

THE PATENTS ACT, 1970

UNDER SECTION 25 (1)

REPRESENTATION OF OPPOSITION

**In the matter of an application for Patent no.
3764/DELNP/2005 filed on 25/08/2005.**

And

**In the matter of representation of opposition
u/s 25(1) of the Patents Act, 1970 as amended**

by Patents (Amendment) Act, 2005

And

**In the matter under rule 55 of the Patent rules, 2003
as amended by the Patents (Amendment) rules, 2006.**

Schering Aktiengesellschaft,.....Applicant

Sun Pharmaceuticals Industries Limited.....Opponent

Hearing Held on May 28, 2009

Present:

Dr. Deepa Tikku Attorney for the Applicant

Ms. Richa Pandey..... Attorney for the Applicant

Ms. Swati Pahuja.....Attorney for the Applicant

Shri. S.Majumdar.....Attorney for Opponent

Dr. Sanchita Ganguli..... Attorney for Opponent

Decision

Schering Aktiengesellschaft hereinafter referred as “The Applicant” filed an application having no. 3764/DELNP/2005 on 25/08/2005 for grant of patent and titled as

“Methods and Pharmaceuticals compositions for reliable achievement of acceptable serum testosterone levels.

A representation by way of opposition under section 25(1) of the Patents (Amendment) Act, 2005 was filed by Sun Pharmaceuticals Industries limited hereinafter referred as “The Opponent” through his attorney of S. Majumdar & Co on 30th September,2008 with a request for hearing. Accordingly notice was served upon attorney for the Applicant on 10th October,2008 along with copy of representation. The Applicant submitted their reply statement on 1st January, 2009 within three months from the date of notice.

A hearing was therefore, appointed in this matter on 2nd April,2009 under Rule 55 of the Patent Rule 2003 as amended by Patent (Amendment) Act 2005 which was finally held on May 28, 2009.

Grounds of opposition taken up by the opponent in their representation dated 30 September, 2008 are as follows:

1. that the invention so far as claimed in any claim of the complete specification has been published before the priority date of the claim

(i) In any specification filed in pursuance of an application for a patent made in India on or after on or after the 1st day of January, 1912; or

(ii) in India or elsewhere, in any other document.[Section 25(1)(b)]

2. that the invention so far as claimed in any claim of the complete specification was publicly known or publicly used in India before the priority date of that claim. [Section 25(1) (d)]

3. that the invention so far as claimed in any claim of the complete specification, is obvious and clearly does not involve any inventive step, having regard to the matter published as mentioned in clause (a) or having regard to what was used in India before the Priority date of the applicant’s claim.[25(1)(e)]

4. that the subject of any claim of the complete specification is not an invention within the meaning of this Act, or is not patentable under this Act.[Section 25(1)(f)]

5. that the complete specification does not sufficiently and clearly describe the inventions or the method by which it is to be performed.[25(1)(g)]

Originally 17 claims were filed in the original application in national phase wherein 1-6 related to composition formulated for intramuscular injection comprising a testosterone ester and a vehicle comprising castor oil and claims 7-17 are directed towards the use of composition. The Application came up for examination and the first examination report was issued on 28/02/2008. The Applicant made amendment in claims and filed 4 nos. of amended claims in reply to representation u/s 25(1).

The representation of opposition was argued by the attorney for opponent during the hearing only on following grounds:

1. Section 25(1)(e) obviousness or lack of inventive step,
2. Section 25 (1) (f) not an invention and not patentable;

OBVIOUSNESS/LACK OF INVENTIVE STEP

The opponent relied upon Exhibit 1 to 7 and the additional documents which were sent along with letter dated March 20,2009, namely annexure 1 and annexure 2.

1. GB 1567515 (Exhibit 1)

Opponent's submissions:

The attorney for opponent stated that GB 1567515 document teaches novel esters of testosterone and dosage forms for better androgenic activity which comprises testosterone esters, and castor oil and a co-solvent. The preferred esters are decanoate and undecanoate

which are dissolved in a lipid substance for formulating into a suitable dosage form. The document teaches various lipid substances which include castor oil among others. The parenteral dosage form may contain one or more co-solvents like benzyl alcohol to increase the solubility. The choice of oil, which gives the composition claimed in the present application the alleged benefit of superior stability, is taught in prior art and the co-solvent.

Applicant's Submissions:

The attorney for applicant submitted that the inventive step of the present invention lies in the exact composition of the vehicle and the surprising effect inherent in the composition with the castor oil in a concentration of 25 to 45 vol% and same was neither known nor suggested GB 1567515.

2.US 3164520 (Exhibit 2)

Opponent's submissions:

The attorney for opponent stated that document US 3164520 teaches a parenteral pharmaceutical composition of testosterone and its esters in a pharmaceutically acceptable vehicle of benzoyl benzoate. Example 2, discloses compositions of testosterone palmitate, wherein 2g of testosterone palmitate is dissolved in a vehicle consisting of 40% Castor oil and 60% benzoyl benzoate. Testosterone palmitate is a commonly found ester of hexadecanoic acid (CI 6) derivative of testosterone.

Applicant's Submissions:

The attorney for applicant submitted that the in document US 3164520, testosterone undecanoate is not used in any of the examples and the prolonged stability of testosterone undecanoate is also not disclosed in the document. This was further submitted that in the example with 40% castor oil and 60% benzyl benzoate is a reference example included with the purpose of showing that in those formulations, it is preferable to include higher amounts of benzyl benzoate to minimize irritation at the place of injection of the formulations and hence a skilled person would never contemplate use the same as a starting point for further developments.

3.US 4181721 Exhibit 3

Opponent' submissions:

The attorney for opponent stated that document US 4181721 relates to depot preparations in an oily, unsaturated solution suitable for intramuscular injection. This teaches an intramuscular injection comprising lipophilic steroid ester having 4- 20 carbon atoms having progestational activity dissolved in 1-6ml of a mixture of castor oil and benzyl benzoate. The desired depot effect has been achieved by reducing the viscosity of the vehicle by addition of benzyl benzoate as co-solvent, has been admittedly known to the applicant. The applicants had done nothing more than merely manipulate the concentration of castor oil and benzyl benzoate to an optimum range, and such manipulation is completely within the expertise of a skilled person.

Applicant's Submissions:

The attorney for applicant submitted that the document US 4181721 discloses the examples concerning a testosterone enanthate ester having seven carbon atoms and the stability problem of testosterone ester comprising a C11 alkanoate was not recognized .They further submitted that the surprising finding of the inventors, namely the castor oil in a concentration of **25** to 45 vol% provides a stabilizing effect, was neither known nor suggested .This document does not teach any other ratios of castor oil benzyl benzoate then that 6:4=1:0.66 , corresponding to 60 vol% castor oil and by virtue of this limitation, revised claim 1 and its dependent thereon are inventive.

4.Document WO95/12383 (Exhibit 4)

Opponent's Submissions:

The attorney for opponent submitted that the chinese application teaches an injectable solution comprising testosterone undecanoate as the active component, injectable plant oil and/or benzyl benzoate. The injectable solution can be used to treat the diseases that need androgen therapy and need androgens for long-term therapy or replacement therapy. This document goes to establish that testosterone undecanoate has been known as an active compound to treat hypogonadal males. Even the composition comprising testosterone

undecanoate along with vegetable oil and benzyl benzoate is known in the art, which provides enough motivation to try the same composition and manipulate the concentration of the components to achieve the optimum effect. Such manipulation is mere routine experimentation to a person skilled in the art and does not require any inventive ingenuity.

Applicant's Submissions:

The applicant submits that the document WO/95/12383 discloses the solution containing testosterone undecanoate and injectable plant oil and/or benzyl benzoate and does not disclose the use of castor oil in the formulation.

The present inventors clearly state that the surprising finding in the subject invention lies in the claimed concentration of castor oil which affects the stability of testosterone undecanoate.

5.Document WO 02/15938 (Exhibit 5)

Opponent's Submissions:

The attorney for opponent stated that Document WO 02/15938 teaches a parenteral formulation comprising testosterone decanoate dissolved in a pharmaceutically acceptable oily medium of castor oil and benzyl benzoate. It further teaches that addition of benzyl benzoate as additives in castor oil lowers the viscosity of the formulation and document clearly teaches that castor oil is the preferred oil not only due to the excellent stability that it confers on the composition but also due to its extremely good release profile.

Applicant's Submissions:

The applicant submitted that the document WO 02/15938 does not teach the use of testosterone undecanoate in combination with castor oil and benzyl benzoate. Testosterone undecanoate is only disclosed in the "comparison example as a solution of 100 vol% castor oil . The present invention teaches vehicles having 25 to 45 vol% castor oil and that the range of 25-45 vol% castor oil is not arbitrary range but reflects the surprising finding which affects the stability of testosterone undecanoate and hence the present claim inventive . It is also important to emphasise that testosterone

disclosed is different, i.e., decanoate(C10) as opposed to that in the present invention,i.e., undecanoate(C11).

6.Document (Exhibit 6) “Treatment of male hypogonadism with testrone undecanoate injected at extended intervals of 12 weeks-JOURNAL OF ANDROLOGY, VOL 23, NO,3, MAY/JUNE 2002

Opponent’s submissions:

The attorney for opponent stated that the document discloses testosterone undecanoate 1000 mg (TU) in 4mL castor oil injections resulted in well-maintained androgen-dependent functions without serious side effects of injection intervals up to 12 weeks, for a total period of 3.2 years .

Applicant’s Submissions:

The attorney for Applicant submitted that the document discloses 1000 mg of testosterone undecanoate in 4 mL castor oil.Firstly, the document does not teach the mixing of co-solvent in castor oil. Secondly, that in the present invention range of 25 to 45 vol% of castor oil is not an arbitrary range but reflects the surprising findings of the present inventors that the concentration of castor oil affects the stability of testosterone undecanoate. Hence claim 1 is inventive and its dependents thereon over the said document.

7.Document (Exihibit7) Repeated intramuscular injections of testosterone undecanoate for substitution therapy in hypogonadal men. Clinical Endrocrinology(1999), 5 1, 757-763

Opponent’s submissions:

The opponent stated that exhibit7 teaches intra-muscular injection of testosterone undecanoate (TU) for substitution therapy in hypogonadal men by administering 4 injections of 1000mg TU in 4-ml (250mg/ml) castor oil at 6-week intervals and castor oil is routinely used in the prior art as a vehicle for TU and addition of a co-solvent in the solvent system is completely within the expertise of a skilled person.

Applicant's submissions:

The applicant submitted that the said document discloses 1000 mg of testosterone undecanoate in 4 mL castor oil and whereas, the present invention discloses the range of 25 to 45 vol% of castor oil which is not an arbitrary range but reflects the surprising empirical findings of the present inventors that the concentration of castor oil affects the stability of testosterone undecanoate. Furthermore, the said document does not teach the mixing of co-solvent in castor oil. Hence claim 1 is inventive and its dependents thereon over the said document.

Following mentioned case laws were discussed:

1. EPO Board of Appeals

Case Number; T 0386/89 Date of decision: 24 March 1992

Opponent's submissions:

The Board in the present case concludes that the alleged unexpected effect is not deducible from the application as originally filed cannot be taken into account when determining the problem underlying the invention for the purpose of assessing the issue of inventive step.

Applicant's submissions:

T0386/89 relates to a situation where the Board was of the opinion that there was no basis in the application as originally filed for changing the problem solved. In that case the statement "suitable for use on tractors of high power" did not give basis for effect of enhancement of fatigue life. The present case also differs in this respect as the application as filed clearly states on page 3 in the "Summary of Invention", lines 31-33 that "the compositions are chemically stable with respect to the testosterone ester as well as physically stable with respect to the vehicle for a prolonged time". Thus, the effect of stability was clearly described in the original application as filed. Hence the teachings of T0386/89 do not apply to the present case.

2. EPO Board of Appeals

Case Number: T 0021/81

Date of decision: 10 September 1982

Opponent's submissions:

As far as selection of materials is concerned the Board generally considers it as forming part of the normal activities of the man skilled in the art to select from the materials which are known to him as suitable for a certain purpose the most appropriate one, and this also in the case where he is presented with no more than an unreasoned preference for a specific material in a document forming part of the prior art.

The Board therefore considers that no inventive step is present in the selection of this particular material.

Applicant's submissions:

In T0021/81, a lack of inventive step was found by the Board because "an advantageous effect could be expected to result from the combination of the teachings of the prior art documents" and this was "irrespective of the circumstances that an extra effect (possibly unforeseen) is obtained" (point 6 of the decision). Thus this decision describes the situation where an advantageous effect could be expected when combining the prior art and the finding of further advantageous effects do not amount to the presence of an inventive step. Thus, the present case is completely different from that of T0021/81 because based on the prior art; no advantageous effect is expected when castor.oil is used in a concentration of 25-45 vol%. This is an effect found by the inventors of the present invention. Thus the improved stability found by using castor oil in a concentration of 25-45 vol% is not just a further or extra effect as that of T0021/81. Hence the teachings of T0021/81 do not apply to the present case.

3. EPO Board of Appeals

Case Number; T 1344/05

Date of decision: 17 December 2007

Opponent's submissions:

Since paracetamol and benzyl alcohol both have an alcohol group, the skilled person would not prima facie disregard benzyl alcohol as an additional solvent in a solvent system comprising

mainly Glycerol Formal, particularly because testing such a preparation by mixing the ingredients together is a routine experiment.

Applicant's submissions:

In T1344/05, the only difference between the contested patent and the closest prior art "lies in the presence of benzyl alcohol as solvent instead of ethanol" and "the patent in suit and the respondent's written submissions are silent about any further or equivalent effect achieved by the presence of benzyl alcohol in the formulation instead of ethanol" . Thus the present case clearly differs from that of T1 344/05 because the Applicant has shown by the submitted stability data that both the choice of oil and the concentration of castor oil affect the stability. Hence the teachings of T1344/05 do not apply in the present case.

4. EPO Board of Appeals

Case Number: T 0287/99

Date of decision: 12 March 2003

Opponent's submissions:

For those skilled in the art the first obvious step would thus be to verify by tests whether or not the teaching of (1) is reproducible and the desired aerosol formulations can in fact be obtained using both adjutants in an amount near to the lower end of the ranges which are explicitly recommended in (1) for the amounts of co-solvent (see 8.1.3 above) and surfactant (see 8.1.4 above). Such tests would be routine.

Since a person skilled in the art had absolutely no reason to doubt that the teaching of citation (1) as a whole is reproducible, this person, having carried out the above-mentioned tests, could not really have been surprised to find that even small amounts of co-solvent, say about 1% w/w based on propellant. in combination with small amounts of surfactant, say 1 to 5% w/w based on medicament, are sufficient to achieve the formation of stable homogeneous dispersions of a medicament in an "ozone-friendly" hydrofluorocarbon or hydrochlorofluorocarbon propellant and to obtain the desired inhalation aerosols.

In order to solve the technical problem posed (ie to provide alternative inhalation aerosols), it was then only necessary to carry out the smallest possible and, accordingly, most obvious modification of the closest state of the art, that is to say reducing the amount of co-solvent marginally below that of 1.01% as suggested (1) to any amount less than 1%. eg 0.999%. based on the propellant.

Applicant's submissions:

In T0287/99, a lack of inventive step was found because the claimed range only differed marginally from that disclosed in the prior art; i.e., less than 1% vs. 1.01% and the effect of using a lower concentration was the same as that described in the closest prior art. The present case differs from this decision as the upper value of the concentration of castor oil of 45 vol% is not just marginally different from the compositions disclosed in the prior which contains testosterone undecanoate and castor oil (e.g. castor oil is 100% in WO 2002/015839). Furthermore, the Applicant has submitted further data showing that there is actually an improved stability associated with the claimed concentration of castor oil an effect which was not described in the prior art. Such a surprising effect was not found with the claimed concentration in T 0287/99. Hence the teachings of T0287/99 do not apply to the present case.

5.EPO Board of Appeals

Case Number; T 1034/01

Date of decision: 29 January 2004

Opponent's submissions:

The use of an article of silicon as fluorine scavenger mounted between the window and the substrate, does not involve an inventive step having regard to the combined teachings of documents E1, E3 and E8. A finding of lack of inventive step with respect to one alternative of the invention as claimed however renders the whole claim including different alternatives not allowable. For this reason, it is not necessary to discuss the presence of an inventive step of the other options provided in claim 1. The patent, moreover, does not disclose any technical effect that is achieved by locating the scavenger above the substrate when it is formed by an article of silicon that is not achieved by a scavenger formed by an

article of graphite. Such a limitation in the claim renders the claimed subject-matter new with respect to the state of the art, but is hardly suitable to render it inventive.

Applicant's submissions:

In T1034/01, a lack of inventive step of the whole claim was found because a lack of inventive step with respect to one alternative of the claimed invention was found to lack an inventive step. The only comment that the Applicant has to this decision is that all the alternatives claimed in the present application involve an inventive step over the prior art for the reasons that have been put forward so far. Thus, T1034/01 does not apply in the present case. In view of the foregoing, where the facts of the present case have been clearly distinguished, it is submitted that the Opponent's reliance on this case law stands flawed and misplaced and ought not be considered.

6.EPO Board of Appeals

Case Number: T 920/91

Date of decision: 12 February 1993

Opponent's submissions:

The Board follows decision T 21/81. OJ EPO 1983. 15. paragraph 6. in that, irrespective of a possibly unforeseen extra effect, a claim lacks inventive step if it had already been obvious for a skilled person to arrive at a claimed feature because an advantageous effect could be expected to result from the combination of the teachings of the prior art. Thus, even if the cushioning effect and the improved adherence put forward by the Appellant in paragraph VI(d) above had been disclosed originally, these effects have to be classified as bonus effects, which are not able to give inventiveness to the obvious way from the state of the art to the subject-matter of Claim 1.

Applicant's submissions:

In T0920/91 a lack of inventive step was found because it was based on "use of known

properties of a known material for a known technical purpose". Further it was stated that "an advantageous effect could be expected to result from the combination of the teachings of the prior art". This is clearly in contrast with the present invention as using castor oil in a concentration of 25-45 vol% is not based on a known property as there is no indication anywhere in the prior art that the concentration of castor oil affects the stability and therefore also no advantageous effect could be expected. Hence the teachings of T0920/91 do not apply to the present case.

Findings and Conclusion on inventive step u/s 25(1)(e):

Let me reproduce the amended claims filed by the Applicant, which are follows:

1. A composition formulated for intramuscular injection comprising 15 to 50 % (w/v) testosterone undecanoate and a vehicle comprising castor oil in a concentration of 25 to 45 vol% and benzylbenzoate.
2. The composition as claimed in claim 1, wherein the vehicle comprises 55 to 65 vol% benzylbenzoate.
3. The composition as claimed in claim 1 or 2, wherein the composition comprises 17.5 to 40 % (w/v) testosterone undecanoate.
4. The composition as claimed in claim 3, wherein the composition comprises 25 % (w/v) testosterone undecanoate.

Now I need to analyse these claims for inventive step in light of arguments put forth by both parties over cited documents and the disclosure of the invention in the specification of this present application.

The independent claim 1 of the invention discloses composition having 15 to 50 % (w/v) testosterone undecanoate and a vehicle comprising castor oil in a concentration of 25 to 45 vol% and benzylbenzoate and dependent claims speak about other preferred ranges of testosterone undecanoate and benzylbenzoate.

The attorney for applicant submitted that the present invention relates to providing a testosterone ester e.g. testosterone undecanoate, formulation which is both chemically and physically stable and which is able to maintain physiologically normal serum levels of testosterone for an extended period of time .

The applicant referred to Annexure B and an affidavit by Sabine Fricke to establish enhance effect by comparison of the stability of testosterone undecanoate (TU) in

different mixtures of benzyl benzoate and oils. The stability was assessed on basis of how many ampoules of each mixture that contained precipitates of TU following storage in a refrigerator (2-8°C) and Surprisingly, it was found that the stability of the formulation comprising TU was dependent on the type of oil chosen. This was concluded from the stability data that precipitates are formed in all compositions comprising peanut oil (arachis oil) and Miglyol 8 12 (Triglycerides medium chain). Secondly, it was concluded that the concentration of castor oil has a pronounced effect on the stability of TU. As can be seen, mixtures containing 37% castor oil were perfectly stable even after storage for 34 days, whereas mixtures containing 50% castor oil, and in particular 60% castor oil, were not sufficiently stable. The range of 25-45 vol% castor oil is not arbitrary range but reflects the surprising finding over the stability of testosterone undecanoate.

Let me read through the cited documents by the attorney for opponent in light of arguments made by both parties.

GB 1567515

If I read through the document GB 1567515, I agree with the contention of applicant that this document do not mention about castor oil in a concentration of 25 to 45 vol% in composition formulated for intramuscular injection having testosterone undecanoate and a vehicle benzylbenzoate.

US 3164520

If I read through the document US 3164520, I observe that I agree with contention of attorney for opponent that in example 2 testosterone palmitate is dissolved in a vehicle consisting of 40% Castor oil and 60% benzoyl benzoate but neither testosterone undecanoate is mentioned nor prolonged stability of testosterone undecanoate is discussed.

US 4181721

After reading through the document US4181721 I find that the document discloses a testosterone enanthate ester with a dose of 200 mg in 1 ml of castor oil/benzoate (6:4) with depot effect lasts 12 weeks. It is observed that document do not discloses castor oil in a concentration of **25** to 45 vol% and benzyl benzoate with testosterone undecanoate which provides a stabilizing effect.

WO/95/12383

Upon reading through the document WO/95/12383, I observe that solution containing testosterone undecanoate and injectable plant oil and/or benzyl benzoate is disclosed but castor oil in a concentration of **25** to 45 vol% which provides a stabilizing effect is not disclosed.

WO 02/15938

If I read through the document WO 02/15938, I observe that this discloses testosterone undecanoate, castor oil and benzyl benzoate in formulation but the document do not teaches about 25 to 45 vol% castor oil being used and that the range of 25-45 vol% castor oil is not arbitrary range but reflects the surprising finding which affects the stability of testosterone undecanoate.

Exhibit 6

Upon reading through the document I agree that document discloses testosterone undecanoate 1000 mg (TU) in 4mL castor oil injections resulted in well-maintained androgen-dependent functions without serious side effects of injection intervals up to 12 weeks, for a total period of 3.2 years but it is also understood that this do not discloses 25 to 45 vol% of castor oil surprising finding which affects the stability of testosterone undecanoate.

Exhibit7

After reading through the document I find that the range of 25 to 45 vol% of castor oil used along with mixing of co-solvent resulting in surprising finding is no where taught in the said document.

In absence of any provision under the law over further evidences , I am not bound to discuss; document (D 8) "Effect of prenatal exposure to hydroxyprogesterone on steroidogenic enzymes in male rats"(Annexure 1)and document (D9) castor oil as a

vehicle of parenteral administration of steroids hormones” Riffkin et al article (Annexure2) filed by the attorney for opponent.

But even after reading through these documents, I am not able to find that these documents teaches about surprising effect of use of vehicle comprising castor oil in a concentration of 25 to 45 vol% and benzylbenzoate over stability of testosterone undecanoate.

I observe following on the cited case laws:

Case law T 0386/89

I agree with contention of the attorney for applicant that on page 3 in the "Summary of Invention", lines 31-33 it is stated that "the compositions are chemically stable with respect to the testosterone ester as well as physically stable with respect to the vehicle for a prolonged time".

Case law T 0021/81

I agree with contention of Applicant that an advantageous effect could be expected to result from the combination of the teachings of the prior art documents so as to establish lack of inventive step.

Case law T 1344/05

I find that in Case Number; T 1344/05 further effect achieved by the presence of benzyl alcohol in the formulation instead of ethanol are not discussed.

I also believe that EPO board of Appeals case laws T0287/99, T1034/01 and EPO T920/91 have different technical facts and principals laid down therein shall not be applicable in this matter.

With my findings on above case laws, I conclude that theses case laws may not benefit to the opponent.

Having found that use of vehicle comprising castor oil in a concentration of 25 to 45 vol% and benzylbenzoate resulting in to surprising finding which affects the stability of testosterone undecanoate and in absence of any motivation in the cited documents for a skilled person in the art to arrive at this surprising finding , I conclude that claim 1 and dependent claims thereon are inventive.

NOT AN INVENTION/NOT PATENTABLE u/s 25(l) (f)

The Attorney for opponent raised two issues under this head:

1. Lack of inventive step u/s 2(1)(ja)
2. Lack of synergy thus not patentable u/s 3(e)

I have already discussed the question of inventive step above; therefore I shall now confine myself to question of synergy and non patentability u/s 3(e).

The opponent submitted that the invention claimed is a mere composition of known components lacking any synergy thus non patentable under section 3(e). The opponent further submitted that if synergy has been proved between two classes of compounds, discovering the same cannot be regarded as inventive.

Applicant's Submissions:

The Attorney for applicant submitted that what is being claimed is a novel and synergistic composition with improved and unexpected properties (as such properties were not exhibited by any of the prior art compositions) and not a mere admixture. Accordingly, the said invention does not fall within the prohibition of Section 3(e).

With respect to therapeutic efficacy, they submitted that *in-vivo* efficacy of the claimed composition has been described in the description, examples and Figure 1. Thus, the Opponent's allegation that the description does not have any supporting data for efficacy is incorrect.

Moreover, it is submitted that stability of a composition plays a major role in determining its efficacy, even so when the composition is meant for human use. Accordingly, the subject invention does not fall under Section 3(e) of the Act.

In view of the above, the ground of opposition under Section 25(l)(f) is not maintainable and hence should be rejected.

First of all, the Applicant would like to point out that a corresponding European patent has been granted with claims that are broader than those currently pending in India. During prosecution of the European application, an inventive step was acknowledged by the EPO based on the Applicant's findings of improved stability.

Following case laws to substantiate this ground were quoted by attorney for opponent:

1.EPO Board of Appeals Case

Number: T 191/86 Date of decision:

23 June 1988

Opponent's submissions:

The partial absence of synergism in document (2) is not conclusive as to the question of inventive step in the application. It is not accepted that Table B on page 17 does not show unambiguously that the results obtained from a combination of compound (I) and compound (B) are significantly better than what would be expected on the basis of a merely additive effect. In reality, whether synergism is present or not in the prior art composition is of little importance since their effectiveness is regarded as insufficient.

The synergism of the claimed compositions abundantly demonstrated by the numerous comparative examples provided by the Appellant has never been disputed. The fact is that synergism was expected.

Although the expectation of a synergistic effect is only mentioned in document (I) within a paragraph which in its previous sentence is dealing with insecticides .The Board cannot accept the restrictive interpretation made by the Appellant which consists in separating the insecticides from the fungicides and the herbicides disclosed in the previous paragraph. This

approach would not be in line with the description in general wherein no distinction is made between the various agricultural chemicals used individually or in combination; moreover, the distinction between herbicides and insecticides regarding synergism would mean that the phosphorothioates listed as herbicides are fundamentally different from the phosphorothioates listed as insecticides, which the Appellant has never demonstrated and which would be surprising.

Applicant's submissions

In TO 191/86, a lack of inventive step was found because when combining the compounds, some synergism was expected and actually mentioned in one of the prior art documents . However, it was clearly stated that synergistic effect are generally unpredictable and surprising and that the case of that decision was an exceptional one. We would also like to point out that this decision is as stated in the decision, an exceptional one as the general practice of the EPO is that synergistic effects are an indication of inventive step. However, with regard to the present case, it also differs from this decision in two aspects. First of all, synergistic effect is generally related to the combination of two or more compounds and our invention is not based on a mere combination of castor oil and benzylbenzoate but also the choice of a particular concentration of castor oil. Secondly, there is no hint in the prior art, of a particular effect associated with using castor oil in a concentration of 25-45 vol%, as the improved stability found by the applicant. Hence the teachings of TO 191/86 do not apply to the present case.

2. 2485/DEL/1998 (Boehringer Ineelheim Pharmaceuticals vs INP+ & PWN):

The attorney for opponent in this case submitted that the Ld. Controller mentioned that “at a minimum the applicant must place on record two thing”s: 1) data relating to the therapeutic effect of the known substance and 2) data relating to the therapeutic effect of the claimed substance. The applicant has failed to place on record either of these items. Firstly, the data presented in the applicant's affidavit shows stability data only for the product claimed in the application. There is no data upon which one can conclude that particle size stability is significantly enhanced over the known substance. Secondly the data, at most shows the stability of the nevirapine hemihydrate suspension over various storage

conditions. There is no data upon which one can conclude that improved particle size stability translates into better therapeutic effect. Given this lack of data, there is no basis upon which the Patent Controller can conclude that there is the requisite enhancement in therapeutic efficacy.

The opponent also mentioned that the way in which the Madras High Court has defined 'efficacy', the opponents submitted that it is impossible for alleged improvements in particle size stability no how matter how comprehensively proved and placed on record, to be sufficient to meet the efficacy requirement of section 3(d).

The court stated "

Further to the above, the Ld. Controller held that "I have analyzed the above arguments and have come to the conclusion that the product (composition) claims section 3(d) of the Patents Act in the absence of any data for the composition to show enhanced efficacy."

Applicant's submissions:

The attorney for applicant submitted that the application 2485/DEL/1998 titled 'Pharmaceutical composition" relates to a pediatric suspension of Nevirapine Hemihydrate used for treating HIV. The Opponent has misplaced their reliance by quoting case Number 2485/DEL/98 which relates to a different invention and having different technical features where the efficacy was measured by way of stability data. It is to be noted that the present invention not only exhibits stability as a surprising property but also shows enhanced pharmacokinetic properties as evidenced by data present in the description. Accordingly, the Applicant would like to submit that the judgment in case of 2485/DEL/98 is not relevant for the instant application.

3. Warner Lambert v Torrent (1577/DEL/1996)

Opponent's submissions:

Applicants have admitted during hearing that due to enhanced stability and solubility of the crystalline form III Atorvastatin hydrate, it is more bioavailable as compared to the prior art atorvastatin compound because it degrades less than the prior art compound

and consequently more bio-available. That means, the therapeutic contents of the molecule remain same, and due to more stability, the molecule is more bio-available. Therefore it is clear from the above, the present invention provides a new form of a known substance either in anhydrous or hydrated form III of Atorvastatine having same therapeutic activity and in the same field. It only claims some improvement in physical property, which does not make any change in therapeutic efficacy of the compound as compared to the prior art compound.

The attorney for opponent submitted that from the above decisions it is quite clear that stability does not affect the therapeutic efficacy of the drug in any manner thus the present composition does not provide any therapeutic efficacy over the prior art compositions.

Applicant's submissions:

This Application titled "Form III Crystalline [R-(R*,R*)]-2-(4 fluorophenyl)-, - Dihydroxy-5-(1-Methylethyl)-3-Phenyl-4[(Phenylamino) Carbonyl]-1H-Pyrrol-1-Heptanoic Acid Calcium Salt (2:1)" claims the crystalline form III of Atorvastatin and hydrates, a pharmaceutical composition and omnibus claims, for its use as an inhibitor of the enzyme 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMG-COA reductase) and is thus useful as a hypolipidemic and hypocholesterolemic agent. Needless to say, this case is entirely different in technicalities compared to the present invention. In the said case the Controller observed the following-

"The Applicant has strongly pleaded that the present invention is a crystal polymorph of the prior art atorvastatin salt, having better solubility and stability than the prior art salt. Whereas Opponent has not provided any conclusive evidence that the prior art compound prepared by example 10 & 11 of the US patent 5273,995 is a crystalline anhydrous salt. In absence of any conclusive evidence it is very difficult to agree with Opponent's pleadings. Accordingly, I would prefer not to satisfy with arguments and evidence given by Opponent and allow the applicant's pleading that the present invention which it alleges to be crystal polymorph is novel over the prior art.

Regarding obviousness / lack of inventiveness, I am not very much convinced with the pleading of the Applicant that the Example A of document W094/16693 and example 10 of the US patent 5273,99 which are almost similar process and wherein the process involved large amount of water before it was subjected to recrystallisation in ethyl acetate and hexane to isolate an anhydrous atorvastatin salt. In my opinion the drying condition mentioned in this process appears to be insufficient to produce an anhydrous product. But again in absence of any conclusive evidence that both the process leads to atorvastatin in hydrated crystalline and not in amorphous form, I reluctantly allow the Applicant to get the benefit of doubt in this matter."

As can be seen from the highlighted portion above, on both the counts, the Controller gave a judgment in favour of the Applicant. Accordingly, the Applicant would like to submit that the judgment in this case may not be considered in detriment to the Applicant's interest.

Findings and conclusion over not an invention/not patentable u/s 25(l) (f):

Having discussed the question of lack of inventive step above, I shall not comment over the same issue under this section.

Now to conclude upon the question of synergism u/s 3(e), let me reproduce the section:

Section 3(e) states that:

“A substance obtained by a mere admixture resulting only in the aggregation of properties of the components thereof or a process for producing such substance.”

Therefore it is observed from this section that composition obtained by adding other substances should not demonstrate mere aggregation of properties i.e. this should not be a mere admixture or in other words there should be synergistic effect in the properties of composition.

It is also understood that there is no question of therapeutic efficacy being raised in this section.

I do not have any doubt from the arguments made by both parties that there is a synergistic effect on testosterone undecanoate (TU) in castor oil and benzyl benzoate. The attorney for applicant referred to Annexure B and an affidavit by Sabine Fricke to establish enhance effect by comparison of the stability of testosterone undecanoate (TU) in different mixtures of benzyl benzoate and oils. Further therapeutic efficacy, shown by claimed composition described in the description, examples and Figure 1 establishes this fact.

In view of above, I also observe that the following case laws are less relevant to help the opponent.

In TO 191/86, I agree with argument of attorney for Applicant that synergistic effect is generally related to the combination of two or more compounds. This invention is not only based on a mere combination of castor oil and benzylbenzoate but also on the choice of a particular concentration of castor oil and it relates to a particular effect associated with using castor oil in a concentration of 25-45 vol%, for the improved stability as found by the applicant.

The case laws of application no 2485/DEL/1998 and 1577/DEL/1996 quoted by the attorney for opponent raises a different issue therapeutic efficacy under section 3(d), which has been adequately addressed in the description, examples and Figure 1. Therefore these in my opinion shall not benefit to opponent.

Having understood that synergism being demonstrated by the claimed composition of the present invention and question of inventive step being discussed earlier, I conclude that the ground u/s 25(1)(f) could not be established.

In view of my findings and conclusion drawn on the grounds u/s 25(1)(e) and 25(1)(f) I allow this patent application no. 3764/DELNP/2005 to proceed for grant of patent on four amended claim .

This opposition is disposed off with no cost to either party.

Dated this 11th. Day of November, 2009

(N R Meena)

Asstt. Controller of Patents & Designs

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