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30 NOV 2010
Dated: 30/11/2010

To,
Shri Subramaniam,Nataraj & Associates,
Attorneys at Law
Patent & Trademark Attorneys
E-556,Greater Kailash-II
New Delhi-110048

POD/2010-11/

Subject: **Application no.9661/DELNP/2007**

Sir,

This is with respect to the above mentioned application. I am forwarding the decision issued in respect of the pregrant representation under section 25(1) of Patents Act. 1970, Amendment 2005 filed in this office by M/s Majumdar & Co. on behalf of Cipla Ltd.

This is for your information and further necessary action.

Thanking you,

Yours faithfully

(N.R.Meena)
Asstt.Controller of Patents & Designs

Enclosure: Decision of pregrant representation under section 25(1) of Patents Act,1970, Amendment 2005.

chem/2010/2930

CC: 1) S.Majumdar & Co.5,Harish Mukherjee Road,Kolkatta-700025
2) Legal Cell, Patent Office, Baudhik Sampada Bhavan,Dwarka, New Delhi-110078

RECEIVED
-4 DEC 2010
S. MAJUMDAR & CO.

THE PATENTS ACT, 1970

UNDER SECTION 25 (1)

REPRESENTATION OF OPPOSITION

In the matter of an application for Patent no. 9661/DELNP/2007 filed on 13/12/2007

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.

BRISTOL-MYERS SQUIBB & GILEAD SCIENCES, LLC,..... Applicant

CIPLA Limited.....Opponent

HEARING HELD ON APRIL 13,2010

Present:

G.Natraj & Sonia Pawa.....for Applicant

S.Majumdar, Amrita.Majumdar ,M.Venkatesh,& others..... for Opponent

M/s BRISTOL-MYERS SQUIBB & GILEAD SCIENCES, LLC of 333 Lakeside Drive, Foster City, CA 94404, United States Of America; U.S.A herein after referred as "the Applicant" filed an national phase application no. 9661/DELNP/2007 on 13/12/2007 corresponding to international application no. PCT/US2006/023223 having priority from Applications US 60/690010 dated 13-06-2005 and US 60/771279 dated 7-02-2006 titled as "Stable fixed- Dose Unitary

Formulations Containing Tenofovir, a Surfactant, Efavirenz and Emtricitabine" for grant of patent with originally having 30 claims on record.

This Application no.9661/DELNP/2007 was published on 15-02-2008 and the first examination report (FER) was issued on 1-12-2008. The Agent for applicant filed reply to FER on 24-11-2009 with amended claims 25 nos.

M/s Cipla Limited, 28 Bellasis Road, Mumbai Central Mumbai 400008, India, herein after referred as "the opponent" filed a representation of opposition u/s 25(1) of the Patent Act 1970 on 2-07-2009. The reply statement to the opposition was filed on 22-01-2010 within three months from the date of intimation of opposition i.e. 22-10-2009.

Further reply statement and evidence copy along with amended claims 25 nos. were sent to the agent for applicant on 19-02-2010.
A hearing was appointed on 16-03-2010 in this matter .The hearing was adjourned to 13-04-2010 on request made by the Agent for opponent and finally hearing was held on 13-04-2010.
The opponent withdrew the ground of anticipation and argued on the grounds of obviousness and lack of inventive step, not an invention and not patentable and insufficiency.

The Agent for opponent submitted the written arguments after hearing on 05-05-2010 and whereas the written arguments after hearing were not submitted by the Agent for Applicant.

Upon reading through the specification, it is observed that application under opposition relates to products for the treatment of viral infections, particularly HIV infections using known compounds, namely, efavirenz (EFV); emtricitabine (FTC) and tenofovir DF (TDF) .

HIV therapy using EFV, FTC and TDF is considered desirable .Whereas a triple combination consisting of EFV, FTC and TDF is known through WO 04/64845. The product as per the Applicant was not bioequivalent to the individual compositions of EFV (Sustiva); FTC (Emtriva) and TDF (Viread).

The applicant has, therefore allegedly formulated a composition wherein the stability and bioequivalence objectives for the triple combination product have been achieved by providing a multicomponent dosage form, one component comprising tenofovir DF and, optionally, emtricitabine, and the other comprising at least efavirenz. Also, the surfactant is in destabilizing contact with TDF component.

SECTION 25(I) (e): OBVIOUSNESS/LACK OF INVENTIVE STEP

Opponent's Submissions:

The opponent relied upon the following documents to establish that the alleged invention lacks inventive step and is obvious to a person skilled in the art.

- Exhibit 1: WO2004064845 published on August 5, 2004;
- Exhibit 1A: US20010012518 published on August 9, 2001;
- Exhibit 2: WO2005/021001 published on March 10, 2005;
- Exhibit 3: "Guidance for Industry" by U.S Department of Health and Human Services published in May 2004;
- Exhibit 4: WO2003/059327 published on July 24, 2003.
- Exhibit 5. "The Theory and Practice of Industrial Pharmacy" by Lachman, Lieberman, Kanig; third edition; Indian reprint 1990 published by Varghese Publishing House.
- Annexure B – Sustiva (efavirenz)capsules and tablets--2004
- Annexure C – 3383/DELNP/2005

The Agent for opponent submitted that Exhibit 1 is an acknowledged prior art

which belongs to the applicant itself. As put forth in lines 26 to 28 at page 1, it relates to combinations of compounds with antiviral activity and more specifically with anti-HIV properties. In particular, it relates to chemically stable combinations of structurally diverse antiviral agents. Lines 5 to 9 at page 4 teach that the invention provides a unit dosage form of a therapeutic combination comprising TDF and FTC, which is unexpectedly chemically stable. Further lines 10 to 21 on the same page teach that the unit dosage composition of TDF and FTC comprise a third antiviral agent. Particularly line 21 teaches that the third antiviral agent can be EFV. At page 5, line 12 onwards, chemical stability has been defined which clearly mentions that the combination is substantially stable to chemical degradation.

The opponent further submitted by referring at page 30, lines 10 to 15, the dosage of the components are taught, which can be administered as a ternary unitary dosage, i.e., a single dosage form.

The opponent further referred to claims 50 to 58 of Exhibit 1, particularly claims 51, 53, 54 and 58 which clearly teach that an additional antiviral agent, either a protease inhibitor or a non-nucleotide reverse transcriptase inhibitor, which includes EFV and the tradename of EFV (Sustiva) is also explicitly mentioned in claim 54. Claim 58 is of utmost significance since it unambiguously teaches a combination of TDF, FTC and Sustiva.

The opponent submitted that Sustiva is the tradename of EFV, a label of which is annexed to the representation as Annexure B. It is clear from the description, that both capsules and tablet forms comprise sodium lauryl sulphate (SLS), which is the surfactant.

The Agent for opponent therefore submitted that the triple combination of EFV, FTC and TDF is already a part of prior art. The property that the formulation is chemically stable is also well taught in Exhibit 1. Thus the alleged invention is

completely within the skill of a person skilled in the art and does not involve any inventive feature. Exhibit 1 read with Annexure B renders claim 1 of the impugned application completely obvious.

It was further stated that though the object of the invention was to make a triple combination, claim 1 has been very cleverly drafted so as to seemingly relate to a binary combination of antiviral agents. That the instant invention is completely devoid of any inventive activity and is only mere combination of teachings of prior art. Moreover the applicant has also failed to provide evidence to support the fact that the combination claimed in the impugned application has better stability than the one taught in Exhibit 1. Absence of any comparative data is a further confirmation of the fact that the invention lacks inventive step.

The Agent for opponent submitted that Exhibit 2 teaches combinations of a pyrimidine containing NNRTI with RT inhibitors. Exhibit 2 at page 13 lines 9 teaches a triple composition comprising TMC278 or a stereoisomeric form thereof; or a pharmaceutically acceptable salt thereof; or a prodrug thereof; with emtricitabine and tenofovir disoproxil fumarate. Page 5, line 19 further discloses that TMC278 is a NNRTI, it is submitted that EFV is also a NNRTI, thus the triple combination of the three API as claimed in the impugned application is completely obvious in view of teachings of prior art.

The Agent for opponent submitted that Exhibit 3, which is a publication of the USFDA, clearly teaches that combination therapy is essential for the treatment of HIV/AIDS, preferably three actives from two different classes of antivirals. The publication at page 19 teaches the combination of TDF, FTC and EFV under the proposed three-drug regimens. It is submitted that such combinations, which have been suggested, are supported by clinical data as would be evident from the caption at page 19.

The triple combination *per se* has been contemplated in prior art and

formulating such a combination does not involve any inventive merit. A person skilled in the art in view of the above cited prior art will be motivated or lead to try a triple combination of said components.

As to the incompatibility of the surfactant and TDF, the opponent submitted as under.

Exhibit 1A clearly teaches the fact that EFV composition when formulated with sodium lauryl sulphate as surfactant by wet granulation disintegrates and dissolves rapidly so as to enhance the therapeutic characteristics of the formulation. Thus it was also known that to get the maximum therapeutic activity of EFV it had to be formulated with a surfactant, preferably SLS.

Therefore the problem to be solved by the applicant was to ensure that the incompatible substances, namely, TDF and surfactant do not affect each other when formulated as a single dosage form.

The opponent submitted that Exhibit 5 at page 330 under the paragraph relating to multiple compressed tablets discusses types of multiple layer tablets and reasons for preparing such tablets. It is clearly taught that the one of the reasons for preparing such multiple layered tablets is to separate physically or chemically incompatible ingredients. Further at page 331 it is taught that such separation is often required for stability purposes. Exhibit 5 was published long back in 1987 which indicate that the same ought to be part of common general knowledge of a person in the field of industrial pharmacy. Therefore preparation of a multiple layered tablet when certain ingredients are incompatible is a well known technique in pharmaceutical sciences. The opponent also submitted that Exhibit 4 which teaches a bilayer pharmaceutical tablet comprising telmisartan and a diuretic. Here too, at page 2 the problem pertaining to a combination is discussed. A combination of telmisartan and HCTZ was not possible because of the incompatibility of HCTZ with meglumine which is a component of conventional telmisartan formulations. To

circumvent said problem, the inventors therein prepared a bi-layer tablet whereby the meglumine was not in contact with HCTZ as evident from the summary of the invention at page 3. The paragraph bridging pages 3 and 4 further teaches a process for the preparation of such a bilayer tablet.

Thus the opponent submitted that when two components to be combined in one single dosage form are incompatible, the most obvious way to obviate such problem is to formulate a bi-layer or multilayer tablet so that the incompatible components are not in contact with each other. In the present case, the applicant has alleged that the surfactant (sodium lauryl sulphate) of EFV degrades TDF therefore it has prepared a bilayer tablet wherein the components are in different layers thereby not being in contact. It was submitted that such a solution does not involve any inventive ingenuity since the same has been abundantly taught in prior art viz. Exhibit 4 and Exhibit 5.

Finally they submitted that, the triple combination as sought to be claimed by the applicant is well taught in prior art, particularly the use of the actives are completely obvious in view of Exhibit 1, Exhibit 2 and Exhibit 3. The solution to the problem relating to the incompatibility of the surfactant and TDF is also well taught in prior art as submitted in herein above. Thus the present invention is completely obvious to a person skilled in the art and thus lacks an inventive step.

The opponent also relied upon following decisions/case laws to support his contentions on the ground of lack of inventive step and obviousness.

1. Atlantic Works v. Brady, 107 U.S. 192 (1883)

2..*Bishwanath Prasad Radhey Shyam Vs Hindustan Metal Industries.* (AIR 1982SC1444(1979)2SCC, 1979,2SCR757

3.case number - T 0308/99 - 3.3.2, the EPO Board of Appeals

4. case number - T 0235/97- 3.3.2, the EPO Board of Appeals

5. case number - *T 0956/05*- 3.3.2, the EPO Board of Appeals .

6. case number - *T 0928/06*- 3.3.02, the EPO Board of Appeals .

The Agent for opponent submitted that in light of the clear and unambiguous teachings relating to the triple combination of antiviral agents, it is highly likely that a person skilled in the art would try such combinations. However while trying to formulate a combination, the applicant faced problems relating to incompatibility of actives, which was also solved following the teachings of Exhibit 4 and 5. Thus the invention lacks an inventive step.

Applicant's Submissions:

The Agent for Applicant submitted that different compositions and combinations of antiviral drugs are known in the prior art which contain different antiviral drugs selected from tenofovir, lamivudine, azidothymine, adefovir, efavirenz, etc. However, the chemical stability of such compositions and combinations is of concern as the individual component(s) can interact with each other or with the some external component thereby decreasing the efficacy and stability of the combination. The present application claims a stable pharmaceutical formulation of tenofovir disoproxil fumarate and an Efavirenz formulation and, if desired one or more additional active pharmaceutical ingredients, with pharmaceutical^ acceptable carriers and excipients.

They submitted that Inventive step or obviousness has to be judged by a person skilled in the art and the opponents have failed to enclose any expert evidence on the matter. The Opponents are not the right persons to judge the inventiveness of the present application.

Various combinations of antiviral drugs are known but none of the document combined the drugs, tenofovir and emtricitabine of the present invention to form a

stable co-formulation.

It was further pointed out that the chemical stability of TDF and FTC is of concern due to their low pKa values of 3.75 and 2.65, respectively. TDF is subject to hydrolytic deamination of the exocyclic amine of the adenine nucleobase, and to hydrolysis of one or both of the POC ester groups. TDF not only is a labile ester, it also is the salt with fumaric acid, an organic diacid. Only one carboxyl group of the fumaric acid is consumed for salt formation, the remaining carboxyl would have been expected (in a combination product) to be free to catalyze hydrolytic deamination of 5-fluoro cytosine nucleobase of FTC to form 5-fluoro uridine nucleobase. The acid-catalyzed deamination of FTC forms ammonia, which in turn would have been expected to catalyze the hydrolytic degradation of TDF to mono-POC PMPA (mono-ester of TDF), formaldehyde, isopropanol and carbonic acid. The carbonic acid would have been expected to further degrade the FTC, thereby creating more ammonia. The formaldehyde also would have been expected to crosslink FTC to produce dimers. The result of all this was that one could have expected a substantial prospect of reciprocal catalytic degradation.

They asserted that knowing the combination of TDF and FTC is at risk of catalytic hydrolysis, a person skilled in the art would have been prevented from considering a combination of TDF and FTC. The drugs could have simply been administered separately, or they might have been assembled separately into a patient
package. It would not have been obvious to attempt to formulate TDF and FTC in the same dosage form which is claimed in the present invention. Thus, the present invention is clearly inventive over the cited prior art.

The applicant submitted that the invention lies in the discovery of the problem of incompatibility of the surfactant and the TDF component and the solution which ensues. The applicant with regard to Exhibit 1 contended that the same does not teach a single dosage formulation of the three components, namely, EFV, TDC

and FTC. With regard to the other prior art it contended those are general teachings, which cannot be extrapolated to the present invention.

Findings and Conclusion on SECTION 25(I) (e): OBVIOUSNESS/LACK OF INVENTIVE STEP

Upon reading through the specification WO2004064845 published on August 5, 2004, it is observed that lines 5 to 9 , at page 4 teaches that the invention provides a unit dosage form of a therapeutic combination comprising TDF and FTC, which is unexpectedly chemically stable. Further lines 10 to 21 on the same page teaches that the unit dosage composition of TDF and FTC comprise a third antiviral agent. Particularly line 21 teaches that the third antiviral agent can be EFV. At page 5, line 12 onwards, chemical stability has been discussed. It is further observed at page 30, lines 10 to 15, the dosage of the components are taught, which can be administered as a ternary unitary dosage.

It is further agreed that claims 51, 53, 54 and 58 clearly teaches an additional antiviral agent, either a protease inhibitor or a non-nucleotide reverse transcriptase inhibitor, which includes EFV .The tradename Sustiva of EFV is also explicitly mentioned in claim 54. Claim 58, unambiguously teaches a combination of TDF, FTC and Sustiva.

Exhibit 1A also teaches the fact that EFV composition when formulated with sodium lauryl sulphate as surfactant by wet granulation disintegrates and dissolves rapidly so as to enhance the therapeutic characteristics of the formulation. It also teaches that to get the maximum therapeutic activity of EFV it had to be formulated with a surfactant, preferably SLS.

It is also found that Annexure B discloses Sustiva (EFV), in both capsules and tablet forms comprising sodium lauryl sulphate (SLS), which is the surfactant.

Document WO2005/021001 published on March 10, 2005 (Exhibit 2) teaches combinations of a pyrimidine containing NNRTI with RT inhibitors. Exhibit 2 at page 13 lines 9 teaches a triple composition comprising TMC278 or a stereoisomeric form thereof; or a pharmaceutically acceptable salt thereof; or a prodrug thereof; with emtricitabine and tenofovir disoproxil fumarate. Page 5, line 19 further discloses that TMC278 is a NNRTI (EFV).

Document Exhibit 3, May, 2004, discloses that combination therapy is essential for the treatment of HIV/AIDS, preferably three actives from two different classes of antivirals. The publication at page 19 teaches the combination of TDF, FTC and EFV under the proposed three-drug regimens.

Document Exhibit 5 published long back in 1987 teaches about multiple compressed tablets, discusses types of multiple layer tablets and reasons for preparing such tablets. It is taught that the one of the reasons for preparing such multiple layered tablets is to separate physically or chemically incompatible ingredients and such separation is often required for stability purposes.

Document, Exhibit 4, WO2003/059327 published on July 24, 2003 , teaches a bilayer pharmaceutical tablet comprising telmisartan and a diuretic. A combination of telmisartan and HCTZ was not possible because of the incompatibility of HCTZ with meglumine which is a component of conventional telmisartan formulations. The inventors therein prepared a bi-layer tablet whereby the meglumine was not in contact with HCTZ. The document further teaches the process for the preparation of such a bilayer tablet.

Therefore, it is agreed that triple combination as sought to be claimed by the applicant is well taught in prior art, and is completely obvious in view of Exhibit 1,

Exhibit 2 and Exhibit 3. The solution to the problem relating to the incompatibility of the surfactant and TDF is also well taught in Exhibit 1 A, and Annexure B.

I am also not convinced to the statement that the combination claimed in the impugned application has better stability as compared to the one taught in Exhibit 1

It is further observed that the independent claim 1 remains the same after amendment and in claim 2; the applicant has replaced 'additionally' with 'if desired' and that according to the originally filed claim 2, FTC was an essential component, but according to the amended claim the same has become optional.

It is ambiguous that the triple composition comprising EFV, FTC and TDF as per invention is highly desired, whereas claim 1 of the instant invention relates to only EFV and TDF and claim 2 covers FTC as an optional component.

I also agree to the submission of the Agent for opponent that when two components to be combined in one single dosage form are incompatible, the most obvious way to obviate such problem is to formulate a bi-layer or multilayer tablet so that the incompatible components are not in contact with each other. In the present case, the applicant has alleged that the surfactant (sodium lauryl sulphate) of EFV degrades TDF; therefore it has prepared a bilayer tablet wherein the components are in different layers thereby not being in contact. And that such a solution does not involve any inventive step since the same has been abundantly taught in prior art viz. Exhibit 4 and Exhibit 5.

I am also bound by the principles laid down in various case laws as referred by the agent for opponent .viz. 1. Atlantic Works v. Brady, 107 U.S. 192 (1883) 2.*Bishwanath Prasad Radhey Shyam Vs Hindustan Metal Industries.* (AIR 1982SC1444(1979)2SCC, 1979,2SCR757 ,3.case number - T 0308/99 - 3.3.2, the EPO Board of Appeals 4.. case number - T 0235/97- 3.3.2, the EPO Board of Appeals 5. case number - *T 0956/05*- 3.3.2, the EPO Board of Appeals .6. case number - *T 0928/06*- 3.3.02, the EPO Board of Appeals .

"The design of the patent laws is to reward those who make some substantial discovery or invention, which adds to our knowledge and makes a step in advance in the useful arts..."

"whether the alleged discovery lies so much out of the Track of what was known before as not naturally to suggest itself to a person thinking out of the Track of what was known before as not naturally to suggest itself to a person thinking out of the Track of what was known before as not naturally to suggest itself to a person thinking on the subject, it must not be the obvious or natural suggestion of what was previously known."

"According to established case law of the boards of appeal (see eg T 296/87, OJ EPO 1990, 195) enhanced effects cannot be adduced as evidence of inventive step if they emerge from obvious tests....".

Therefore, I conclude that the claims of this instant application lacks inventive step as this shall be obvious to as person skilled in the art to arrive at what herein has been claimed, having the knowledge of the triple combination of EFV, FTC and TDF, which is already known in the cited prior arts along with the teaching on chemical stability of the combination. Further more, formulating such a combination does not involve any inventive merit in absence of any unexpected results.

NOT AN INVENTION/NOT PATENTABLE Section 25(1)(f)

The ground u/s 25(1)(f) NOT AN INVENTION/NOT PATENTABLE needs to be read with section 3(d) and section 3(e) respectively.

Opponent's submissions:

The Agent for opponent stated that the claimed invention as per Section 3 (d) which states that *"the mere discovery of a new form of a known substance which does not result in the enhancement of known efficacy of that substance or the mere discovery of any new property or new use for a known substance or of the mere*

use of a known process results in a new product or employs at least one new reactant" is not patentable under this Act. Isomers, complexes, combinations and other derivatives of known substance shall be considered to be the same substance, unless they differ significantly in properties with regard to efficacy. The Agent for opponent stated that tenofovir as Viread, emtricitabine as Emtriva and efavirenz as Sustiva were available in the market earlier to the impugned application. The applicant has not supported the impugned application with any data demonstrating enhanced efficacy allegedly claimed of the composition as against the activity of the individual actives. The applicant has thus grossly failed to show improvement in therapeutic efficacy of the allegedly claimed composition.

The Agent for opponent referred to and relied upon the judgment dated August 6, 2007 in W.P.24760/06 passed by the Hon'ble High Court of Judicature at Madras in the case of Novartis AG Vs Union of India and others. The Hon,ble court held that:

"As we understand the amended section, it only declares that the very discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance, will not be treated as an invention".

The position therefore is, if the discovery of a new form of a known substance must be treated as an invention, then the Patent applicant should show that the substance so discovered has a better therapeutic effect. Darland's Medical Dictionary defines the expression "efficacy" in the field of Pharmacology as "the ability of a drug to produce the desired therapeutic effect" and "efficacy" is independent of potency of the drug.

Dictionary meaning of "Therapeutic" is healing of disease - having a good effect on the body." Going by the meaning for the word "efficacy" and "therapeutic" extracted above, what the patent applicant is expected to show is, how effective the new discovery made would be in healing a disease / having a good effect on the body?

The Agent for opponent further stated that the claimed invention falls under Section 3

(e), which clearly states that "a *substance obtained by a mere admixture resulting only in the aggregation of the properties of the components thereof or a process for producing such substance"* is not patentable under this Act.

The impugned application describes composition of tenofovir, emtricitabine and efavirenz. The Agent for opponent stated that claim 4 and claim 5 of the impugned application are directed to the components of composition being *"physically discrete"* and in *"layers."* Claim 14 is essentially directed to marketed products, Truvada and Sustiva. Moreover the AUC and C max of claimed composition is similar to FDA approved products as admitted by the applicant. The applicant is therefore claiming a composition of known active agents of similar therapeutic efficacy. Evidently, the applicant has failed to demonstrate any synergy between the active ingreadiants of the composition. In absence of any data on synergy, the composition is thus a mere admixture of known active agents. The application is therefore liable to be rejected on this ground alone.

The Agent for opponent bought to the notice the extracts of the following Indian patent decisions:

In the matter of application no. 2485/DEL/1998

"at a minimum the applicant must place on record two things: 1) data relating to the therapeutic effect of the known substance and 2) data relating to the therapeutic effect of the claimed substance….".

In the matter of application no. 1577/DEL/1996

"This means there has to be an improvement in the therapeutic content or capacity in a same amount of drug compound of the present invention vis-a-vis prior art compound….."

In the matter of application no. 315/DEL/2000

"find that the present specification does not show any efficacy data of the claimed compound while reference is made only to stability of the claimed compound. The improved stability cannot be counted as enhanced efficacy

Applicant's Submissions:

The Agent for Applicant submitted that unexpected enhanced stability of pharmaceutical co-formulation of the present invention provides for an improved property as compared to the properties of the individual ingredients. The pharmaceutical acceptable carriers included in the formulation prevent the formation of eutectic mixture of TDF and FTC. The eutectic mixture has lower melting point and thus is amorphous and not as stable as the original individual crystal forms of the starting materials. Thus, increased stability of the co-formulation by incorporation of the carrier makes the co-formulation a synergistic co-formulation and not a mere admixture of the active ingredients. Therefore, these grounds do not hold relevance for the present application.

Findings and Conclusion on 25(1)(f): NOT AN INVENTION/NOT PATENTABLE

I observe that tenofovir as Viread, emtricitabine as Emtriva and efavirenz as Sustiva are well known in the prior arts as discussed earlier. I also agree to the opponent statement that the applicant has not supported the impugned application with any data demonstrating enhanced efficacy allegedly claimed of the composition as against the activity of the individual actives. Therefore, the applicant has grossly failed to show improvement in therapeutic efficacy of the allegedly claimed composition.

I am bound by the directions of Hon'ble High court that :

"*As we understand the amended section, it only declares that the very discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance, will not be treated as an invention…*".

In view of the argument that the combination being admittedly known in the prior arts and no data has been produced to substantiate the enhanced efficacy of the combination over the previously known combination as taught in Exhibit 1, the present invention falls under Section 3(d) of the Patent Act. and therefore not

patentable.

I can agree to the contention of the agent for applicant that the pharmaceutical acceptable carriers included in the formulation prevent the formation of eutectic mixture of TDF and FTC. The eutectic mixture has lower melting point and thus is amorphous and not as stable as the original individual crystal forms of the starting materials. Thus, increased stability of the co-formulation by incorporation of the carrier makes the co-formulation a synergistic co-formulation and not a mere admixture of the active ingredients. The increased stability of the co-formulation by incorporation of the carrier may make the co-formulation a synergistic co-formulation and not a mere admixture of known compounds as alleged by the Opponents. Therefore, the claims do not fall(s) U/s 3(e)

SECTION 25(I) (g): INSUFFICIENCY

Opponent's Submissions:

The Agent for opponent stated that claims of the impugned application are not fairly based on the disclosures of the impugned application. Claim 1 of the impugned application is directed to combination of two API viz tenofovir and efavirenz. However, the specification is directed to bilayer formulation of tenofovir DF, emtricitabine and efavirenz-surfactant. The impugned application provides no description on bilayer tabletting of tenofovir and efavirenz combination in accordance with its claim 1. Thus subject matter of invention claimed is not fairly based upon description.

Secondly, as per claim 5 and claim 7 of the impugned application, the composition is a bilayer tablet. Claim 5 and 7 are supported by table 3 on page 17 of the impugned application. However, the impugned application on page 23, lines 11-13, refers to blending of its components; stated as *"Efavirenz granulation and emtricitabine/tenofovir DF dry granulation were blended in a 3 cubic foot V-blender for 10 minutes.""* *At* page 23, lines 21 -24

it reads as compression of efavirenz/emtricitabine/tenofovir DF final powder blend in bilayer tablet press. Here it is not clear how this achieves its objective of bioequivalence and stability by providing multicompartment dosage forms thereby preventing "unexpected incompatibility" of tenofovir DF with surfactant of Sustiva. However, the act of blending powder blends of two components (as claimed in claim 3) as final powder blend defeats the sole purpose of the alleged invention, since a homogenized powder blend simply cannot be compressed into a bilayer tablet. The specification is therefore unclear as to how a bilayer tablet is compressed from the final blend.

The Agent for opponent further stated that claim 14 of the impugned patent application claims a composition where in efavirenz, emtricitabine and tenofovir DF are provided to a patient upon oral administration at substantially the same AUC and Cmax as the FDA approved product of Truvada and Sustiva. However, no data has been provided by the applicant to demonstrate that the claimed composition exhibits same AUC and Cmax as the FDA approved product of Truvada and Sustiva. 15.5 From the aforesaid, it is clear that the specification lacks clarity on the fundamental aspects of the alleged invention.

The opponent further submitted that although the claims recite that the composition is a bilayer tablet and the examples also go to show the same, the paragraph under final blends at page 23 mentions that the EFV granulation and the TDF/FTC dry granulation were blended. The opponent submitted that blending the TDC/FTC granulation and EFV granulation would never yield a bilayer composition of TDC/FTC and EFV. Blending very clearly implies that the components are mixed together which is not in accordance with the claims and the other examples and disclosure of the specification. It was also pointed out that claim 1 recites a combination EFV along with surfactant and TDF, which has no enablement in the disclosure.

The Agent for opponent further stated that blending wet granulated efavirenz and surfactant with dry granulated tenofovir DF and emtricitabine would

definitely result in a homogenous blend (page 23, lines 9 to 20), thereby, exposing tenofovir DF to surfactant component of efavirenz. This is again contradictory to statements made by the applicant, page 1 lines 29-33 which states homogenous composition of three APIs failed to produce chemically stable tablet; and page 2 lines 14-19 which states that combination tablets prepared from the mixture of dry granulated tenofovir and emtricitabine and wet granulated efavirenz and surfactant failed to achieve desired bioequivalence.

Applicant's Submissions:

The Agent for applicant submitted that opponent have not mentioned which part of the application is not fully enabled. They also have failed to specify which part of the specification is not clear to a man skilled in the art. This allegation is spurious, mischievous and made with a malignant intent without proper verification. The statements of the Opponents' are groundless and uncorroborated. The compositions claimed in the present application have been described very clearly and in sufficient detail in the specification. All the examples mentioned in the specification are fully enabled and workable as claimed under the specified physical and chemical conditions and can be performed by a man skilled in the art.

Findings and Conclusion on ground u/s 25(l) (g): INSUFFICIENCY

As to sufficiency and clarity of the specification, I am of the opinion that sufficiency of the disclosure needs to be judged from the angle of the person skilled in the art and applicant is supposed to disclose the best method known to him.

I do agree that data regarding therapeutic efficacy has not been provided by the applicant as to the requirement under section 3(d), but I doubt that data is essentially needed to demonstrate that the claimed composition exhibits same AUC and Cmax as the FDA approved product of Truvada and Sustiva.

Upon reading through the specification, I observe that disclosure is sufficient and claims are fairly based on the disclosure. I also do not see any anomaly in terms of contradictions as stated by the Agent for opponent, when understood in right context.

Therefore, I conclude that this ground u/s 25(1)) (g) is not maintainable.

In view of my above findings and facts on records, I refuse to grant patent on this patent application no.9661/DELNP/2007 on the ground of lack of inventive step section 25(1) e read with section 2(1)(ja) and not patentable invention under section 25(f) read with section 3(d) of the Patent Act 1970.

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

Dated this 30th.November,2010

(N.R.MEENA)
ASSISTT. CONTROLLER FPATENTS & DESIGNS

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