The Controller of Patents
The Patent Office,
New Delhi

Kind Attention:
Mr. N.R. Meena
Assistant Controller of Patents & Designs.

Dear Sir,

Re: Opposition under Section 25(1) against
Applicant: Bristol-Myers Squibb and Gilead Sciences,
Opponent: Cipla Limited
Our Ref No: PI1-310

As directed by the Ld. Controller we submit herewith Written Arguments on behalf of Cipla Limited in duplicate in respect of the hearing held on April 13, 2010 in connection with the above identified cases.

The above documents may kindly be taken on record.

Yours faithfully,

Mythili Venkatesh
Of S. Majumdar & Co.
(Agent for the Opponent).

Encl: 1. Written arguments (in duplicate).
BEFORE THE CONTROLLER OF PATENTS,
NEW DELHI

Opposition to Patents Application No. 9661/DELNP/2007 dated December 13, 2007

BRISTOL-MYERS SQUIBB & GILEAD SCIENCES, LLC,

.....Applicant

-And-

CIPLA Limited

.....Opponent

WRITTEN ARGUMENTS OF THE OPPONENT BASED ON THE HEARING
HELD ON APRIL 13, 2010 AT PATENT OFFICE, NEW DELHI

As directed by the Ld. Controller, Cipla Limited, 289 Bellasis Road, Mumbai Central
Mumbai 400008, India, being the opponent in the present opposition proceedings hereby
submits written arguments on the submissions made at the hearing in the aforesaid
opposition.

The submissions at the hearing were made on the basis of the impugned Patent
application and the pleadings of the parties.

1. At the outset the opponent withdrew the ground of anticipation.

2. The grounds argued were obviousness and lack of inventive step, not an invention
and not patentable and insufficiency.

3. Before making submissions on the specific grounds of opposition, the opponent
discussed the specification. The application under opposition relates to products for
the treatment of viral infections, particularly HIV infections using known compounds, namely, efavirenz (referred to as EFV hereinafter); emtricitabine (referred to as FTC hereinafter) and tenofovir DF (referred to as TDF hereinafter) as mentioned at page 2 of the impugned specification. The background of the invention was also briefly discussed so as to understand the difference between prior art and present application which subsequently aids in ascertaining the inventive step. The prior art products known at the time of the priority date of the invention is as under.

- Chemically stable dosage form comprising FTC and TDF (also known by its tradename Truvada). The product was prepared by wet granulation. (lines 16-18 at page 2)
- HIV therapy using EFV, FTC and TDF considered desirable and a triple combination consisting of EFV, FTC and TDF known by way of WO 04/64845. However according to the applicant the product was not bioequivalent to the individual compositions of EFV (Sustiva); FTC (Emtriva) and TDF (Viread).

4. The applicant allegedly found that the reason behind such loss in bioequivalence was the chemical instability of TDF when in contact with the surfactant (sodium lauryl sulfate) of the EFV composition. The applicant then attempted to formulate a triple combination without a surfactant; however the EFV’s bioequivalence was reduced. Thus it was concluded that EFV cannot be formulated without a surfactant. Wet granulation of EFV with a surfactant and dry granulating Truvada and then mixing the granules together also did not yield a composition with the desired bioequivalence.

5. Wet granulation of the three components also unexpectedly resulted in a composition where the TDF was found to be highly unstable. The co-pending application (U.S.S.N. 60/771,353) addresses the reason for the same, it was attributed to the formation of a eutectic mixture of FTC and TDF due to wet granulation and where
after on drying the eutectic mixture forms a glassy or amorphous product in which the 
TDF is chemically unstable.

6. Thus the applicant has 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.

7. The opponent submitted that the specification was originally filed with a set of 30 
claims and was later amended to 25 claims. The independent claim 1 remains the 
same after amendment, although in claim 2, the applicant has replaced ‘additionally’ 
with ‘if desired’. It is submitted that according to the originally filed claim 2 FTC was 
an essential component, but according to the amended claim the same has become 
optional.

8. The opponent further submitted that the triple composition comprising EFV, FTC and 
TDF is highly desired although claim 1 of the instant invention relates to only EFV 
and TDF and claim 2 covers FTC as an optional component.

9. SECTION 25(1)(e): OBVIOUSNESS/LACK OF INVENTIVE STEP

9.1 The opponent relied upon the various prior art referred to in its representation to 
establish that the alleged invention lacks inventive step and is obvious to a person 
skilled in the art.

9.2 The 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 anti-
viral 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.

9.3 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.

9.4 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.

9.5 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.

9.6 The 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 claim1 of the impugned application completely obvious.
9.7 It is 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. It is submitted 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.

9.8 The 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.

9.9 Likewise 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.

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

9.12 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.

9.13 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.

9.14 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 indicates 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.
9.15 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 is 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.

9.16 To sum up, 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.

9.17 Claim 14 of the amended claims clearly recite that the combination of EFV, TDF and FTC as claimed in claims 1 and 2 have substantially the same AUC and Cmax as that of the individual compositions, i.e., Truvada and Sustiva. It is submitted that this clearly shows that the present composition does not have a superior activity as compared to the art known compositions. Hence, it falls under within the scope of section 3(d). This also substantiates the fact that the present application is more of a patient compliance invention, which does not involve any inventive merit.

9.18 The opponent also relied upon a few decisions/case laws to support its contentions on the ground of lack of inventive step and obviousness. Specific portions of which have been extracted herein below for reference:

*Atlantic Works v. Brady, 107 U.S. 192 (1883)*
Page 8/12 and 9/13
"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. Such inventors are worthy of all favour. It was never the object of those laws to grant a monopoly for every trifling device, every shadow of a shade of an idea, which would naturally and spontaneously occur to any skilled mechanic or operator in the ordinary progress of manufactures. Such an indiscriminate creation of exclusive privileges tends rather to obstruct than to stimulate invention. It creates a class of speculative schemers who make it their business to watch the advancing wave of improvement and gather its foam in the form of patented monopolies which enable them to lay a heavy tax upon the industry of the country without contributing anything to the real advancement of the art. It embarrasses the honest pursuit of business with fears and apprehensions of concealed liens and unknown liabilities to law suits and vexatious accountings for profits made in good faith."

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

21. It is important to bear in mind that in order to be patentable an improvement on something known before or a combination of different matters already known, should be something more than a mere workshop improvement; and must independently satisfy the test of invention or an 'inventive step'. To be patentable the improvement or the combination must produce a new result, or a new article or a better or cheaper article than before. The combination of old known integers may be so combined that by their working in relation they produce a new process or improved result. Mere collocation of more than one integers or things, not involving, the exercise of any inventive faculty, does not qualify for the grant of a patent. 'It is not enough', said Lord Davey in Rickmann v. Thierry (1896) 14 Pat. Ca. 105 'that the purpose is new or that there is novelty in the application, so that the article produced is in that sense new, but there must be novelty in the mode of application. By that, I understand that in adopting the old contrivance to the new purpose, there must be difficulties to be overcome, requiring what is called invention, or there must be some ingenuity in the mode of making the adoption'. As Cotton L J put in Blackey v Latham (1888) 6 Pat. Ca. 184, to be new in the patent sense, the novelty must show invention". In other words, in order to be patentable, the new subject matter must involve 'invention' over what is old. Determination of this question, which in reality is a crucial test, has been one of the most difficult aspects of Patent Law, and has led to considerable conflict of judicial opinion.

22. This aspect of the law relating to patentable inventions, as prevailing in Britain, has been neatly summed up in Encyclopaedia Britannica, Vol 17, page 453. Since in India, also the law on the subject is substantially the same, it will be profitable to extract the same hereunder:

23. "A patent can be granted only for ‘manner of new manufacture’ and although an invention may be ‘new’ and relate to a ‘manner of manufacture’ it is not necessarily a ‘manner of new manufacture’ – it may be only a normal development of an existing manufacture. It is a necessary qualification of a craftsman that he should have the
knowledge and ability to vary his methods to meet the task before him a tailor must cut
his cloth to suit the fashion of the day and any monopoly that would interfere with the
craftsman’s use of his skill and knowledge would be intolerable. 24. “A patentable
invention, therefore, must involve something which is outside the probable capacity of a
craftsman which is expressed by saying it must have ‘subject matter’ or involve an
‘inventive step’. Novelty and subject matter are obviously closely allied... Although these
issues must be pleaded separately, both are invariably raised by a defendant, and in fact
‘subject matter’ is the crucial test, for which they may well be novelty not involving an
‘inventive step’, it is hard to conceive how there can be an ‘inventive step’ without
novelty.

25. Whether an alleged invention involves novelty and an ‘inventive step’ is a mixed
question of law and fact, depending largely on the circumstances of the case. Although no
absolute test uniformly applicable in all circumstances can be devised, certain broad
criteria can be indicated.

26. The expression “does not involve any inventive step” used in Section 26(1)(a) of the
Act and its equivalent word “obvious”, have acquired special significance in the
terminology of Patent Law. The ‘obviousness’ has to be strictly and objectively judged.
For this determination several forms of the question have been suggested. The one
suggested by Salmond LJ in Rado v John Tye & Son Ltd (1967) RPC 297 is apposite. It
is: ‘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.

38. We have ourselves examined the evidence on record with the aid of the Ld Counsel
for the parties, and have ourselves compared the machines (Ex CC and Ex XVI) which
were produced before us. We do not want to rehash the evidence. Suffice it to say, we do
not find that any piece of evidence has been misread, overlooked or omitted from
consideration. The view taken by the Trial Court was quite reasonable and entitled to due
weight. In our opinion, it did not suffer from any infirmity or serious flaw which would
have warranted interference by the Appellate Bench.

39. Be that as it may, from the discussion that follows, the conclusion is inescapable that
the invention got patented by M/s. Hindustan metal Industries, respondent herein, was
neither a manner of new manufacture, nor a distinctive Improvement on the old
contrivance involving any novelty or inventive step having regard to what was already
known and practiced in the country for a long time before 1951.

The opponent submitted that both these cases basically hold that patents applied for
trivial inventions, mere workshop improvements, which do not progress the art, are not to
be granted. In the present case, the applicant has formulated a triple combination, the
inventive concept behind such a triple combination is also well taught in prior art as
evident from Exhibit 1, 2 and 3. Thus the combination involves no inventive step. The
problem relating to the incompatibility and its subsequent solution also involves no
inventive step. It is submitted that the solution to problems pertaining to incompatibility of APIs and excipients are well documented in prior art as evident from Exhibit 4 and 5. The applicants have merely applied such teachings of prior art in order to achieve the composition having the desired bioavailability. Thus the present invention does not progress the art forward and should be rejected.

In case number - T 0308/99 - 3.3.2, the EPO Board of Appeals held as under.

In the present situation, the prior art pointed the notional skilled person in the direction of the claimed use, and it only remained to confirm experimentally by a small number of routine tests that the thoroughly obvious result, namely that water-soluble hylans and water-insoluble cross-linked HA according to claim 1 can act as drug release controlling agents, was in fact obtained. However, the necessity of experimentally confirming a reasonably expected result does not render an invention unobvious. The board is aware that the respondent has found in the comparative tests referred to in 6.1 above some slightly enhanced effects associated with the use of water-soluble hylans and a water-insoluble (but non-DVS) cross-linked HA as drug release controlling agents in comparison with HA or its salts and esters used in the cited state of the art. If, as here, the aim was to find for known water-soluble cross-linked HA derivatives (ie hylans) and water-insoluble cross-linked HA derivatives a further usable property (see 6 above), the first self-evident step - before any thought is given, say, to finding some other valuable properties for these HA derivatives - is to test whether they exhibit that property which would have been expected and envisaged by the skilled person in the light of the cited state of the art and which in the present case is, as shown above, straightforwardly obvious. Such tests are routine. 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.

In the present matter the triple combination was well contemplated in prior art as evident from Exhibits 1, 2 and 3. It is to be noted that Exhibit 1 also taught the exact combination as sought by the present applicants. Although claim 1 does not specifically mention TDF, EFV and FTC the object of the invention was to achieve a triple combination without loss in bioavailability. Thus the applicants had to experimentally confirm the activity of such a well-taught combination. While doing so it faced problems of incompatibility between the surfactant and TDF, which was also successfully solved by employing methods routinely practiced in the industry (Exhibit 4 and 5). Thus the entire invention is an experimental confirmation of the teachings of prior art. Admittedly, Exhibit 1 is the
closest prior art however no evidence by way of comparative data has adduced to corroborate the superiority of the present invention.

9.19 The opponent further relied upon a few decisions/case laws to support its contentions on the ground of lack of inventive step and obviousness. Specific portions of which have been extracted herein below for reference:

In case number - T 0235/97- 3.3.2, the EPO Board of Appeals held as under.

Having regard to this clear and strong suggestion to pursue tests on the basis of the teaching of document (7), the Board is convinced that the skilled person faced with the problem as defined above and knowing both documents (7) and (13) would have tried with a reasonable expectation of success to use 2-HPCD as stabilizer in aqueous EPO solutions, knowing in particular that he would at the same time overcome the toxicity problems linked to the use of HSA.

4.10 Contrary to the Appellant's point of view the Board sees no prejudice against the claimed solution on the basis of the disclosure of document (12) contained in document (7) as a cross reference and showing that proteins employed in parenteral formulations may vary tremendously in their properties. It is highly probable that a skilled person trying to improve the unsatisfactory results obtained with one stabilizer would first try to replace completely the unsatisfactory ingredients and would not fall back on a combination of the unsatisfactory ingredient with other stabilizers already known as components in aqueous EPO solutions. In view of the toxicity problems linked to the administration of HSA he would in any case be encouraged to find a product which is described as being non-toxic.

Moreover, the skilled person would note in particular that the authors of document (7), even in the light of the warning in document (12) of the specificity of the behaviour of each protein, nevertheless give an express and strong hint to pursue the tests with 2-HPCD.

When coming to the above conclusions, the Board did not overlook that document (7) describes a large palette of stabilizing and solubilizing effects by testing inter alia small molecule drugs and the effect of inhibiting protein aggregation of insulin, which is not a glycosylated protein like EPO. However, once there is such a strong expectation of success when continuing experimental work, it is most unlikely that there would be a particular prejudice against tests with EPO for a skilled person.

The Board is convinced that in the present case the skilled person would try to complete the palette of tested drugs proposed in document (7) by EPO.

Also, the teaching of document (9), referred to by the Appellant in favour of an inventive step, is not so relevant that the skilled person would not try what is strongly suggested by document (7). In fact, document (9) clearly relates to non-derivatized cyclodextrin (see particularly column 3, Table I, and column 5, Table II) with all the disadvantages known from document (7) and thus the skilled person would indeed set aside this document, but
only so as not to continue tests with pure cycloextrin. Therefore, contrary to the
Appellant's argumentation, document (9) can be regarded as a further incentive to
continue test series with the modified cycloextrin of document (7). The Board has
consequently come to the conclusion that the replacement of HSA by the derivatized
cycloextrin of the invention in order to increase the stability of EPO in aqueous solution
was obvious to a skilled person. The claimed formulations therefore lack the required
inventive step under Article 56 EPC.

In case number - T 0956/05- 3.3.2, the EPO Board of Appeals held as under.

3.1.2 Document (6) represents the closest state of the art. According to the introduction
in the description, page 1, paragraph 1, together with claim 1 of (6), the subject-matter of
that prior art corresponds to medicinal aerosol formulations which are at least
substantially free of chlorofluorocarbons and in particular to such formulations
comprising a medicament and 1,1,1,2-tetrafluoroethane (HFC 134a). On page 8 of
the description, a formulation is disclosed as example 24A, consisting of 0.012g (0.23 wt%)
of "salbutamol", 0.058g (1.10 wt%) of ethanol, 0.005g (0.09 wt%) of a surfactant and the
rest (5.220g) of HFC 134a as the single propellant. Salbutamol is a synonym for
albuterol and on page 5, line 57, in document (6) the term "salbutamol" in the table of
contents is defined for example 24a as "salbutamol sulfate B.P., micronised". Based on
this definition, in document (6) the term "salbutamol" represents micronised albuterol
sulfate in the same way as BDP represents isopropyl alcohol solvate, micronised, or in
the same way as DSCG stands for sodium cromoglycate B.P., micronised (see (6), page
6, lines 1 and 2).

In line 57 on page 8 of (6) the test samples are described as stable suspensions.
Therefore, in document (6) a suspension aerosol formulation is disclosed comprising
from 0.2 to 0.5% by weight of micronised albuterol sulfate and HFC 134a instead of
HFC 227 as the only propellant.

3.1.3 In the absence of any comparative example referring to the closest state of the art,
represented by example 24A of (6) (see point 3.1.2 above), the technical problem
underlying the patent in suit can only be seen in the provision of a further suspension
aerosol formulation. The solution to this problem is the provision of a suspension aerosol
formulation exhibiting the features of claim 1 of the main request or of the second
auxiliary request.

3.1.4 Having regard to worked example 2 of the patent in suit and in the absence of any
counter-evidence provided by the appellant, the board is convinced that the problem
has been plausibly solved.

3.1.5 However, in order to supply merely a further suspension aerosol formulation with
respect to the formulation disclosed in document (6), it is obvious to the skilled person to
substitute HFC 134a by the other propellant that was well known at the time of the
priority of the patent in suit as non-damaging to the ozone-layer of the atmosphere and
as a good candidate for production of aerosol formulations in this context (it was for
instance mentioned in document (16), in particular in the lines 7 to 10 of the abstract and
in the headlines on pages 185 and 186).
3.1.6 Accordingly, the board can only conclude that the subject-matter of each of the claims 1 of the main request or of the second auxiliary request does not involve an inventive step, as it merely amounts to taking the other of a pair of two well known propellants in the context of avoiding ozone-damaging propellants of the chlorinated hydrocarbon type.

In case number - T 0928/06- 3.3.02, the EPO Board of Appeals held as under.

According to the description of the patent in suit, the claimed formulation enhances bioavailability and increases compliance and colour stability. During the oral proceedings, the appellant-patent proprietor, referring to document (22), an extract of the Austrian codex for pharmacists, submitted that it was well-known in the field relating to this drug that the treatment required intake of the drug with meals to increase its bioavailability. As to the effect on colour stability, the Board observes, as objected by the appellant-opponents and the respondent, that this alleged effect is not at all substantiated, either in the patent itself or in the file. Moreover, the Board notes that the amount of iron oxide, an agent used to achieve colour stability, in the examples of the patent and in the example of document (4B) is similar. As to the effect relating to bioavailability and compliance, the Board considers, in favour of the appellant-patent proprietors, that this is confirmed by the results published in annex 3 filed during the appeal proceedings, which shows that a formulation according to claim 1 has an increased bioavailability so that it can be taken with or without food. Accordingly, vis-à-vis document (4B), the technical problem can therefore only be formulated as the provision of a formulation of oxacarbazepine with increased bioavailability so that it can be taken at any time.

2.3.2 This problem is solved by the use of a formulation having the technical features of claim 1. In the light of results published in Annex 3 filed with the appellant-opponent's 2 statement of grounds of appeal, the Board is satisfied that the problem has been solved (page 532, last paragraph).

2.3.3 Thus the question to be answered is whether the proposed solution would have been obvious to the skilled person in the light of the prior art. Document (4B) discloses only the average particle size of the compacted product, i.e. 400 μm, so that no information is available concerning the actual particle size before compaction. However, as this document does not mention any particular method of preparation, the Board has no reason to doubt, as argued by the appellant-patent proprietors, that example 1 of document (4B), which corresponds to its own previously marketed product Trileptal®, was prepared by a conventional method (i.e. not by micronisation), and has a median particle size well above 2 to 12 μm, namely 50 to 70 μm as accepted by the Opposition Division.

Having regard to document (7) for instance (page 51, left column, third paragraph), it appears that there is indeed a general teaching that the drug dissolves more rapidly, which results in a more rapid and complete absorption - conditions which increase the bioavailability - when its surface area is increased, so that poorly soluble or slowly dissolving drugs are micronized in order to reduce the particle size of the drug (page 51, left column, third paragraph).
Indeed, it is also known, for instance from document (24), that ocarbazepine is a drug having a very low solubility in water (see e.g. (24), page 913, right column, first paragraph). Accordingly, the skilled person would arrive at the claimed subject-matter in order to solve the above defined problem without inventive step, merely by following the clear teaching provided in document (7). Accordingly, the subject-matter of claim 1 does not fulfil the requirements of inventive step.

The 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.

10. NOT AN INVENTION/NOT PATENTABLE

10.1 The opponent adopted its written pleadings as found in paragraphs 10, 12 and 13 for lack of invention step (u/s 2(1)(ja)); section 3(d) and section 3(e) respectively.

10.2 The opponent also submitted two decisions of the Indian Patent Office to support its contentions under the ground of 3(d) and section 3(e) of which extracts are being provided herein below.

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

(page 12) "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. 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 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 fall under section
3(d) of the Patents Act in the absence of any data for the composition to show enhanced
efficacy."

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

Section 3(d) provides "mere discovery of a new form of a known substance which does
not result in the enhancement of the known efficacy of the substance, are not patentable
u/s 3(d). Explanation provides that "For the purpose of this clause, Salts, esters, ethers,
polymorph, metabolites, pure form, particle, size isomers, mixture of 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. It is
clear from the above that even the new form including polymorph can be patentable
provided they show the substantial improvement in the therapeutic efficacy as compared
to the prior art. 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. Applicants have admitted during hearing that due to enhanced stability and
solubility of the crystalline form III Atorvastatin hydrate, it is more bio available 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, & 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 Atorvastatin 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. Therefore this new form does not qualify the
requirement under section 3(d).

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

5.4.11 I 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. According to the section 3(d)
of the Patent Act, 1970, a new form, which does not show significant efficacy, is not
patentable and the presently claimed compound (polymorph) fail to pass the test of
enhanced efficacy.

5.4.12 Referring to the argument of the applicant that the same application has been
granted in US and EP, I view that the Indian patent law has been amended from time to
time since r山庄ia became a signatory to the TRIPS and the current amendment of section
3(d) clearly makes the Indian patent law distinct from the laws in US and EP. The
provisions of Indian Patent law is customized and industrial needs in India and are not
guided and dictated by the laws in other countries.

In the present matter, the combination admittedly has substantially same bioequivalence
as Truvada and Sustiva, which are already part of prior art. Therefore there is not increase
in bioavailability and no data has been produced to substantiate the enhanced efficacy of
the combination over the previously known combination as taught in Exhibit 1. Thus the
present invention falls under the mischief of Section 3(d) and ought to be rejected.

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

I agree with the opponent that the applicant has failed to show neither in specification
nor through the submissions that novel pharmaceutical composition claimed exhibits any
of the properties above and beyond the aggregation of the constituent parts.
So claims fall under Section 3(e) of the Act are not patentable.

It is submitted that the present invention also fails to provide any data to corroborate that
the combination claimed has a synergistic effect. Moreover the applicant has itself
mentioned that the combination claimed is bioequivalent to the individual components
which go to show that it is no more than an additive effect. Thus the invention falls under
the mischief of Section 3(e) and ought to be rejected.

11. SECTION 25(1)(g): INSUFFICIENCY

11.1 The opponent submitted that it would adopt its written pleadings and for the sake
of brevity the same is not being reiterated. However the opponent drew the attention of
the Ld. Controller to two significant issues, which are to be carefully considered.
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 bi-
layer 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.

12. APPLICANT'S CASE AND REBUTTAL

It is to be noted that the applicant filed a reply statement, the contents of which are in reply to some other opposition and not the present one. Paragraphs 1 to 10 are the only relevant paragraphs which are in response to the present representation.

The opponent placed the relevant provisions of the CPC which relate to pleadings. It is stated that the Rules quite clearly state that when there is no specific or evasive denial on the part of the applicant the contents of the plaint (in this case the representation) are admitted. By not denying the contentions/allegations in the plaint the respondent admits the same. So in the present case, the reply statement has not denied the contentions of the representation which ought to amount to admission of the same.

Order VIII, Rules 3 to 5

R3. Denial to be specific

It shall not be sufficient for a defendant in his written statement to deny generally the grounds alleged by the plaintiff, but the defendant must deal specifically with each allegation of fact of which he does not admit the truth, except damages.

R4. Evasive denial

Where a defendant denies an allegation of fact in the plaint, he must not do so evasively, but answer the point of substance. Thus, if it is alleged that he received a certain sum of money, it shall not be sufficient to deny that he received that particular amount, but he must deny that he received that sum or any part thereof, or else set out how much he received. And if an allegation is made with diverse circumstances, it shall not be sufficient to deny it along with those circumstances.
R5. Specific denial

(1) Every allegation of fact in the plaint, if not denied specifically or by necessary implication, or stated to be not admitted in the pleading of the defendant, shall be taken to be admitted except as against a person under disability:

Provided that the Court may in its discretion require any fact so admitted to be proved otherwise than by such admission.

(2) Where the defendant has not filed a pleading, it shall be lawful for the Court to pronounce judgment on the basis of the facts contained in the plaint, except as against a person under a disability, but the Court may, in its discretion require any such fact to be proved.

(3) In exercising its discretion under the proviso to sub-rule (1) or under sub-rule (2), the Court shall have due regard to the fact whether the defendant could have, or has, engaged a pleader.

(4) Whenever a judgment is pronounced under this rule, a decree shall be drawn up in accordance with such judgment and such decree shall bear the date on which the judgment was pronounced.

The applicant stated that Section 25(1) proceedings are not strictly legal in nature and therefore such rules do not apply.

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.
The opponent submitted that Exhibit 1 at page 30, lines 10 to 15 clearly and unambiguously teaches a ternary unitary dosage, i.e., a single dosage form.

The opponent would further rely upon the decision passed by the Ld. Controller in the matter of 3383/DELNP/2005, which corresponds to Exhibit 1 of the instant opposition. The opponent submitted that claim 58 wherein which related to the exact triple combination as claimed in the instant application was also rejected. The said decision was annexed to the representation as Annexure C.

In view of the above the patent application may be rejected in toto as it is in breach of the various provisions of the Act as placed before the Ld. Controller with the representation as well as at the hearing.

Dated this the 04th Day of May 2010.

[Signature]
Mythili Venkatesh
Of S. Majumdar & Co
Opponents Agent