer needed.

Furthermore, Article 54(4) EPC, which allows a same medicament to be patented for a second therapeutic effect, is totally silent on the possibility of patenting a certain dosage so that the Enlarged Board of Appeal's answer according to which "such patenting is also not excluded where a dosage regime is the only feature claimed which is not comprised in the state of the art", cannot be inferred from the Convention but from an interpretation of what a dosage is, that is, a second therapeutic application, which plainly it is not.

A specific dosage for the treatment of an illness constitutes neither a first nor a second therapeutic application but simply an indication of the range within which this substance is efficacious so as to treat such or such an illness in light of the tests and research completed and explained in the patent.

The therapeutic application is therefore limited to the use of a substance to treat a specific illness and not to the choice of such or such a dosage within a range of efficacious dosages.

The practitioner then has the task of determining in his therapeutic approach and in light of the other many factors to be taken into account (age, weight and gender of the patient, history and other illnesses, other treatments followed) which dosage is adapted to the treatment of the illness treated by this substance.

The ideal dosage as the only indication belongs to the virtual world and the doctor alone has the right to determine the dosage adapted to the patient by confronting his theoretical knowledge in the field of illnesses and medicaments with the particular case of his patient as he knows it, with all the interactions which the latter is subject to.

Also, it matters little that the medicament thus protected is marketed by the company which owns the patent or its licensees with a leaflet recommending a certain dosage since such information is merely an indication and only the doctor, in a therapeutic approach, has the right to prescribe the dosage adapted to each patient.

In addition, the leaflet which is required for marketing any medicament with an MA, contains the warning in France that these dosages are merely indicative and that a doctor should be consulted.

In the same way, all the cases where the medicament must not be taken and all the warnings relating to the counter-indications due to other illnesses and other treatments or other prohibitions are listed.

In any case, the marketing of the medicament is not a relevant criterion for assessing its patentability.

Consequently, it is possible to patent a medicament for the treatment of a first and then a second illness but not a dosage adapted to the treatment of those illnesses as by doing so, one attempts to patent a therapeutic method, which is excluded in order to belong to the field of care and to depend only on the concomitant freedom and responsibility of each doctor.

As stated by the *Bundespatentgericht*, "to develop a specific therapeutic care plan for a patient which includes the prescription and the dosage of the medicaments is an essential part of the treating doctor's activity. The determination of a dosage as an integral part of the therapeutic process is therefore removed from the patent protection."

Claim 1 of patent EP 0 724 444, which is novel over the prior art only because of the specified dosage, is therefore excluded from patentability and should consequently be held invalid pursuant to Article 53(c) EPC 2000.

Claim 2 which is a dependent use of claim 1 wherein the dosage is 1.0 mg and claim 3 dependent on claims 1 and 2 wherein the treatment is for male pattern baldness will be held invalid for the same reasons since only the dosage taught is a novel feature over the prior art.

Furthermore, it should be added that the very requirements of patentability admitted by the EPO were not met since the problem-solution approach is not applicable.

In fact, a particular problem in the therapeutic application of finasteride to androgenic alopecia in light of the skilled person's scientific knowledge was not claimed since side effects which the new dosage would have remedied are not described, nor are the reasons which would have prevented a researcher from continuing to work on finasteride as an efficacious treatment against hair loss caused by hyperandrogenic conditions.

"To administer the lowest dosage possible of a pharmaceutical compound to a patient and still maintain therapeutic efficacy" cannot be considered on its own as a specific problem to be resolved when the application of a medicament is already known and has already been protected.

On the other requests

The provisional enforcement of the decision is compatible with the nature of the case, it is necessary and will be ordered.

The conditions are met to award Actavis and A.E.T the sum of €30,000 each pursuant to Article 700 of the French Code of Civil Procedure.

ON THESE GROUNDS

Ruling by making the decision available at the Court Clerk's office, after due hearing of the parties and in first instance,

Hold that claims 1, 2 and 3 of the French designation of Merck & Co. Ltd's Patent EP 0 724 444 are invalid for being excluded from the scope of patentability in accordance with the provisions of Article 53(c) EPC 2000.

Order the registration of this judgment, once it has become final, in the *RNB* held at the *INPI*, at the request of the most diligent party.

Order Merck & Co. Ltd to pay Actavis and A.E.T the sum of €30,000 each on the basis of Article 700 of the French Code of Civil Procedure.

Order Merck & Co. Ltd to bear the entire costs of these proceedings, which will be recovered by Mr Bizollon, pursuant to Article 699 of the French Code of Civil Procedure.

ORDERED AND ADJUDGED IN PARIS ON THE TWENTY-EIGHTH OF SEPTEMBER TWO THOUSAND AND TEN./.

The Court Clerk	**The Presiding Judge**
Signature	*signature*