BEFORE CONTROLLER OF PATENTS

THE PATENT OFFICE, DELHI

In the matter of pre-grant opposition by way of representation under section 25(1) of The Patents Act, 1970 as amended by The Patents (Amendment) Act, 2005

And

In the matter of rule 55 of The Patents Rules, 2003 as amended by The Patents (Amendment) Rules, 2006

And

In the matter of Application No: 1960/DELNP/2007

APPLICANT: BAYER HEALTHCARE AG, GERMANY.

Present in hearing:

Dr. Sanjay Kumar (Agent representing the Applicant)

OPPONENT I: NATCO PHARMA LIMITED, HYDERABAD.

Hearing held on 24th December, 2014

Present in hearing:

Dr.Chitra Anand (Agent representing the Opponent)

OPPONENT II: FRESENIUS KABI ONCOLOGY LIMITED, GURGAON,

Hearing held on 05th February, 2015.

Present in hearing:

Mr. Vishal Sudan (**Agent representing the Opponent).**

Dr.A.P.Singh (Examiner of Patents & Designs)

An application for a patent bearing number **1960/DELNP/2007** was filed in Patent Office, Delhi on 14th March, 2007 entitled "THERMODYNAMICALLY STABLE FORM OF A TOSYLATE SALT". A request for examination under Section 11-B was filed on 22nd September, 2008 and was assigned a Request No. 9316/RQ-DEL/2008. As per the provision under Section 11-A of Patents Act, the said application was published on 17th August, 2008.

The said application was examined according to the provisions in force of the Patents Act, 1970 (as amended) and First Examination Report (herein after called as FER) was issued to the Applicant's Agent on 16th September, 2013.The applicant filed reply to FER on 04th March, 2014 with amended set of claims.

It is to be noted that two pre-grant oppositions under section 25(1) were filed against this application, first by

1) Natco Pharma Limited, Hyderabad represented by Rajeshwari & Associates on 14th October, 2011. The said pre-grant opposition was forwarded to the applicant on 16th September, 2013 & the applicant filed reply statement & evidence on 16th December, 2013 within three months from issuing of pre-grant opposition. Hearing in this matter was held on 24th December, 2014 **(Herein after Opponent I)** and second one by

2) Fresenius Kabi Oncology Limited, Gurgaon represented by the company itself. The said pre-grant opposition was forwarded to the applicant on 21st October, 2014 & the applicant filed reply statement & evidence on 19th January, 2015 within three months from issuing of pre-grant opposition. Hearing in this matter was held on 05th February, 2015. **(Herein**

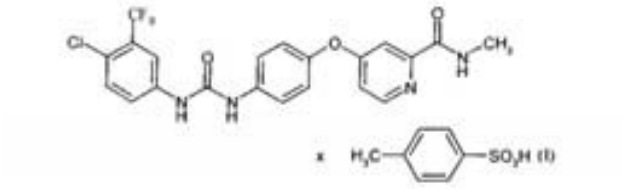
after Opponent II)

Prior to hearing on this matter several dates of hearing to dispose of the said pre-grant oppositions were fixed by this Office as adjournments were taken by the applicant several times.

Having dealt with the hearings independently I will discuss the contents independently & finally decide the matter commonly.

The amended claims as filed on 04th March 2014 which are opposed are as follows

1) A tosylate salt of 4-{4-[({[4-chloro-3 (trifluoromethyl) phenyl] amino} carbonyl) amino] phenoxy}-N-methylpyridine-2- carboxamide compound



in the polymorph **I.**

2) A preparation of the compound of the formula (I) in the polymorph I, which comprises effecting the compound of the formula (I) in the polymorph II in an inert solvent until quantitative conversion to the polymorph **I.**

3) The preparation of the compound of the formula (I) in the polymorph I as claimed in claim 2, wherein the compound of the formula (I) in the polymorph II is effected in an inert solvent and seeded with crystals of the compound of the formula (I) in the polymorph **I.**

4) The preparation of the compound of the formula (I) in the polymorph I, wherein the compound of the formula (I) in the polymorph II is heated

to from 195 to 222°C at a heating rate of from 10 to 30°C per minute and subsequently cooled to from 10 to 30°C at a cooling rate of from 1 to 4° C per minute.

5) A pharmaceutical composition comprising the compound of the formula (I) mainly in the polymorph I and no significant fractions of another form of the compound of the formula (I).

6) The pharmaceutical composition as claimed in claim 5 containing more than 90 percent by weight of the compound of the formula (I) in the polymorph I related to the total amount of the compound of the formula (I) present in the composition.

7) The pharmaceutical composition as claimed in claim 5 comprising one or more inert, nontoxic, pharmaceutically suitable excipients.

8) A compound of the formula (I) in the polymorph I, obtainable by dissolving or suspending the compound of the formula (I) in the polymorph II in an inert solvent and stirring or shaking it until quantitative conversion to the polymorph I.

9) A compound of the formula (I) as claimed in claim 8 obtainable by dissolving or suspending the compound of the formula (I) in the polymorph II in an inert solvent and seeding it with crystals of the compound of the formula (I) in the polymorph I.

10) A combination comprising the compound of the formula (I) in the polymorph I and one or more other pharmaceutical agents.

11) The combination as claimed in claim 10 wherein the one or more other pharmaceutical agents are cytotoxic agents, signal transduction inhibitors, anti- cancer agents or antiemetics.

12) The pharmaceutical composition as claimed in one of the claims 5 and 6 comprising one or more other pharmaceutical agents.

13) The pharmaceutical composition as claimed in claim 12 wherein the one or more other pharmaceutical agents are cytotoxic agents, signal transduction inhibitors, anti cancer agent, or antiemetics.

Documents relied by Natco Pharma Limited, Hyderabad (Opponent I)

Before proceeding the opponents has relied on the cited documents which are as follows

1) Representation u/s 25(1) by the Petitioner/Opponent
2) Annexure-A: Specification as mentioned in impugned Indian National Phase Application 1960/DELNP/2007.
3) Annexure-B: A printout of WO 00/42012.
4) Annexure-C: A printout of WO 03/068228.
5) Annexure-D: A printout of WO 03/047579.
6) Annexure-E: A printout of article 'Current Pharmaceutical Design 2002. 8, 2255-57' titled 'Bay 43-9006: Preclinical Data' by Scott Wilhelm et al.
7) Annexure-F: A printout of W0/1996/027592.
8) Annexure-G: A printout of W0/1999/00 1444.

I further proceed on the grounds on which the actual opposition is based.

GROUNDS OF OPPOSITION:

GROUND I

lA) Section 3(c): Subject of claims 1-18 of the complete specification is not patentable under this Act

Claims 1-18 are drawn to polymorphic forms of 4-{4-[({[4-chloro-3- trifluoromethyl) phenyl] amino} carbony) amino] phenoxy}-N-methyl pyridine-2-carboxamide, also known as Sorafenib. Sorafenib is a known substance as admitted by the Applicant in the impugned specification -

the said compound is known from WO 00/42012 (Annexure B), WO 03/068228 (Annexure C) and WO 03/047579 (Annexure D). The Applicant also admits that a polymorphic form is already prepared in WO 00/42012 and hence the purported new polymorphic forms of this substance claimed in the impugned application are at best characterization of certain known properties of a known substance. Hence claim 1-18, falls squarely within the mischief and prohibition of Section 3(c) and therefore not patentable at all.

IB) Section 3(d): Subject of claims 1-18 of the complete specification is not patentable under this Act.

Claims 1-18 are drawn to polymorphic forms of 4-{4-[({[4-chloro-3- trifluoromethyl) phenyl] amino} carbony) amino] phenoxy}-N-methyl pyridine-2-carboxamide. The compound as claimed in the impugned application is already known as sorafenib and is also admitted by the Applicant as explained in the foregoing paragraphs.

As per section 3(d) of the Indian Patents Act, *1970,* the mere discovery of a new form of a known substance that does not result in the enhancement of the known efficacy of the substance is not patentable. The alleged invention of polymorphic form I, as claimed, is not supported by any examples or any other data of enhanced efficacy over that of known substances, including the metastable form.

In the absence of any evidence in the specification and given that the stable form (form I} is nothing but the stable form of metastable form disclosed in W000/42012, it must be assumed that the polymorphic form I as claimed in claim I of the impugned application does not differ significantly in properties with regard to efficacy as compared to the polymorphic form II.

Hence the form I as claimed is not patentable under section 3(d) of the

Indian Patent Act of 1970. Moreover the process for the preparation of sorafenib tosylate polymorph I as claimed in claims 2-4 neither involve any new reactant nor result in any new product. Thus the claimed invention falls within the scope and mischief of Section 3 (d)

IC) Section 3(e): Subject of claims 7, 8 and 12 and 15-18 of the complete specification is not patentable under this Act.

It is submitted that claims *7,* 8 and 12 and 15-18 are drawn to a pharmaceutical compositions, the composition comprises of the polymorphs of claims 1 along with a pharmaceutically acceptable excipient. However, there are no examples to indicate that the composition is synergistic. The specification does not provide any data to substantiate the statement that the combination as claimed is synergistic. In the absence of such data, the composition is a mere admixture that results in the aggregation of the properties of the two known substances. Accordingly, the composition as claimed is a mere admixture and on this ground alone ought to be rejected.

ID) Section 3(i): Subject of claims 5 to 6 and 9 to 11 of the complete specification is not patentable under this Act.

Claims 5-6 and 9-11 correspond to method of treatment and are not patentable under sec 3(i). It is submitted that under the act, any method for treatment of an animal or human cannot be patented. The said claims fall within the said provision and hence should be rejected.

GROUND II

II) Section 25(1) (b)/(c): Lack of novelty

The invention as claimed in claims 1-18 lacks novelty and are not patentable under Section 25(1) (b)-(c) of the Patents Act, 1970 (as amended in 2005; hereinafter referred to as "the Act"). It is submitted that none of the claims

of 1960/DELNP/2007 are novel and they are all liable to be rejected on this ground alone.

PRIOR USE

It is submitted that sorafenib tosylate is well known and widely used before the date of the impugned application and hence the polymorph as claimed by the impugned specification is known from prior art disclosures. It is further submitted that sorafenib tosylate (in the form I as claimed in the impugned application) has been subject of extensive prior use by the Applicant. Such prior use has been well documented as in Current Pharmaceutical Design 2002, 8, 2255-57 titled 'Bay 43-9006: Preclinical Data' by Scott Wilhelm et al.

The said article narrates the use of the compound Bay43-9006 in pre-clinical settings (Annexure E). The compound would exist and would have been used naturally in its most stable form i.e. form I. Such documents constitute prior use of the polymorphic compound claimed. Thus, all claims stand anticipated by disclosure in prior art, prior claiming and by prior use and hence this application, ought to be rejected.

GROUND Ill

Ill) Section 25(1) (e): Lack of inventive step

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 (b) or having regard to what was used in India before the priority date of the claim. It is submitted that the claims of the impugned application are not inventive and obvious.

The impugned application admits at WO 00/42012 that one form of the polymorph is already disclosed. *"The compound of the formula {II} is prepared in the manner described in WO 00/42012. The compound of the*

formula {I} is prepared according to a general standard method for the preparation of tosylate salts, as described in example I of the working examples. In this method, the compound of the formula {I) is obtained in one crystal polymorph which is referred to herein below as polymorph II. Polymorph II has a transition point of 194°C and a characteristic X-ray diffractogram, IR spectrum, Raman spectrum, FIR spectrum and NIR spectrum (Tab. 1-6, Fig. 1-6}. It has been found that polymorph II is metastable." (see para 1 of page 3 of the impugned specification).

Assuming but not conceding that the impugned application pertains to the conversion of one polymorphic form to another polymorphic form, it is submitted that the conversion of one crystalline form to another crystalline form is known from various prior arts which are in public domain since a long time and much before the priority date of impugned patent application.

For instance W0/1996/027592(attached herewith as **Annexure F)** published on 12 September 1996 teaches process for the preparation of polymorphic B form of (E)-4-[[3-[2-(4-cyclobutyl-2-thiazolyl) ethenyl] phenyl] amino]-2, 2-diethyl-4-oxobutanoic acid by agitating Polymorphic Form A in a solvent and adding the seed crystals of Form B.

Also, a disclosure in W0/1999/001444 (attached herewith as **Annexure G)** published on 14 January 1999 (Example 23) teaches process for the preparation of thermodynamically stable polymorphic form I of the tachykinin receptor antagonist 2-(r)-(1-(r) -(3,5-bis(trifluoromethyl) phenyl)ethoxy)-3-(s)-(4-fluoro) phenyl-4-(3-5 (-oxo-1hAh-1,2A,-triazolo) methylmorpholine by effecting the compound of Form II in methanol and seeded with crystals of Polymorphic form I.

Thus, the conversion of one polymorphic form of compound to another is

spontaneous and is also known from prior art and is within the routine skills of a person skilled in the art. Moreover, the use of inert solvent and seeding technology, which appears to be the crux of claims 2-4 of impugned application, is also in the public domain.

Claims 2-4 and claims 13-14 of the impugned patent application deal with process for the preparation of polymorphic form I of sorafenib tosylate. Claim

13- 14 deal with the process of converting from polymorph II to polymorph I. *"The process involves effecting the polymorphic form II of sorafenib tosylate in an inert solvent and stirring or shaking until Polymorphic Form I was obtained".*

It is submitted that stirring and shaking are but means to accelerate the conversion and even without such process, the polymorphic form II is automatically converted to polymorphic form I. Polymorph-I of sorafenib tosylate is found to be the most stable crystal form and claimed as a compound in claim-1 of the impugned application. The pharmaceutical composition and method of use claims in the said application, all deal with polymorph-I only as this is 'stable'.

The process and methods used for making polymorphs or converting a metastable polymorph into a stable polymorph is well documented in literature. For any a chapter from the book "Advanced Pharmaceutical Solids" by Jens T. Carstensen, published by Marcel Dekker Inc, ©2001 -(see Annexure H) clearly discloses the various experimentation techniques to obtain polymorphs and to convert metastable polymorphs into stable polymorphs.

Thus from the above following are established

1. The conversion of one polymorphic form to another polymorphic form

is well known in prior art.

2. The use of the inert solvent and seeding technology for the conversion one polymorphic form to another polymorphic form is known from the prior art. Hence, the process of conversion of polymorphs and the resultant polymorphic form is well known from prior art. On this ground alone all claims ought to be rejected.

GROUND IV

IV) Section 25(1) (f): Subject of claims 1 to 3 is not an invention within the meaning of this Act or is not patentable under this Act.

It is submitted that since claims 1-18 are not novel, are not inventive and lack industrial application, they do not constitute an 'invention' under the Act. In this regard, the Opponent craves leave to refer and rely on submission made in Grounds 1-VI above which are not being repeated for the sake of brevity.

i) Subject of claims are not patentable under section 2(1) (ja) of this act:

The claimed invention falls under the mischief of Section 2(1)(ja) being devoid of inventive step as according to definition of inventive step, the invention should have a technical advancement over the prior art or it should show economical significance or both and should not be obvious to a person skilled in the art. The alleged invention as claimed is not a technical advancement.

GROUND V

V} Section 25 (l) (g}: The complete specification does not sufficiently and clearly describe the invention or the method by which it is to be performed.

It is submitted that the complete specification of 1960/DELNP/2007 does not describe the invention claimed or the method by which it is be performed.

The particulars thereof are as under:

Claims 1-18 of the application at hand bitterly suffer from lack of adequate description and are liable to be rejected.

GROUND VI

VII) Section 25(1) (h): The patentee has failed to disclose to the Controller the information required under Section 8:

It is submitted that the Applicant-Respondent has failed to disclose the details of corresponding foreign applications filed and on this ground alone the patent application should be rejected.

The applicant is required to provide all the information regarding the prosecution of the equivalent applications till the grant of the Indian application to the Controller in writing from time to time and also within the prescribed time. The applicant has failed to furnish the details of National phase applications filed in USA, Europe etc, which are still under examination and not granted. Therefore the applicant has failed to comply with the requirements of the section 8 of the act and the opponent demands rejection on this ground also

Documents relied by Fresenius Kabi Oncology Limited, New-Delhi (Opponent II)

Documents relied upon

1) Representation u/s 25 (1) by the opponent 1-30.

2) Annexure- I: Claims of 1960/DELNP/2007 31-33.

3) WO 03/068228 (referred to hereinafter as D1) published on August 21, 34-110, 2003; annexed hereto as Exhibit 1.

4) WO 03/050111 (referred to hereinafter as D2) published on Jun 19, 2003; 111-132 annexed hereto as Exhibit 2.

5) A document downloaded from the EMA website (hereinafter referred to

as133-181 D3) which is annexed hereto as Exhibit 3.

6) A document downloaded from the FDA website (hereinafter referred to as 182-186 D4) which is annexed hereto as Exhibit 4.

7) Chemistry & industry, 1989, pages 527-529 (hereinafter D5) which is 187-189 annexed hereto as Exhibit 5

8) Pharmaceutical Research, vol. 12, No. 7, pages 1995, 945-954 (hereinafter 190-199 D6) which is annexed hereto as Exhibit 6.

9) X-Ray diffraction data of products obtained by repeating (four times) the 200-example 1 of the impugned application are annexed hereto as Exhibit 7 to 203-214 Exhibit 10.

10) X-Ray diffraction data of product obtained by following the method of D2215-217 is annexed hereto as Exhibit 11.

11) Affidavits of Ms. Sandeep Kaur, who repeated the experiment of example 1, 218-218 of the impugned application is annexed hereto as Exhibit 12

12) Affidavits of Mr.Nikunj Kachhadia, who repeated the expt. of 219- 219 example 1 of the impugned application is annexed hereto as Exhibit 13

13) Affidavit of Mr. Varun Sharma who performed the method as given in D2 220 is annexed hereto as Exhibit 14

GROUNDS OF OPPOSITION OF OPPONENT II

1. The application is opposed on the following grounds:

a). Section 25(1) (b): Novelty *I* Anticipation

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 the 1st day of January, 1912; or

(ii) In India or elsewhere, in any other document: Provided that the

ground specified in sub-clause (ii) shall not be available where such publication does not constitute an anticipation of the invention by virtue of sub-section (2) or subsection (3) of section 29;

b). Section 25(1) (d): Prior Knowledge / Prior Use

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.

Explanation.-For the purposes of this clause, an invention relating to a process for which a patent is claimed shall be deemed to have been publicly known or publicly used in India before the priority date of the claim if a product made by that process had already been imported into India before that date except where such importation has been for the purpose of reasonable trial or experiment only;

c). Section 25(1) (e): Obviousness I lack of inventive step

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 (b) or having regard to what was used in India before the priority date of the applicant's claim;

d). Section 25(1) (f): Not Patentable Subject Matter

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;

e) Section 25(1) (g): **Insufficient disclosure**

That the complete specification does not sufficiently and clearly describe the invention or the method by which it is to be performed;

ARGUMENTS ON MERITS AND HEARING SUBMISSIONS

Now here I will discuss the argument of opponent I & opponent II & its rebuttal by the Applicant on the opposition grounds jointly.

GROUND 1: CLAIMS NOT PATENTABLE UNDER SECTION 3(c)

Opponent I arguments & hearing submission

The opponent 1 contends that the claims drawn to the polymorph 1 are not patentable under Section 3(c) of the Act. It is an admitted fact that the specification admits that Sorafenib tosylate is an own substance disclosed by the WO 00/42012, WO 03/068228 and WO 03/47579. It is admitted in the specification that a polymorphic form is prepared in WO 00/42012. No attempt has been made by the Applicant to distinguish the properties of the polymorphic form disclosed in WO 00/42012. In the absence of such data and information, it must be presumed that the polymorph 1 claimed in the present application is the same polymorph as disclosed in WO 00/42012 and therefore, the claimed polymorph is known. Since no claim can be made to a known substance, or properties of such known substance, the claims are liable to be rejected. In the alternative and without prejudice, it is submitted that the polymorphic form claimed in the present application is nothing but characterization of the properties of the polymorph already disclosed in WO 00/42012.

Opponent II arguments & hearing submission

The opponent II has not pressed this ground

Applicants Argument & hearing submission to Opponent I

With regard to Section 3(c) of the Patents Act, it is submitted that the contents of paragraph 1A of the present representation are misleading, lack proper interpretation of law, science and are based on assumptions · and presumptions and therefore, are vehemently denied. Opponent is wrong when he says that the present claims 1 to 18 are drawn to polymorphic forms of 4-{4-[({[(4-chloro-3-trifluoromethyl) phenyl] amino} carbonyl) amino] phenoxy} –N-methylpyridine-2-carboxamide which is sorafenib. The correct statement would be that the present claims relate to the polymorphic forms of the tosylate salt of sorafenib which is different from sorafenib itself, in particular when polymorphic forms are discussed. WO 00/42012 (referred to as Annexure B in the Opponent's statement) does not describe any polymorphic form of sorafenib tosylate salt. WO 03/047579 (referred to, as Annexure Din the Opponent's statement) and WO 03/068228 (referred to as Annexure C in the Opponent's statement) describe a tosylate salt of sorafenib but without any specification of the polymorphic form. The polymorphic form I of the tosylate salt of sorafenib as claimed in the present application is not disclosed in any of the cited documents by the Opponent. It is pertinent to mention here that the submissions made by the Opponent are based on conjectures and surmises in as much as the Opponent has not placed on record any evidence/ document whatsoever, which establishes the possibility of polymorphism, is sorafenib tosylate. There has been human intervention in the inventing subject matter of the present invention. Therefore, the subject matter claimed by any stretch of imagination cannot be considered a mere discovery of a scientific principle as alleged or at all and therefore, provision of Section 3(c) of the Patents Act is not attracted in the present case in hand.

GROUND 2 OPPOSTION UNDER SECTION 25 (1) (g)

THAT THE COMPLETE SPECIFICATION DOES NOT SUFFICIENTLY AND CLEARLY DESCRIBE THE INVENTION OR THE METHOD BY WHICH IT IS TO BE PERFORMED

Opponent I arguments & hearing submission

Though the opponent had pressed this ground in pre-grant opposition but has withdrawn this ground during hearing.

Opponents II arguments & & hearing submission

The opponent submitted, that the whole objective of a patent grant is that a *quid pro quo* system is followed, whereby the Patent Office grants a patent to an inventor when he discloses the mode and method of performing an invention, along with details pertaining to the invention such as prior art, description etc. The very basis of granting a patent is to provide monopoly right to the inventor/applicant in lieu of the disclosure of the working of the invention to enable an unimaginative individual having sufficient skill in the art, to perform the invention in its best embodiment.

Application describes that polymorph-II is the starting material for the preparation of polymorph-I of Sorafenib tosylate. In this regard, impugned application provides five examples for the preparation of polymorph-I starting from polymorph-II.

However, as stated earlier which is not repeated here for the sake of brevity that there is no best method disclosed for the preparation of polymorph-II. As explained earlier, reworking of example 1 or general standard method does not lead to the formation of polymorph-II. This leads to an unsolvable problem to the skilled person in the field. In fact, general standard methods known in the

art do not lead to the formation of polymorph-II of Sorafenib tosylate.

Opponent highlighted during the hearing that when there is an opposition filed by the instant opponent, Applicant mentioned various theories/points or measures to consider while preparing polymorph-II e.g. **special measures, unintentional seeding, disappearing polymorphs, uncontaminated laboratories etc.** However, there is no whisper of such special measures, unintentional seeding, disappearing polymorphs, uncontaminated laboratories etc. in the specifications of the impugned application.

Applicants arguments & submission to opponent II

The Applicant would like to draw the attention of the learned Controller to the relevant provision of the Patents Act which governs the field, i.e. Section 10(4) *of* the Patent Act which is reproduced herein below:

10. *Contents of specifications.-*

..... (4) Even; complete specification shall-

(a) fully and particularly describe the invention and its operation or use and the method by which it is to be performed;

(b) disclose the best method of performing the invention which is known to the applicant and for which he is entitled to claim protection; and

(c) end with a claim or claims defining the scope of the invention for which protection is claimed; (d) be accompanied by an abstract to provide technical information on the invention:

It is submitted that the Applicant is under a mandate to comply with Section 10(4) of the Patents Act in so far as its complete specification of the patent application is concerned. It is submitted that since the Applicant has followed the requirements as mandated by Section 10(4) of the Patents Act, the Opponent's objection on this ground is baseless and should be rejected outrightly.

It is submitted that the said ground has been taken in a mechanical manner by the Opponent without reference to the facts at hand. It must be kept in mind that over 40 patents have been granted on corresponding applications filed in various countries where the complete specification fulfilled the test of describing the invention sufficiently and the best mode of carrying out the invention.

It is submitted that the complete specification filed by the Applicant sufficiently describes the invention as claimed in the claims of the patent application. It is submitted that the Opponent has failed to provide any particular detail which a person skilled in art should know to work the invention, and which is not so disclosed. Therefore, in absence of any such particular information, the averments are mere *ipse dixit* and are liable to be ignored by the learned Controller. However, the Applicant would like to draw the attention of the learned Controller to the fact that the polymorphic forms of sorafenib tosylate are sufficiently and clearly described in the description in tables 2 to 6 by X-ray diffractometry, IR spectroscopy, Raman spectroscopy, FIR spectroscopy and NIR spectroscopy.

It is submitted that the complete specification filed by the Applicant sufficiently describes the invention as claimed in the claims of the alleged patent application.

It is submitted that the polymorph of example 1, i.e., polymorph ll, is not part of the invention claimed in the patent application. If the whole preparation process is conducted according to the description which is the process of example 1 combined with the process of example 2, polymorph I is yielded and the Opponent has confirmed this. The Opponent is trying to approbate and reprobate at the same time which cannot be allowed by the learned Controller. Therefore, the disclosed process provides the claimed subject matter

(polymorph I) sufficiently and there is no lack of enablement as alleged or at all.

In view of the above, it is submitted that the complete specification of the patent application sufficiently and clearly describes the invention as well as the method by which it is to be performed. Therefore, the Opponent's objection on this ground as well should be rejected outrightly.

In this regard, the Applicant also refers to and relies upon oppositions filed by the parent Company of the Opponent and Biofer S.P.A. before the EPO against corresponding European patent. (Reference in this regard is made to the internal pages *4* and 5 of the communication dated October 31, 2013 by Attorneys for the Patentee before the EPO and internal page 6 and pages 7 and 8 of the communication dated May 28, 2014 of the EPO and internal pages 2 and 3 of the communication dated December 5, 2014 by Attorneys for the Patentee before the EPO).

GROUND 3: CLAIMS NOT PATENTABLE UNDER SECTION 3(i)

In view of deletion of claims 5 to 6 and 9 to 11, which were related to the use of the compound of claim **1** or a pharmaceutical composition thereof for the treatment of certain disorders or diseases during reply to First Examination Report dated 04th March; 2014.**The opposition ground is rendered moot.**

GROUND 4: CLAIMS NOT PATENTABLE UNDER SECTION 3(e)

Opponent I arguments & hearing submission

The opponent 1 submitted that claims of the impugned application are drawn to polymorphic form 1 as well as the composition comprising such form as well as combinations containing such form I. However, the specification does not provide any examples for preparation of such composition nor are there any examples to demonstrate that the compositions claimed are

synergistic. Therefore, the composition is no more than a mere admixture and is liable to be rejected.

Applicant's arguments & hearing submission to applicant I

The applicant submitted that the Opponent is trying to mislead the learned Controller with wrong interpretation of the claims of the Patent Application. It is submitted that as long as the polymorphic form I of compound of formula I itself is patentable, any composition comprising said polymorphic form I ought to be patentable as well and as such provision of Section 3(e) are not attracted in the present case in hand.

Opponent II arguments & & hearing submission

The opponent 2 asserts that claims 5-7 claimed in the specification of the impugned application fail to provide any data to support the statement that these pharmaceutical compositions or combinations provide any synergistic effect. In the absence of such data, the compositions or combinations in these claims are a mere admixture of the known substances. Hence, such claims ought to be rejected solely on the basis of this ground.

Applicants arguments & hearing submission to Opponent II

The applicant submitted that the Opponent is trying to mislead the learned Controller with wrong interpretation of revised claims 5, 6, 7, 10 to 13 on record (which correspond to earlier claims 7, 8, 12, 15-18) of the patent application. It is submitted that as long as the polymorphic form I of compound of formula I itself is patentable, any composition comprising said polymorphic form I ought to be patentable as well and as such the provision of Section 3(e) is not attracted in the present case in hand.

GROUND 5- CLAIMS NOT PATENTABLE AS LACKING NOVELTY UNDER SECTION 25(1) (b)/(c)

Opponent I arguments & & hearing submission

The opponent contends that the patent application itself discloses and admits that Sorafenib tosylate salt is disclosed by WO 00/42012, WO 03/47579 and

WO 03/068228. Scott Wilhelm et al narrate the use of the compound BA43-9006 in clinical settings- the same constitutes a specific use of the compound BA43-9006. The said compound would have existed in its most stable form i.e. Form 1. In the absence of any data to the contrary, it must be presumed that the above documents disclosed the polymorph 1 as claimed in the impugned application and hence, polymorph 1 stands anticipated by aforesaid prior art.

Applicants' arguments & hearing submission to Opponent I

The applicant submitted that the present claims relate to the polymorphic form I of the tosylate salt of sorafenib. WO 00/42012 does not describe any polymorphic form of sorafenib tosylate salt. WO 03/047579 and WO 03/068228 describe a tosylate salt of sorafenib but without any specification of the polymorphic form. The polymorphic form I of the tosylate salt of sorafenib as claimed in the present application is not disclosed in any of the documents cited by Opponent. Therefore, the subject matter claimed is novel.

The applicant also submitted that the patent application discloses an invention which pilots to higher stability and better physical characteristics of Sorafenib in the form of polymorph I of tosylate salt. It is important to distinguish the present invention from the disclosure in the prior art document which pertains to Sorafenib to cure cancer.

It is submitted that none of the cited documents read alone or in combination disclose any polymorph of sorafenib tosylate, let alone polymorphic form I, any pharmaceutical composition thereof or any process for making the said polymorphic form. A person skilled in the· art cannot predict the polymorphism and prepare the subject compound from the available disclosure therein. Therefore, polymorphic form I of sorafenib tosylate is not anticipated in view of the cited documents.

Opponent II arguments & hearing submission

Claim 1

Claim 1 of the impugned application relates to polymorph-I of Sorafenib tosylate (in general referred to as compound of claim 1).

Applicant states that polymorph-I can be prepared by converting polymorph-II of Sorafenib tosylate. Applicant states that polymorph-II is obtained while converting Sorafenib free base to Sorafenib tosylate via following any general standard method for the preparation of tosylate salts or by following the procedure given in example 1 of the impugned application (see page 2, first paragraph and example 1 of the impugned application).

As explained in the representation, Opponent repeated the said example 1 and observed that polymorph-I was obtained in contrary to the Applicant's statement. To ensure the reproducibility example 1 was repeated four times; however in all the experiments Polymorph-I was obtained (refer to chromatographs submitted with the representation).

To follow the Applicant's statements, Opponent also followed a general standard method for the preparation of Sorafenib tosylate. In this regard, Opponent prepared the tosylate salt of Sorafenib by following an alternative method known in the art that is found in document D2 (see page 11, example 3).The said example 3 of D2 was re-worked replacing the thiazolidine compound by Sorafenib, and again polymorph-I of Sorafenib tosylate was obtained (see chromatographs submitted with the representation).

From above, it is clear that by following any method for the preparation of Sorafenib tosylate from Sorafenib, polymorph-I is obtainable. Accordingly, it was submitted that D1 which is an admitted prior art and which discloses Sorafenib tosylate is nothing other than polymorph-I.

Therefore, it was submitted that the subject matter of claim 1 of the impugned

application is not new. Hence, D1 (which is an admitted prior art) disclosing Sorafenib tosylate inherently anticipates subject matter of claim 1.

Also, reference to the counterpart of the instant application in Europe under opposition was made by the Opponent. Wherein, counterpart of the impugned application is under opposition filed by the two opponents'. Among two of the opponents, one is the parent company of the instant Opponent and second named as Biofer SpA. It was observed and submitted before the Ld. Controller that Biofer SpA also arrived at polymorph-I of Sorafenib tosylate by following general standard method OR example 1 of the impugned application and polymorph-II is not obtainable by methods described in the impugned application.

In this regard, Applicant submitted that such phenomenon is caused by an unintentional **seeding or disappearing polymorph theory** (see page 18, line 07 of "Statement and Evidence").

Again, Applicant states that polymorph II can only be produced **when taking special measures** or might only be reproduced in **uncontaminated laboratories** (see page 18, line 15 onwards of "Statement and Evidence").

It was submitted by the Opponent that there is no whisper of such **special measures, unintentional seeding, disappearing polymorphs, uncontaminated laboratories etc.** in the specifications of the impugned application.

Opponent submitted that there is no need to take special measures while following a prior art. Accordingly, if by following a prior art someone arrives at the subject matter of the instant application then it should be considered as novelty destroying prior art.

In this regard, Applicant relied upon following case law for support which was handed-out during the hearing. The relevant paragraphs there

from are set-out for ready reference:

- SMITHKLINE BEECHAM CORPORATION and BEECHAM GROUP, P.L.C., V. APOTEX CORP., APOTEX, INC., and TORPHARM, INC

Factual background of the case:

In 1970s, a British company, Ferrosan, invented a compound known as paroxetine, See U.S. Patent No. 4,007,196 ('196 patent). Ferrosan eventually developed a process to produce the **crystalline hydrochloride salt of paroxetine**, or paroxetine hydrochloride (PHC).

In 1980, Ferrosan licensed the '196 patent and its other PHC-related technology to SmithKline. SmithKline began manufacturing PHC in its Harlow plant in England.

In 1985, Alan Curzons, a chemist in SmithKline's Worthing, England laboratory discovered a **new crystalline form of PHC** while attempting to improve PHC production.

"Curzons's test results established that the new product was the hemihydrous form of PHC (PHC hemihydrate). Ferrosan's original form was anhydrous PHC (PHC anhydrate)."

"In 1985, SmithKline filed a patent application in the British Patent Office relating to "crystalline paroxetine hydrochloride, its preparation and its uses as a therapeutic agent." The British application identified the invention as both the hemihydrate and the anhydrate form of PHC, as well as mixtures that contain a major portion of either form.

One year later, on October 23, 1986, SmithKline filed a U.S. application claiming priority to the British application that issued as the '723 patent in 1988. The '723 patent does not claim PHC anhydrate and does not claim mixtures of the two PHC forms. The only claim at issue in this case is claim 1,

which reads in its entirety: "Crystalline paroxetine hydrochloride hemihydrate."

In 1998, Aptex while seeking approval to market its own PHC identified the active ingredient in its antidepressant as **PHC anhydrate.**

In 1998, SmithKline asserts that Apotex will infringe by manufacturing PHC anhydrate tablets that necessarily contain, by a conversion process discussed below, at least trace amounts of PHC hemihydrate.

Page 05, 2nd para:

"*To show that manufacture of PHC anhydrate tablets necessarily creates PHC hemihydrates: SmithKline proffered expert testimony on the* ***so-called "seeding" or "disappearing polymorph" theory.*** *Under this theory, Ferrosan may have originally created a crystalline compound, namely PHC anhydrate, in a relatively unstable form. For presently unknown reasons, the PHC anhydrate "morphed" into a more stable form, namely the PHC hemihydrate discovered in SmithKline's facilities. With this new form or polymorph in existence, SmithKline's experts explained, the general environment became "seeded" with crystals of PHC hemihydrate.* ***In this seeded environment, the PHC anhydrate converts to the PHC hemihydrate upon its inevitable contact with seeds of PHC hemihydrate. In other words, the creation of pure PHC anhydrate became extremely difficult, if not impossible; the old polymorph, PCH anhydrate, has effectively disappeared in its pure form because it changes naturally into the new polymorph, PCH hemihydrate."***

Page 16, 2nd para

"SmithKline argues that practicing the '196 patent infringes claim 1 of the '723 patent, but that the '196 patent does not anticipate claim 1 of the '723 patent. SmithKline uses the "disappearing polymorph" theory to justify its apparently inconsistent positions. On the one hand, SmithKline asserts that

the creation of a prior art compound will result in a product containing at least trace amounts of their patented compound. On the other hand, SmithKline contends that the creation of the prior art compound before SmithKline's discovery of its compound did not have the same result."

Page 18, last para:

The '196 patent is undisputed prior art under 35 U.S.C. § 102(b), even though the '196 patent discloses how to make PHC anhydrate and does not discuss PHC hemihydrate. PHC hemihydrate was not even discovered until years after the '196 patent was filed. Nonetheless, the '196 patent anticipates claim 1 of the '723 patent because the '196 inherently discloses PHC hemihydrate.

Page 20, line 06 onwards:

Apotex did not need to prove that it was impossible to make PHC anhydrate in the United States that contained no PHC hemihydrate, but merely that "the disclosure [of the prior art] is sufficient to show that the natural result flowing from the operation as taught [in the prior art] would result in" the claimed product. In re Oelrich, 666 F.2d 578, 581 (CCPA 1981); accord Mehl/Biophile Int'l Corp., 192 F.3d at 1366; see also Atlas Powder, 190 F.3d at 1349-50 (affirming the district court's finding of inherent anticipation despite a finding that the inherent element could be avoided by taking "extraordinary measures" when practicing the prior art).

Page 21, first line:

723 held invalid for anticipation by the 196 patent.

Page 22

SmithKline did not offer any evidence that pure PHC anhydrate can be produced in facilities that are not seeded.

Page 24

This court's law does not require Apotex to take extraordinary measures to practice the prior art without infringing claim 1 of the '723 patent. See Atlas Powder, 190 F.3d at 1349-50 (affirming the district court's finding of inherent anticipation despite a finding that the inherent element could be avoided by taking "extraordinary measures" when practicing the prior art).

Therefore, drawing the analogy with the instant case, if so called disappearing polymorph theory exists, then eventually at some stage before the filling of instant application Polymorph-I must have formed. Also, court in the above cited case made clear that there is no need to take special measures while following a prior art. Therefore, it was submitted that subject matter of the instant claim cannot be considered novel on view of D1.

- **SUBMISSIONS IN RELATION TO NOVELTY [U/S 25(1) (b)]**

Claim 1

Opponent submitted that it is evident from D3 that Modification-3 of Sorafenib tosylate was used in the clinical studies. Again, D3 makes it clear that a tablet formulation of Sorafenib tosylate was used in the clinical studies. Also, from D4 it is evident that clinical studies were conducted before the priority date of the impugned application.

In this regard, it was submitted that it's a common general knowledge that only a stable form of a compound can be used in the formulation of a composition. Applicant admitted the same that "***compounds in most stable form are required for efficacious and stable drug formulation*"** (refer to Page 12, para 21, line 05-06 of the "Statement and Evidence").

Therefore, it was submitted that any composition of Sorafenib tosylate would certainly use stable form which is as per Applicant's statement is polymorph I.

Accordingly, D1 (see page 60, line 04 -08 of D1) which is Applicant's own international application and which discloses the tablet compositions of Sorafenib tosylate would certainly use the stable form for the efficacious and stable drug formulation. Therefore, subject matter of the claim 1 lacks novelty over D1.

Claims 5-7 and 10-13

D1, inter alia discloses the subject matter of claims 5-7 and 10-13 as presented in table 2 of the representation which is not repeated herein for the sake of brevity.

Applicant's arguments & hearing submission to Opponent II

It is submitted that grounds of opposition under Section 25(1)(e) of the Patents Act does not relate to novelty/anticipation as has been the understanding of the Opponent, but to inventive step. The Opponent has wrongly relied upon Section 25(1) (e) to challenge the novelty of claim 1.

lt is submitted that Example 1 according to the patent application describes the preparation process of the metastable polymorph II of sorafenib tosylate. However, the present invention is about the stable polymorph I of sorafenib tosylate. Therefore, example 1is not an example to support the claims but is to demonstrate which polymorphic form was obtained at the time the invention was made, i.e., prior to the filing date, when conducting the process as described in examples. The figures and tables of the patent application show the analytical data obtained for said polymorph ll. Therefore, evidence is provided for the existence of polymorph II.

It is submitted that the Opponent now asserts that they could not reproduce polymorph II when conducting the process described in example 1 as per the declaration. It is submitted that while the said declarations have no recognition under the law and are inadmissible as evidence for the reasons as

stated in the preliminary paragraph, the process of example 1 was not carried in a proper manner. Accordingly, this could have happened for the following reason. It is known that established methods may sometimes result in a different crystalline product than usually expected, although all process parameters and starting materials have remained identical. Such phenomenon is caused by an “unintentional seeding (‘‘Disappearing Polymorphs", Ace. Chem. Res., voL 28, 1995, 193-200 which is annexed with the statement Annexure A). In the field of the art, this phenomenon is explained by minimal concentrations of a certain crystalline modification that serves as a seeding nucleus and thus, prevents the development of another crystalline form that had always been obtained up to then. Consequently, this phenomenon can be ascribed to a contamination of the laboratories and lab equipment. It is clear that particularly in the laboratories of the Opponent, polymorph I was already handled before the reproduction of Example 1, causing the results obtained by the Opponent. However, this does not mean that polymorph II can never be produced by the method according to Example 1, but that Example 1 might only be reproduced in uncontaminated laboratories (i.e. in laboratories different from those of the Opponent).

With regard to the submissions made by the Opponent re Dl (WO 3/068228), it is submitted that it merely mentions a tosylate salt of sorafenib by name but without any further disclosure, i.e., it neither describes a method for its preparation nor provides a specification of the any polymorphic form. That means none of the now identified polymorphic forms I, II and II were disclosed in Dl and this is true in particular for the polymorphic fom1 I of the tosylate salt of sorafenib as claimed in the patent application. Prior to the present invention of polymorph 1, a standard procedure was performed by the Applicant for the preparation of sorafenib tosylate which had yielded

polymorph II as described in example 1of the patent application. One of the reasons why the Opponent could not have reproduced polymorph II is explained above. The only information the public domain had at the filing date of the patent application was that sorafenib tosylate exists, but without any information about the polymorphic forms. Therefore, D1 cannot destroy the novelty of claim 1or any other claims of the patent application on record as alleged or at all.

With regard to the submissions made by the Opponent re 02, it is submitted that example 3 of D2 cannot anticipate the subject matter of the patent application, since the example is not directed to the preparation of "sorafenib" tosylate and 02 discloses a crystalline tosylate salt and a method for its preparation, which does not contain any reference of the compound "sorafenib". Therefore, D2 cannot destroy the novelty of claim 1 or any other claims of the patent application on record as alleged or at all. (Reference in this regard is made to the pages 17 to 19 paragraphs 33 to 37 of the statement in support of the application)

CLAIMS 5 TO 12- LACK OF NOVELTY [SECTION 25(1) (b)

It is submitted that claims 5, 6, 9, 10 and 11 referred to by the Opponent have already been deleted while filing response to the First Examination Report dated March 4, 2013. Therefore, the assertions by the Opponent in paragraph under reply in relation to the claims 5, 6, 9, 10 and 11do not survive anymore. In so far as the submissions made by the Opponent re claims 7, 8 and 12 (renumbered as claims 5, 6 and 7 respectively) are concerned, it is submitted that for the reasons as stated in the preceding paragraphs, since polymorph I of sorafenib tosylate is novel, claims 7, 8 and 12 (renumbered as claims 5, 6 and 7 respectively) are novel as well. In view of the above, it is submitted that the submissions made by the Opponent in paragraph under reply are baseless

and ought not to be taken cognizance of by the learned Controller. (Reference in this regard is made to the pages 22 to 23 paragraphs 45 and 46 of the statement in support of the application).

In this regard, the Applicant also refers to and relies upon oppositions filed by the parent Company of the Opponent and Biofer S. P.A. before the EPO against the corresponding European patent The communication dated October 31, 2013 by Attorneys for the Patentee before the EPO, the communication dated May 28, 2014 of the EPO, the communication dated December 5, 2014 by Attorneys for the Patentee before the EPO along with the documents/evidence filed in support of its submissions made therein are annexed hereto and marked as Annexure 11 (colly). (Reference in this regard is made to the internal pages 10 and 11 of the communication dated Octobe31, 2013 by Attorneys for the Patentee before the EPO and internal page 8 paragraph12.4 of the communication dated May 28, 2014 of the EPO).

GROUND 6: PRIOR USE SECTION 25(1) (d)

Opponent I arguments & hearing submission

It is submitted that sorafenib tosylate is well known and widely used before the date of the impugned application and hence the polymorph as claimed by the impugned specification is known from prior art disclosures. It is further submitted that sorafenib tosylate (in the form I as claimed in the impugned application) has been subject of extensive prior use by the Applicant. Such prior use has been well documented as in Current Pharmaceutical Design 2002, 8, 2255-57 titled 'Bay 43-9006: Preclinical Data' by Scott Wilhelm et al. The said article narrates the use of the compound Bay43-9006 in pre-clinical settings (Annexure E). The compound would exist and would have been used naturally in its most stable form i.e. form I. Such documents constitute prior

use of the polymorphic compound claimed.

Thus, all claims stand anticipated by disclosure in prior art, prior claiming and by prior use and hence this application, ought to be rejected.

Applicant's arguments & hearing submission to Opponent I

It is submitted that the Opponent wrongly asserts that the polymorphic form I of sorafenib tosylate is known from prior art disclosures. It is correct that sorafenib tosylate is mentioned in WO 03/047579 and WO 03/068228 but without any specification of the polymorphic form. The Opponent does not provide evidence of any prior use of the polymorphic form I of sorafenib tosylate. The document Scott Wilhelm.et al. "Current Pharmaceutical Design 2002" [referred to as Annexure E in the Opponent's statement] only describes the use of the compound BAY 43-9006 which is sorafenib itself but it is not even the tosylate of sorafenib, let alone arty polymorphic form thereof. It is submitted that none of the prior mentions the use any polymorphic form of sorafenib tosylate, which is the subject matter of the present invention. Therefore, no evidence is provided by the opponent for prior use of the polymorphic form I of sorafenib tosylate.

The contention of the Opponent that the present invention stands anticipated by prior use is a bald averment in the absence of any evidence to the contrary, and therefore, this ground of the Opponent is liable to be rejected.

Opponent II arguments & hearing submission to applicant

Compound of Claim 1 i.e. polymorph-1 of Sorafenib tosylate was well known and widely used before the priority date of the impugned application.

D3 and D4 are post published documents; however, it is a well set rule that publication is not necessary to establish prior knowledge or prior use. A matter may be publicly known even if unpublished, if for instance, it is publicly used.

Hence, these documents can be used as proof of evidence to establish prior use or prior knowledge of polymorph-I of Sorafenib tosylate.

D3 describes the use of the compound of claim 1 before the priority date of the impugned application. D3 on page 3/49 under the heading, *"Active Substance"* describes that, *"The active substance exhibits polymorphism and it crystallizes in three different modifications (Mod I, Mod II and Mod III).* "

Under the heading, *"Manufacture",* it states that, *"The active substance is visually tested for appearance and its identity is confirmed by NIR and HPLC, and the desired modification of Sorafenib tosylate (Mod I) is confirmed by Raman spectroscopy.* Also, it discloses that (on page 4/49), *"The potential for polymorphism was investigated by Raman spectroscopy and found to be unchanged"*

D3, on page 28/49 under the heading, *"Main studies",* it relates to the studies 100391 and 11213 performed during Phase II and Phase III trials. Also, it has been acknowledged on page 30/49 under the heading, *"Blinding (masking)"* that, *"The active and placebo tablets were identical in appearance".*

Hence, from the above, it is clear that polymorph-I of Sorafenib tosylate was used in phase II and phase III clinical studies.

From D4, it is evident that the clinical studies 100391 and 11213 for Sorafenib tosylate were started on September 25, 2002 and November 15, 2003 (Page 3, Point 5) respectively, i.e. before the priority date of the impugned application. It is also known that the product which is ultimately approved is necessarily the one which has been clinically tested, this being a strict requirement of drug approving agencies such as the FDA or EMA.

Hence, it is concluded that, during phase-II and Phase-III studies polymorph-I of Sorafenib tosylate was handed out to the patients prior to the priority date of the impugned application.

In *Bilcare Limited v. Amartara (P) Ltd.* (lA Nos. 10848/2006, 1397112006 and 11160/2006 in CSOS No.l847/2006), *"Prior public knowledge of the alleged invention which would disqualify the grant of patent can be by word of mouth or by publication through books or other media. If the public once become possessed of an invention, says Hindmarch on Patents, by any means whatsoever, no subsequent patent for it can be granted either to the true or first inventor himself or any other person, for the public cannot be deprived of the right to use the invention ... the public already possessing everything that he could give" [Source www.judis.nic. in]*.

As shown above, the subject matter of impugned application was in possession of the public before the priority date of the impugned application, hence lacks novelty *VIS* 25(1) (d), and hence, ought to be rejected on this ground too.

Applicants argument & hearing submission to Opponent II

It is submitted that the Opponent cites two clinical studies 100391 and 11213 which had started prior to the filing date. However, the Opponent does not provide any information on both studies which were published prior to the filing date. The later published EMEA document refers back to both studies but this information was not available prior to the filing date. The Opponent asserts that both studies cause a public prior use of polymorph I of sorafenib tosylate. This is not shown by dear *I* cogent evidence. The clinical studies were not conducted in the public domain but were subject to a specific confidentiality. In other words, neither the physicians, nor the clinical staff, nor the patients were allowed to give the tablets used in the study into the public. The tablets had to be used only in connection with the clinical study, which was confidential Therefore; no tablet went into the public domain. It is submitted that the Opponent failed to give clear *I* cogent evidence re how *I* to

whom/ where and when a tablet had been provided to the public prior to the filing date.

Without prejudice to what has been stated above, it is submitted that D3 relates to a scientific discussion of the pharmacological activity of sorafenib in treating cancer, published by the EMEA in 2006, i.e. after the filing date of the present patent application. D3 reports on two clinical studies 100391 (phase II study) and 11213 (phase III study), allegedly using film-coated tablets containing 274 mg of sorafenib tosylate, microcrystalline cellulose,croscarmellose, hypromellose sodium lauryl sulphate, magnesium stearate, water, titanium dioxide and red ferric oxide (03, page 2149, last paragraph).

D3 mentions that the active substance exhibits polymorphism and crystallizes in three different modifications (modification t It and III) (D3, page 3 *j* 49, first paragraph). However, D3 does not give any hint as to which of the modifications have been used for the clinical studies (page 29/49, second paragraph and page 36/ 49).

The Opponent further refers to document D4 (approval letter by FDA). From D4, it arises that the studies were carried out between September 25, 2002 and September 2006 (study 100391) and between November 19, 2003 and September 2006 (study 11213) (see e.g. 04, page 3, item 5).

D4 mentions the date when the clinical studies started. However, the date of delivery of the sorafenib tosylate tablets, i.e. the actual *"use",* does not necessarily correspond to the date of the start of the study. A *"use" of* the subject matter of the invention before the priority date of the present patent application (September 29, 2004) has not been evidenced.

It is submitted that the Opponent does not provide any information to prove that both the studies were published and were in public domain prior to the

filing date of the present application. The later published EMEA document (D3) refers back to both the studies but this information was not available prior to the filing date of the present application. Additionally, neither D3 nor D4 evidences that sorafenib tosylate in the form of polymorphic form I has been used in the clinical trials. It is also submitted that the clinical studies were not conducted in the public domain, but were subject to a specific confidentiality. The medical investigators were obliged to keep any information as to the study strictly confidential

Without prejudice to what has been stated hereinabove, it is submitted that for the purpose of Section 25(1)(d), the invention so far as claimed in any claim of the complete specification should have been publicly known or publicly used in India before the priority date of the claim. In view of the fact that the Opponent has not provided any evidence cogent or otherwise, as to the prior use of the invention disclosed in the patent application before the priority date of the claim, the present ground is baseless and has no merit and accordingly, ought not to be taken cognizance of by the learned Controller.(Reference in this regard is made to the pages 19 to 22 paragraphs 38 and 44 of the statement in support of the application).

It is submitted that it is a settled proposition of law that the onus was on the applicant to show that the prior use was known and not secret. Further, *if* published information does no more than disclose the existence of product which is not physically obtainable by the public, that product cannot have been said to have been "made available" unless and until the public has been told how it can be produced. In this regard the Applicant refers to and relies upon the case titled *Air Master Equipments India (P) Ltd v Ramesh Nana Mhatre* (2011) SCC online IPAB 31 at paragraph 31 which is annexed hereto and marked as Annexure·12.

At this stage, it is once again pertinent to draw the attention of the learned Controller to the oppositions filed by the parent Company of the Opponent and Biofer S.P.A. before the EPO against corresponding European patent wherein the Applicant had placed evidence on record by way of an affidavit of Ms Jeanne Lewis wherein she confirmed that all materials used for staff training were marked as "confidential", assuring the content to be the Applicant's property. (Reference in this regard is made to the internal pages 6 to 10 of the communication dated October 31, 2013 by Attorneys for the Patentee before the EPO, internal page 6 and pages 8 and 9 of the communication dated May 28, 2014 of the EPO and internal pages 3 to 6 of the communication dated December 5, 2014 by Attorneys for the Patentee before the EPO).

GROUND 7: CLAIMS LACK INVENTIVE STEP UNDER SECTION 25(1)(e)

Opponent I arguments & hearing submission

The opponent has relied on the documents

The impugned application admits at WO 00/42012 that one form of the polymorph is already disclosed. "The compound of the formula {II} is prepared in the manner described in WO 00/42012. The compound of the formula {I} is prepared according to a general standard method for the preparation of tosylate salts, as described in example I of the working examples. In this method, the compound of the formula {I) is obtained in one crystal polymorph which is referred to herein below as polymorph II. Polymorph II has a transition point of 194°C and a characteristic X-ray diffractogram, IR spectrum, Raman spectrum, FIR spectrum and NIR spectrum (Tab. 1-6, Fig. 1- 6}. It has been found that polymorph II is

metastable." (See para 1 of page 3 of the impugned specification)

Assuming but not conceding that the impugned application pertains to the conversion of one polymorphic form to another polymorphic form, it is submitted that the conversion of one crystalline form to another crystalline form is known from various prior arts which are in public domain since a long time and much before the priority date of impugned patent application.

For instance W0/1996/027592(attached herewith as **Annexure F**) published on 12 September 1996 teaches process for the preparation of polymorphic B form of (E)-4-[[3-[2-(4-cyclobutyl-2-thiazolyl)ethenyl]phenyl]amino]-2,2-diethyl-4-oxobutanoic acid by agitating Polymorphic Form A in a solvent and adding the seed crystals of Form B. Also, a disclosure in W0/1999/001444 (attached herewith as **Annexure G)** published on 14 January 1999 (Example 23) teaches process for the preparation of thermodynamically stable polymorphic form I of the tachykinin receptor antagonist 2-(r)-(1-(r) -(3,5-bis(trifluoromethyl) phenyl)ethoxy)-3-(s)-(4-fluoro) phenyl-4-(3-5 (-oxo-1hAh-1,2A,-triazolo) methylmorpholine by effecting the compound of Form II in methanol and seeded with crystals of Polymorphic form I.

Thus, the conversion of one polymorphic form of compound to another is spontaneous and is also known from prior art and is within the routine skills of a person skilled in the art. Moreover, the use of inert solvent and seeding technology, which appears to be the crux of claims 2-4 of impugned application, is also in the public domain.

Claims 2-4 and claims 13-14 of the impugned patent application deal with process for the preparation of polymorphic form I of sorafenib tosylate. Claim 13- 14 deal with the process of converting from polymorph II to polymorph I.*"The process involves effecting the polymorphic form II of sorafenib tosylate in an inert solvent and stirring or shaking until Polymorphic Form I was*

obtained".

It is submitted that stirring and shaking are but means to accelerate the conversion and even without such process, the polymorphic form II is automatically converted to polymorphic form I.

Polymorph-I of sorafenib tosylate is found to be the most stable crystal form and claimed as a compound in claim-1 of the impugned application. The pharmaceutical composition and method of use claims in the said application, all deal with polymorph-I only as this is 'stable'.

The process and methods used for making polymorphs or converting a metastable polymorph into a stable polymorph is well documented in literature. For any a chapter from the book "Advanced Pharmaceutical Solids" by Jens T. Carstensen, published by Marcel Dekker Inc, ©2001""" -(see Annexure H) clearly discloses the various experimentation techniques to obtain polymorphs and to convert metastable polymorphs into stable polymorphs.

Thus from the above following are established

1. The conversion of one polymorphic form to another polymorphic form is well known in prior art.

2. The use of the inert solvent and seeding technology for the conversion one polymorphic form to another polymorphic form is known from the prior art.

Hence, the process of conversion of polymorphs and the resultant polymorphic form is well known from prior art. On this ground alone all claims ought to be rejected.

It is submitted that the claims of the impugned application are obvious in view of what was already known in the art. The Applicant admits at WO 00/42012 that a certain polymorph of tosylate salt of Sorafenib is known. Techniques for development of polymorphic forms were already known in the prior art.

Techniques for conversion of 1 polymorphic form to another were also known and taught - for example *WO 1996/027592 (which teaches preparation of polymorphic B form of (E)-4-[[3-[2-(4-cyclobutyl-2 -thiazolyl) ethenyl] phenyl] amino]-2, 2-diathyl-4-oxobutanoic acid by agitating Polymorphic Form A in a solvent and adding the seed crystals of Form B).*Similarly, WO 1999/001444 teaches a process of converting thermodynamically stable polymorph 1 of tachykinin receptor antagonist to Form 2 by treatment in methanol and seeding.

It is submitted that conversion of one polymorphic form of a compound to another polymorphic form is often spontaneous and even if induced, the conditions for such conversions were practices routinely and well within the skills of a person skilled in the art. No inventive step is found in such conversion. The process claims merely recite the conversion of form 2 of Sorafenib tosylate in an inert solvent which shaking/stirring in order to obtain Polymorphic Form 1. Such processes are very common in the prior art. Jens T. Carstensel 2001 in the book "Advance Pharmaceutical solvents" discloses various techniques for conversion of metastable form into stable polymorphs. Therefore, obtaining stable polymorphic form of Sorafenib tosylate was the result of the techniques already known in the prior art and no inventive step resides in the same. There is no merit or force in the argument of the Applicant that finding the most stable and superior polymorphic form is inventive nor force in the argument that the prior art does not describe conversion of any polymorphic form of Sorafenib tosylate. Because, even if the prior art does not expressly teach preparation of Sorafenib tosylate polymorphic form, the techniques for preparation thereof were well known and therefore, Sorafenib tosylate polymorph as well as processes for its preparation were obvious and within the routine skills of a person skilled in

the art. In view of the above, the claims are obvious and liable to be rejected on this ground alone.

Applicant's argument & hearing submission to opponent 1

The contents of paragraph III of the statement of opposition are denied *in toto* and are wrong. Claims of the present Application are valid and involve inventive step.

Document WO 00/42012 does not describe the polymorphic form I of the tosylate salt of sorafenib. None of the cited documents describe any type of polymorphic form of sorafenib tosylate. The Opponent is wrong when he starts the discussion with the conversion of polymorph II of sorafenib tosylate into polymorph I. Even polymorph II was not described in the prior art. Also the documents WO 1996/027592 (referred to as Annexure F in the Opponent's statement) and WO 1999/001444 (referred to as Annexure G in the Opponent's statement) are not relevant because they do not refer to sorafenib at all and only describe the conversion of one polymorph into another polymorph of a different chemical compound. The question regarding inventive step is not a question whether the process of conversion of one polymorph into another polymorph is obvious but it is the question what are the polymorphic forms and which form is surprisingly superior over the other polymorphs. The discussion whether the conversion of one polymorph into another would be obvious is not eligible here because no polymorphic form of sorafenib tosylate is known in the prior art.

In general there are substances which only appear in a single crystal form but there are also substances which can form two, three or even more polymorphous crystal modifications. It is just as difficult to calculate or predict this possible morphological and structural variety and the respective physico-chemical, especially thermodynamic stability thereof on a scientific-mathematical basis, as it is to calculate or predict their different behaviour. The relevant polymorphism of an organo-chemical substance is always unpredictable in respect of the number of polymorphs, the stability thereof and their behaviour. Due to the unpredictability the screening for polymorphs is not a routine work. The finding of new polymorphs having improved properties does not constitute a mere discovery but fulfils all

criteria needed for an invention.

The problem to be solved by the present subject matter was to provide a form of sorafenib tosylate which has superior properties regarding manufacturing, storage and administration. It is very important for a pharmaceutical product to have always the same constant properties. Therefore, there is a need to find the most stable form of a compound because only the most stable form can ensure that all properties and characteristics regarding stability, dissolution rate, shelf life and bioavailability remain constant during manufacturing, storage and administration. The problem is solved by the polymorph I which surprisingly is the stable form among the two other polymorphs which are meta-stable. The superior properties of polymorph I over polymorph II is demonstrated in the mechanical stress test as per the affidavit of Dr. Britta Olenik in Annexure C.

Because polymorph I of sorafenib tosylate is not obvious, its preparation is not obvious as well. Therefore, it is adequately clear that the claimed subject matter is inventive over the cited prior art and this ground of Opponent is liable to be rejected.

Without prejudice to what has been stated above, it is submitted that the conclusion drawn by Opponent that the conversion of one polymorphic form to another is spontaneous, is technically flawed. It is well understood in the art that the spontaneity of a molecule is determined through change in free energy of the molecule when it transits from one thermodynamic stage to another thermodynamic stage. This free energy, in fact, depends upon many factors like intermolecular forces, types of bonds between atoms, van-der wall forces and the like which varies according to the type and orientation of the molecule in space. It cannot be generalized that the conversion of molecule from one polymorph to another polymorph form is spontaneous based on the analysis of a molecule different in structure or properties from the molecule in question.

In regard to Annexure H, it is submitted that Annexure H elaborates the principles of polymorphism and scientific theories underlying the phenomenon of polymorphism and as such, does not further the case of the

Opponent in any manner whatsoever.

Therefore, all the assertions and conclusions made by the Opponent in ground III of the statement of opposition are wrong and are liable to be rejected *in toto.*

The claimed subject matter involves an inventive step and is not obvious to person skilled in the art.

Opponent II arguments & hearing submission

Claims 2,3,4,8 and 9

It was submitted that D5, which reflects the common general knowledge in the field of polymorphism**,** discloses that, *"The thermodynamically stable polymorph needs to be identified. If the compound is enantiotropic, there will be two or more stable polymorphs and transition temperatures as well. These can be identified by simple techniques, for example by stirring or shaking excess solid with solid at different temperatures"* (see D5, page 528, column 02).

Thus in view of D5, a thermodynamically stable polymorph of a known compound can be identified by mere stirring and shaking the said compound at different temperatures.

Also, Applicant states that polymorph-I is obtained by shaking or stirring at a temperature of from 50^0C up to the reflux temperature of the solvent (see page 15 and bridging para at page 16).

Opponent submitted that D1 (admitted prior art) which is Applicant's own application must have prepared Sorafenib tosylate as per general standard method or as mentioned by the Applicant in the impugned application. If considering the Applicant's statement that Polymorph-II is obtainable by a general standard method, it is clear that D1 discloses polymorph-II of Sorafenib tosylate.

Therefore, it was submitted that starting from D1 (inherently disclosing polymorph-II) conversion of a known compound to another thermodynamically stable polymorph cannot be considered as inventive in view of D5.

Additionally, D6 provides a review of strategic approaches to remove much of uncertainty by presenting concepts and ideas in the form of flow charts to control the crystal form (polymorph) of drug substance.

D6 specifically mentions the use of solvents such as water, methanol, ethanol, propanal, isopropanol, acetone, acetonitrile, ethyl acetate, hexane and mixtures, which are the same as employed in the examples of the impugned application.

Therefore, it was submitted that in view of above, a person skilled in the art setting out to convert one polymorph to another polymorph would find the teachings of D5 as highly relevant prior art. Further to this, D6 further removes uncertainty and provides the list of selected solvents useful in the formation of polymorphs. Thus combining the teachings of D5 and D6, a person having ordinary skill in the art would reach the impugned process without ingenuity of thought.

Opponent submitted that in the Draft Manual of Patent Practice and Procedure (2008) page 34, under 3.10.7, it is explained that "*The term "obvious" means that the invention does not go beyond the normal progress of technology but merely follows* ***plainly or logically from the prior art****, i.e. something which does not involve the exercise of any skill or ability beyond that to be expected of the person skilled in the art. For this purpose a person skilled in the art is presumed to be an ordinary practitioner aware of what was general common knowledge in the relevant art at the relevant date. In some cases the person skilled in the art may be thought of as a group or team of persons rather than*

as a single person."

The revised Manual of Patent Office Practice and procedure Version 01.11 as modified on March 22, 2011 states on page 79 - the general principle of inventive step:

"e) If an invention lies merely in verifying the previous predictions, without substantially adding anything for technical advancement or economic significance in the art, the inventive step is lacking."

"g) *If the invention is predictable based on the available prior art, merely requiring workshop improvement by a person skilled in the art, the inventive step is lacking."*

Therefore, in view of the given teachings of prior art, it is evident that the impugned process does not involve the exercise of any skill or ability beyond which is expected of the person of ordinary skill.

Thus, based on facts presented above, the subject matter of claims 2, 3, 4, 8 and 9 lacks inventiveness (under the Act) and hence ought to be rejected.

- **In this regards, Applicant states that "**It is difficult to predict or calculate physic-chemical behaviour. The relevant polymorphism of an organo-chemical substance is always unpredictable in respect of number of polymorphs, the stability thereof and their behaviour. Due to unpredictability, screening for polymorphs is not routine work" (running page 23, para 49 of the Statement and Evidence).

Opponent submitted that obviousness cannot be avoided simply by showing of some degree of unpredictability in the art so long as there was a reasonable probability of success**.**

- **Opponent relied upon IPAB Order: OA/8/2009/PT/CH for support which was handed-out during the hearing. The relevant paragraphs there from are set-out for ready reference:**

Page 50, First Paragraph of the Order:

Board cited, Pfizer, Inc. v. Apotex, Inc. in 20061261 Federal Circuit decision

The Court held that "*a suggestion, teaching or motivation to combine the relevant prior art teachings to achieve the claimed invention does not have to be found explicitly in the prior art references sought to be combined, but rather 'may be found in any number of sources, including common knowledge, the prior art as a whole, or the nature of the problem itself".*

The Court held that "obviousness cannot be avoided simply by showing of some degree of unpredictability in the art so long as there was a reasonable probability of success.

The Court held that indeed, a rule of law equating unpredictability to patentability, applied in this case, would mean that any new salt – including those specifically listed in the '909 patent itself – would be separately patentable, simply because the formation and properties of each salt must be verified through testing. This cannot be the proper standard "since the expectation of success need only be reasonable, not absolute.

- Applicant states that the preparation and identification of a polymorph depend upon a plurality of parameters (see page 25, para 53 of the Statement and Evidence). Applicant states that there are four flow charts namely polymorphs, hydrates, solvates, amorphous. Applicant says that D6 provides only guidelines to characterise and synthesized. Applicant states that no

information to from D1 as to how to make different forms of Sorafenib tosylate (refer to Page 25, para 54 and 55 of Statement and Evidence).

In this regard, IPAB in order OA/8/2009/PT/CH made it clear that the unpredictability of success cannot rule out obviousness (refer to para 38 of the order)

For further clarity, IPAB cited KSR v. Teleflex case (see page 39)

It stated that the *"Court for seeing obviousness need not seek out precise teaching, but it can consider the inferences and creative steps that a person of ordinary skill in the art would employ". The Court erred in concluding that a patent claim cannot be proved obvious merely by showing that the combination of elements was obvious to try. When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.*

Para 42, Line 10-18:

In KSR, the US *Supreme Court held that the analysis of obviousness must be made explicit, and the reasoning to support the conclusion of obviousness must be articulated with rational underpinnings, the Court may have to look at the interrelated teachings of the multiple patents, the effect of demands known to the design community and the background knowledge possessed by a person having ordinary skill in the art. So the determination on obviousness is a legal one. The Court has to see a) what is the prior art b) the differences between the prior art and the invention and c) the skill of the imaginary ordinary man.*

Further, Hon'ble Board made it clear that who is a person having

ordinary skill in the art

Last lines of the para 42 and bridging para on next page:

Who is a person having ordinary skill in the art:

"We must remember that this ordinary man has skill in this art. He is not ignorant of its basics, nor is he ignorant of the activities in the particular field. He is also not ignorant of the demand on this art. "He is just an average man..... Well... just an ordinary man." ***But he is no dullard****. He has read the prior art and knows how to proceed in the normal course of research with what he knows of the state of the art.* ***He does not need to by guided along step by step.***

He reads the prior arts as a whole and allows himself to be taught by what is contained therein. He is neither picking out the" teaching towards passages" like the challenger, nor is he seeking out the "teaching away passages" like the defender."

Page 55 of the order:

Exhibit A speaks of using lower alkyl group for Pegylation.

Ex.B says that PEG modification has several advantages. We have already referred to this prior art.

Ex C is referred in Monfardini as encouraging use of high molecular weight.

So these materials provided the knowledge to the person skilled in the art regarding the advantages of branched Pegylation of IFN. He would use the conventional methods as did the inventor. If the methods used are conventional, there is no difficulty in the methods. Even if one grants a degree of unpredictability in the behavior of interferon there was a greater reason to expect success.....

Therefore, drawing analogy with the present case,

- **D1 discloses Sorafenib tosylate**

- **D5 describes the methodology for the identification of thermodynamically stable form of a compound.**
- **D6 disclosed the selected solvents mainly used in polymorphism development.**

Therefore, in view of the given teachings of the prior art, it is evident that the impugned process does not involve the exercise of any skill or ability beyond which is expected of the person skilled in the art.

- **With regard to Applicant's concern on Hindsight, Opponent relied upon Application of Gerald McLAUGHLIN, Patent Appeal No. 8474, United States Court of Customs and Patent Appeals:**

On page 03, para 21:

We have taken the above argument into consideration and do find that it has some merit. Nevertheless, it is not convincing. It should be too well settled now to require citation or discussion that the test for combining references is not what the individual references themselves suggest but rather what the combination of disclosures taken as a whole would suggest to one of ordinary skill in the art. Any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning, but so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made and does not include knowledge gleaned only from applicant's disclosure, such a reconstruction is proper. The Cook patent does indicate that the car shown therein is suitable for carrying palletized loads with lift trucks being used for the loading and unloading, including stacking of the pallets. Since the secondary references show that it was well known to use side filler panels and bulkheads to confine palletized loads to prevent lateral and longitudinal shifting, we agree that those references would have suggested use of such panels and bulkheads with the

Cook car for the same purpose.

From above, it is clear that judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning, but so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, such a reconstruction is permissible.

In the present case, D5 provides a general method for the identification of a thermodynamically stable polymorph and D6 teaches about preferred solvents useful in the polymorphism development. Therefore, in the present case common knowledge was readily available and combination of disclosures taken as a whole suggest to one of ordinary skill in the art to arrive at a thermodynamically stable form of a compound. Accordingly, there is no question of improper hindsight in the present case.

SUBMISSIONS U/S 2(1) (ja):

It was submitted that there is neither any technical advancement nor economic significance in the impugned invention. There is no data in the impugned application that establishes the advantageous effects of the claimed matter over the prior art. It was submitted that Applicant failed to provide any comparative data with recent previous prior art compound

Applicants argument & hearing submission to opponent II

CLAIMS 2, 3, 4, 8 AND 9- OBVIOUSNESS AND LACK OF INVENTIVE STEP [Section 25(1)(e)]

It is submitted that the question regarding inventive step is not a question of whether the process of conversion of one polymorph into another polymorph is obvious. The question is what are the polymorphic forms, and which form is surprisingly superior over the other polymorphs. The discussion whether the conversion of one polymorph into another would be obvious is not eligible here because no polymorphic form of sorafenib tosylate is known in the prior

art.

In general, there are substances which only appear in a single crystal form but there are also substances which can form two, three, or even more polymorphous crystal modifications. It is just as difficult to calculate or predict this possible morphological and structural variety and the respective physico-chemical, especially thermodynamic stability thereof on a scientific mathematical basis, as it is to calculate or predict their different behaviour.

The relevant polymorphism of an organo-chemical substance is always unpredictable in respect of the number of polymorphs, the stability thereof and their behaviour. Due to the unpredictability, screening for polymorphs is not routine work. The finding of new polymorphs having improved properties does not constitute a mere discovery but fulfils all criteria needed for an invention.

The problem is solved by the polymorphic form I which surprisingly is the stable form among the two other polymorphs which are meta-stable. The superior properties of polymorphic form I over polymorphic form II is demonstrated in the mechanical stress test as per the affidavit of Dr. Britta Olenik, a copy of which is annexed with the statement as Annexure B. In so far as submissions made by the Opponent re Dl is concerned, it is submitted that D1 does not give any hint as to the preparation of any sorafenib salt, let alone of sorafenib tosylate. Accordingly, the skilled worker has no idea of whether sorafenib tosylate is amorphous or crystalline and, in the latter case, crystallizes in more than one crystalline modification (polymorph).

ln so far as submissions made by the Opponent re D5 is concerned, it is denied that claim 1 is not inventive taking D1 and D5 together. It is submitted that D5 focuses on the polymorphs of compounds SK&F 94120 which is structurally completely different from sorafenib (D5, page 529, left-hand column,

"Figure"). D5 clarifies that: *"The process of crystallization and the factors governing the appearance of* individual *polymorphs are still poorly understood. Crystals are in equilibrium only with a saturated solution but crystallisation requires supersaturation, so that the Phase Rule is not applicable. Which of several possible polymorphs is obtained seems to depend upon various factors: the temperature at which crystallization occurs, the nature of the solvent (Hydrophilic, hydrophobic) and the degree of supersaturation when crystallization commenced. The use of seed crystals can be helpful in obtaining a desired polymorph. Manufacturing processes seem to be worked out by trial and error aided b11 serendipity, and then adhered to rigidly."* (05, page 527, right-hand column, 2nd paragraph)

The authors further explain that:

"the methods used in attempting to obtain polymorphs include crystallization from a range of solvents (polar and non-polar, hydrophilic and hydrophobic) at different temperatures, for chilling solutions rapidly, by adding a second solvent in which tire solute is sparingly soluble, by vigorously stirring excess solid with solvent, by heati11g excess solid ·with a high boiling solvent, by sublimation, and by very rapidly changing the pH of a solution to precipitate acidic or basic substances." (D5, page 528, left-hand column, 1st paragraph)

It is submitted that D5 clearly evidences that preparation and identification of the most stable polymorph depends on a plurality of different parameters, which might result in the desired crystal modification- with serendipity. It is submitted that D5 clearly contradicts the submissions made by the Opponent in paragraph under reply that the identification of polymorphs is mere routine experimentation.

In so far as the submissions made by the Opponent re D6 is concerned, it is submitted that it is a review article describing a conceptual approach to the

characterization of pharmaceutical solids. The document suggests four flow charts dealing with the most common solid forms, namely polymorphs, hydrates, desolvated solvates and amorphous forms. On eight pages, the authors explain, how pharmaceutical solids can be characterized in a more direct approach (D6, Abstract). The fact that in 1995, a review article has been published in a scientific paper shows that the identification of pharmaceutical solids in no way constituted routine experimentation. It is submitted that D6 admits that the decision trees do not necessarily lead to a result (06, page 945, right-hand column, second paragraph). 06 is rather regarded as a guideline as to how different forms of solids may be characterized and, if necessary, synthesized. No reference to sorafenib tosylate can be found in D6.

Even the combination of Dl and D6 would not lead the skilled person to the subject-matter of claim 1, since the skilled person receives no information or guidance from D1 as to how to make different forms of sorafenib tosylate, nor any information as to which are the polymorphs of sorafenib tosylate. The skilled person would first have to develop the right method of preparation before running through the four decision trees of D6. Even then, it is highly doubtful whether the skilled person would identify polymorphic form I.

In view of what has been stated hereinabove, the Applicant submits that none of the documents cited by the opponent (D1, D5 and D6) either alone or in combination with the other suggest or teach the present invention nor do they enable a person skilled in the art to arrive at the present invention.

In this regard, the Applicant also refers to and relies upon the following scientific literature which is annexed hereto and marked as Annexure-13.

Accordingly, the subject matter of original claims 1, 2, 3, 4, 13 and 14 involve inventive step and is not obvious to a person skilled in the art as alleged or at all (Reference in this regard is made to the pages 23 to 27

paragraphs 47 and 57 of the statement in support of the application).

The Applicant would like to draw the attention of the Learned Controller to the following observation made by the Intellectual Property Appellate Board in case titled *Novartis AG l' Union of India* & *Ors Order No. 100/2009,* wherein Hon'ble Dr. P.C. Chakraborty, Technical Member, explained the phenomenon of polymorphism as follows, which is annexed hereto and marked as Annexure-14:

"The phenomenon of polymorphism is not universal. Its existence has to be discovered by finding out its different forms by way of research and human intervention."

In the same order, Dr. Chakraborty further held: *"It is the fact that no one could predict the possibility of existence of polymorphism in imatinib mesylate before the impugned application. There was no motivation also by an uninventive man to try for finding out different polymorphic forms and their relative properties suitable for preparing for solid dosage formulation for cancer drug."*

Applying the same principle to the facts of the present case, the applicant submits that the possibility of existence of polymorphism in sorafenib tosylate could not have been predicted before the present invention. In fact, none of the cited documents either individually or collectively disclose or give any idea of any specific polymorph of sorafenib tosylate, let alone polymorphic form I, any pharmaceutical composition containing the same or any process for making the said polymorphic form I.

It is further submitted that the Opponent has made assertions based on conjecture and surmises without any cogent evidence in support thereof. In this regard, the Applicant refers to and relies upon the case titled *Raj Prakash v 'Mangat Ram Chowdhry* & *Ors (R.F.A. (OS)* 2 *of1973)* which is already

annexed hereto and marked as Annexure 9, the case titled *F. Hoffman -La Roche Ltd. V Cipla Ltd. CS (OS) 89/2008 and* C. C. *52/2008* which is annexed and marked as Annexure-9. Therefore, all the assertions and conclusions made by the Opponent for lack of inventive step in the present representation are wrong and are liable to be rejected in *toto.* The claimed subject matter involves an inventive step and I not obvious to person skilled in the art.

After going through the submissions of both the parties it is clear

Document D1 (WO 03/068228) as cited by the opponent 2, also disclosed in the impugned patent specification discloses tosylate salt of sorafenib and its use in the treatment of disorders in which angiogenesis plays an important role for example in tumor growth. The teaching that flows from this document is that tosylate salt of sorafenib is known.

D5 as cited by the opponent is research article published in Chemistry & industry, 1989, pages 527-529 is a general article which discloses the common general knowledge in the field of polymorphism surely discloses that ***"The thermodynamically stable polymorph needs to be identified. If the compound is enantiotropic, there will be two or more stable polymorphs and transition temperatures as well. These can be identified by simple techniques, for example by stirring or shaking excess solid with solid at different temperatures.*** "(See on page 528, column 02). The same article also on page 527, column 02 under section *"Crystals and Crystallisation", "The use of seed crystals can be helpful in obtaining a desired polymorph. Manufacturing processes seem to be worked out by trial and error aided by serendipity, and then adhered to rigidity.* "

The teaching that certainly flows from this article clearly suggests that stirring or shaking and seeding technology is very well known in the art prior can be used to prepare a thermodynamically stable polymorph.

Thus a person skilled in the art can easily combine the teachings D1& D5 to arrive at thermodynamically stable polymorph 1 of sorafenib tosylate. Therefore claim 1 lacks inventiveness.

Claims 2, 3, 4, 8 and 9 relates to the conversion of one polymorph to another thermodynamically stable polymorph, particularly a process for the conversion of polymorph-II to polymorph-I.

The disclosure on page 15 & 16 on the specification of the impugned invention discloses the process for the conversion of polymorph-II to polymorph-I of Sorafenib tosylate; *"Preference is given to preparing the compound of the formula (I) in the polymorph I by effecting the compound of the formula (I) in the polymorph (1l) obtained as described in example 1, in methanol, ethanol, a mixture of both solvents or a mixture of both solvents with water, preferably a 1:1 mixture with water, and shaking or stirring at a temperature of from 50°C up to the reflux temperature of the*

Solvent, preferably at from 60 to 80°C, in the absence of crystals of a solvate of the compound of the formula (I), for example in the absence of crystals of the methanol solvate or the ethanol solvate of the compound of formula (I),for up to one day. The crystals are cooled to from -30°C to room temperature, preferably from -25 to 1 0°C, isolated and dried The compound of the formula (I) is thus obtained in the polymorph I Most preferably isopropanol, ethyl acetate or a mixture thereof is used as solvent.

"Preference is likewise given to preparing the compound of the formula (I) in the polymorph I by effecting the compound of the formula (I) in the polymorph II, obtained as described in example 1, in methanol, ethanol, a mixture of both solvents or a mixture of both solvents with water, and shaking or stirring at a temperature of from 1 0°C up to the reflux temperature of the solvent, preferably at room temperature, for up to 1 day. The mixture is subsequently

seeded with crystals of the compound of the formula (I) in the polymorph I and stirred or shaken, for example at room temperature, for from 1 hour to 14 days, preferably from 2 hours to 7 days. The crystals are isolated and dried. The compound of the formula (1) is thus obtained in the polymorph I most preferably isopropanol, ethyl acetate or a mixture thereof is used as solvent"

Thus from the disclosures Dl in view of D5 it is clear that, polymorph-I of Sorafenib tosylate is obtained by heating the polymorph-II of Sorafenib tosylate in an inert solvent. Subsequently, it mentions that seeding is preferred for obtaining the polymorph-I of Sorafenib tosylate.

Also referring to the disclosure page 02, first paragraph of the impugned application & the admittance of the fact that Sorafenib tosylate of Dl exist in polymorph-II, starting from Dl conversion of a known compound to another thermodynamically stable polymorph certainly obvious in view of D5.Therefore the process as claimed in the claims 2, 3, 4, 8 and 9 of impugned application involves no inventive step of any sort and does not satisfy the criteria of non-obviousness.

Document D6 relates to review article published Pharmaceutical Research, vol. 12, No. 7, pages 1995, 945-954 provides a review of strategic approaches to remove much of uncertainty by presenting concepts and ideas in the form of flow charts to control the crystal form (polymorph) of drug substance. D6 provides a review of strategic approaches to remove much of uncertainty by presenting concepts and ideas in the form of flow charts to control the crystal form (polymorph) of drug substance.

It outlines investigations of the formation of polymorphs and the controls needed to ensure the integrity of the drug substance containing either a single or mixture of polymorphs. D6 on page 946, under the heading; *"Formation of Polymorphs - Have Polymorphs Been Discovered?"The first step in the*

polymorph decision tree is to crystallize the substance from a number of different solvents in order to answer the question: Are polymorphs possible? Solvents should include those used in the final crystallization steps and those used during formulation and processing and may also include water, methanol, ethanol, propanal, isopropanol, acetone, acetonitrile, ethyl acetate, hexane and mixtures if appropriate. New crystal forms can often be obtained by cooling hot saturated solutions or partly evaporating clear saturated solutions. ..... "

The teaching that flow from this document D6 is the use of specific solvents during preparation of polymorphs & specifically mentions the use of solvents such as water, methanol, ethanol, propanal, isopropanol, acetone, acetonitrile, ethyl acetate, hexane and mixtures. Here I see that same solvents has been used by the applicants in preparing the polymorph I of Sorafenib tosylate in the working examples of the impugned application

Thus by combining teachings of D5 & D6, a skilled artisan it is practically possible to arrive at a process of converting one polymorph to another polymorph using the solvents mentioned in the D6. Thus process claims lack inventive merit.

GROUND 8: CLAIMS NOT PATENTABLE UNDER SECTION 3(d)

Opponent I & hearing submission

(a) The amended claims are drawn to polymorphic form 1 of Sorafenib tosylate (4-(4-[({[4-chloro-3-trifluoromethy) phenyl] amino} carbony) amino] phenoxy)-N-methylpyridine-2-carboxamide (hereinafter referred to as "polymorph of Sorafenib tosylate"). It is submitted that the claims are not patentable under Section 3(d). In the case of Novartis vs. Union of India [AIR 2013 SC 1311], the Supreme Court was concerned with the patentability of polymorphic form of imatinib mesylate. It was contented by the

Applicant/Petitioner, Novartis before the Supreme Court that the crystal form has better physical properties including that it is thermodynamically more stable, less hydroscopic and has lower hygroscopicity (page 63, para 168). This was supported by expert evidence submitted by the Appellant-Novartis. Comparison was made of these physical properties of the crystal form with the base and it was contended that because the crystal form exhibits better solubility, the same should be taken as a measure of increased bioavailability and hence, improved therapeutic efficacy. It was contended that the crystal showed 30% improvement in bioavailability as compared to the free base (para 168-169, page 63). The Supreme Court considered these submissions in paragraphs 175-190 and at paragraph 180, especially paragraph 187 the Supreme Court has held that *"In whatever way therapeutic efficacy may be interpreted, this much absolutely clear that the physic-chemical properties of beta crystalline form of Imatinib Mesylate, namely (i) more beneficial flow properties, (ii) better thermodynamic stability, and (iii) lower hygroscopicity, may be otherwise beneficial but these properties cannot even be taken into account for the purpose of the test of Section 3(d) of the Act, since these properties have nothing to do with therapeutic efficacy".* The Supreme Court has also held in paragraph 188 that *"Bioavailability falls outside the area of efficacy in case of a medicine…."*. Further, in paragraph 189, the Court held that *"... the position that emerges is that just increased bioavailability alone may not necessarily lead to an enhancement of therapeutic efficacy…."*. The Supreme Court has also held that *"... whether or not an increased in bioavailability leads to enhancement of therapeutic efficacy in any given case must be specifically claimed and established by research data…."*.

(b) In other words, the Supreme Court has rejected mere comparison of base with a claimed form as sufficient for establishing therapeutic efficacy and

held that therapeutic efficacy must be established by submitting appropriate research and clinical data.

(c) In the case at hand, the claimed polymorph 1 fails to pass the test of Section 3(d) as interpreted by the Supreme Court because:

(i) No material on record to establish therapeutic efficacy: Apart from the averments in the Reply statement, there is no document or material on record to establish therapeutic efficacy as required by the Supreme Court. No research data is presented to fortify the conclusion that polymorph 1 exhibits better therapeutic efficacy. There is nothing in the patent application to support this conclusion.

(ii) Affidavits of Britta Olenik and of Kerstin Pauli do not provide any research data to support therapeutic efficacy: These affidavits submitted by the Applicant do not further the case of the Applicant insofar as therapeutic efficacy is concerned. They only compare the dissolution rate of Sorafenib tosylate salt with the base Bay-43-9006. Dr. Pauli on the basis of better dissolution rate of the polymorph 1 concludes that the efficacy of the said polymorph 1 is higher than Sorafenib base. The conclusion is not reached on the basis of any research data as required by the Supreme Court, and is a mere conclusion without any basis on data.

(iii) Affidavits defective, unreliable:

Even otherwise, the dissolution rate as presented by these experts cannot automatically lead to an inference of better therapeutic efficacy because the affidavits do not present any data for the same.

Affidavit of Dr. Kerstin Pauli: this compares the formulation of Sorafenib (BAY 43-9006 micron) and formulation of Sorafenib tosylate polymorph I (BAY 54-9085 micron). Prima facie, it may be noted that both formulations are not similar and that the quantity of Avicel PH101 is much higher when the

formulation is based on Sorafenib. Perhaps, the quantity of Avicel has been increased in the Sorafenib based formulation in order to match the weight of the tablet containing Sorafenib tosylate polymorph I. Avicel by itself has an effect on the dissolution property of the tablet and an increased quantity of a Avicel decreases the rate of disintegration and thereby the dissolution. Such difference has not been accounted for in the final result i.e. there is nothing to suggest that the high dissolution is only on account of Polymorph-1 and not due to Avicel.

Non-disclosure of conditions nor the experiment: Further, the conditions under which the dissolution test was conducted are not disclosed in the affidavit.

No data to show that improved dissolution = enhanced efficacy: The results of the dissolution studies are only limited to the dissolution of the samples and there is no data to show how the said improvement in the dissolution would actually result in increased safety or efficacy. No automatic assumption of therapeutic efficacy can be made unless substantiated by "research data"

Comparison of base with polymorph is inappropriate – real comparison is between two polymorphs: Dissolution of the Sorafenib tosylate polymorph I over that of the base cannot demonstrate any efficacy- the real the standard for comparison has to be Sorafenib tosylate polymorph II being the closest prior art compound.

Affidavit of Dr. Britta Olenik: In this affidavit, it is stated that the polymorph I of Sorafenib tosylate was subject to mechanical stress, i.e. by grinding in hand for about 30 seconds and compared with unground or untreated samples. Similarly, polymorph II was also compared before grinding and after grinding. This affidavit does not depict when the data was measured and does not rule out automatic conversion from form II to form I. This comparison is nothing but comparison of a physicochemical parameter i.e. stability of the

polymorphic form. There is nothing data to conclude that such stability contributes to therapeutic efficacy which is the requirement for patentability under Section 3(d).

Assuming but not conceding that polymorph II is more sensitive to mechanical stress in comparison of polymorph I, a measure of mechanical stress cannot be said to contribute or translate into therapeutic efficacy, which is required under Section 3(d).

(d) Comparison of base versus polymorph-1: Not proper and does not satisfy Section 3(d) requirements

As mentioned above, the Supreme Court has already laid down that therapeutic efficacy must be established by submission of appropriate data. In the case at hand as well as in the case before the Supreme Court, the dissolution rate was presented as a measure of enhanced bioavailability and comparison was made of the polymorph with the base. Such comparison was specifically rejected by the Supreme Court in paragraph 188. Therefore, the comparison prima facie is against the law laid down by the Supreme Court.

(e) Bioavailability does not automatically mean therapeutic efficacy:

It was contended that bioavailability is a measure of therapeutic efficacy. In this regard, it is submitted that therapeutic efficacy and bioavailability are two different parameters and are required to be specifically demonstrated through data. Bioavailability is pharmacokinetic parameter whereas therapeutic efficacy is a pharmacodynamic parameter. Even as per the Supreme Court, therapeutic efficacy must be specifically establish through data, which has not been put forth in the present case.

(f) The impugned application makes no claim of enhanced therapeutic efficacy:

The specification of the impugned application sets out the properties and advantages of polymorph 1. It clearly states that the invention is drawn to a thermodynamically stable form of Sorafenib tosylate salt. The inventive feature is the finding of the polymorphic form 1, which is stable enough and does not convert into another polymorphic form and prevents changes in solubility or bioavailability profile. Nowhere is it contended in the entire specification that the polymorph 1 of Sorafenib tosylate salt exhibits better therapeutic efficacy and treats/contributes to an improvement in the treatment of cancer. Obviously, the Applicant at this stage of the Opposition cannot advance contentions contrary to or not pleaded in their own specification.

In view of the above, it is submitted that the claims drawn to polymorph 1 of Sorafenib tosylate salt are not patentable and liable to be rejected.

Applicants Argument to Opponent I

With regard to Section 3(d) of the Patents Act, it is submitted that the assertions made by the Opponent in the present representation are based on conjectures and surmises without corroborative evidence in support thereof.

It is submitted that it is a settled proposition of law that it is for the Opponent to discharge the onus that *inter alia,* the invention claimed by the Applicant is new form of the known substance and mere submissions will not axiomatically permit the Court to believe that the invention claimed by the Applicant is new form of the known substance unless shown clinically with some evidence. It is submitted that in the present case, the Opponent has failed to corroborate its submissions by placing some cogent evidence on record and therefore, has terribly failed to discharge its onus. On this ground alone, the present opposition deserves to be rejected outrightly. In support of its submissions, the Applicant refers to and relies upon the case titled *F.Hoffman -La Roche Ltd. V Cipla Ltd. CS(OS) 89/2008 and* C.C. *52(2.008* which is

annexed hereto and marked as Annexure-6.

It is further submitted that the assertions made by the Opponent in the present representation are misleading, lack proper interpretation of law, science and are based on assumptions and presumptions and therefore, are vehemently denied. The Opponent is once again wrong when he states that the present claims 1 to 18 are drawn to polymorphic forms of 4-{4-[({[(4-chloro-3-trilluoromethyl) phenyI] amino} carbonyl) amino] phenoxy} -N-methylpyridine-2-carboxamide which is sorafenib. The correct statement would be that the present claims relate to the polymorphic forms of the tosylate salt of sorafenib which is different from sorafenib itself.

The efficacy of the tosylate salt of sorafenib in polymorphic form is higher than its base sorafenib due to a higher dissolution in tablets containing both drugs each. In, this regard, the Applicant refers and relies upon the evidence in the form of technical affidavit deposed by Dr. Kerstin Pauli that was submitted along with the statement in support of the application. Therefore, the present invention is patentable and none of the claims fa1ls within the prohibition of Section 3(d).

Furthermore, it is very important for a pharmaceutical product to always have the same constant properties to guarantee constant and reliable efficacy. There is a need to find the most stable form of a compound because only the most stable form can ensure that all properties and characteristics regarding stability, dissolution rate, shelf life, efficacy, and bioavailability remain constant during manufacturing, storage, and administration. The polymorphic form I of sorafenib tosylate of the present invention is surprisingly more stable than the other polymorphs found and ensures a constant & reliable efficacy, therapeutic or otherwise. 1n this regard, the Applicant refers to & relies upon the evidence in the form of technical affidavit deposed by Dr. Britta Olenik

that was submitted along with the statement in support of the application.

Therefore, the present invention is patentable and none of the claims fall within the prohibition of Section 3(d). When the polymorphic form I of tosylate salt of sorafenib itself is patentable, its preparation ought to be patentable as well.

Opponent II Arguments & hearing submission

It was submitted that the subject matter of the impugned application is not an invention within the meaning of Section 3(d) of the Act because the claimed invention falls within the mischief of Section 3(d). It states that:

"the mere discovery of a new form of a known substance which does not result in the enhancement of the 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, machine or apparatus unless such known process results in a new product or employs at least one new reactant.

Applicant relies upon affidavit of Dr. Kerstin Pauli to fulfill the requirement of Section 3(d). Opponent submitted that reliance to the affidavits of Dr. Pauli and Dr. Olenic should not be taken due to the reasons mentions under preliminary submissions.

Opponent submitted that, in any case if reliance can be taken to these affidavits, still the requirements U/S 3(d) are not fulfilled. Affidavit of Dr. Pauli shows the comparative dissolution data of Sorafenib free base and Sorafenib tosylate.

- **In this regard, Opponent referred to Hon'ble Supreme Court decision on Gleevac case, which was handed out during the hearing. The relevant paragraphs there from are set-out for ready reference:**

Page 88, Para 171:

"That being the position, the appellant was obliged to show the enhanced

efficacy of the beta crystalline form of Imatinib Mesylate over Imatinib Mesylate (non-crystalline). There is, however, no material in the subject application or in the supporting affidavits to make any comparison of efficacy, or even solubility, between the beta crystalline form of Imatinib Mesylate and Imatinib Mesylate (non-crystalline).

Drawing analogy for the instant case, there is no comparison between Sorafenib tosylate prepared by general standard method i.e. D1 with Sorafenib tosylate of present claims.

Affidavit of Dr. Pauli shows that there is difference in dissolution profile of Sorafenib and sorafenib tosylate Form-I.

In this regard, it was submitted that, salt formation is the most common and effective method of increasing solubility and dissolution rates of acidic and basic drugs.

Also, Supreme Court made it clear that

172. As regards the averments made in the two affidavits, for all one knows the higher solubility that is attributed to the beta crystalline form of Imatinib Mesylate may actually be a property of Imatinib Mesylate itself. One does not have to be an expert in chemistry to know that salts normally have much better solubility than compounds in free base form. If that be so, the additional properties that may be attributed to the beta crystalline form of Imatinib Mesylate would be limited to the following:

i. More beneficial flow properties,

ii. Better thermodynamic stability, and

iii. Lower hygroscopicity

173. The aforesaid properties, ("physical attributes" according to Manley), would give the subject product improved processability and better and longer storability but, as we shall see presently, on the basis of those properties

alone, the beta crystalline form of Imatinib Mesylate certainly cannot be said to possess enhanced efficacy over Imatinib Mesylate, the known substance immediately preceding it, within the meaning of section 3(d) of the Act (see Page 88).

Therefore, requirements of section 3(d) are not fulfilled. Hence, ought to be rejected on this ground too.

- **Additionally, affidavit of Dr. Olenik has been cited by the applicant. However, it is submitted that Mechanical stress is not a criterion to show efficacy of a drug.**

Supreme Court on Page 94, 187 further states that:

187. In whatever way therapeutic efficacy may be interpreted, this much is absolutely clear: that the physico-chemical properties of beta crystalline form of Imatinib Mesylate, namely (i) more beneficial flow properties, (ii) better thermodynamic stability, and (iii) lower hygroscopicity, may be otherwise beneficial but these properties cannot even be taken into account for the purpose of the test of section 3(d) of the Act, since these ***properties have nothing to do with therapeutic efficacy****.*

Last lines of para 188:

"It is not the intent of a bio-availability study to demonstrate effectiveness, but to determine the rate and extent of absorption. If a drug product is not bioavailable, it cannot be regarded as effective. However a determination that a drug product is bio-available is not in itself a determination of effectiveness."

Opponent submitted that, since Supreme Court has provided clear directions to overcome the barrier of Section 3(d). However, in the present case Applicant failed to submit such data and therefore deserves to be rejected outrightly.

Applicants argument & hearing submission to Opponent II

With regard to Section 3(d) of the Patents Act, it is submitted that the assertions made by the Opponent in the present representation are based on conjectures and surmises without corroborative evidence in support thereof. It is submitted that it is a settled proposition of law that it is for the Opponent to discharge the onus that *inter alia,* the invention claimed by the Applicant is new form of the known substance and mere submissions will not axiomatically permit the Court to believe that the invention claimed by the Applicant is new form of the known substance unless shown clinically with some evidence. It is submitted that in the present case, the Opponent has failed to corroborate its submissions by placing some cogent evidence on record and therefore, has terribly failed to discharge its onus. On this ground alone, the present opposition deserves to be rejected outrightly. In support of its submissions, the Applicant refers to and relies upon the case titled *F. Hoffman -La Roche Ltd. V Cipla Ltd. CS(OS) 89/2008 and* C.C. *52/2008* which is already annexed hereto and marked as Annexure-15.

It is further submitted that the assertions made by the Opponent in the present representation are misleading, lack proper interpretation of law, science and are based on assumptions and presumptions and therefore, are vehemently denied.

It is submitted that the efficacy of the tosylate salt of sorafenib in polymorphic form l is higher than its base sorafenib due to a higher dissolution in tablets containing both drugs each. In this regard, the Applicant refers and relies upon the evidence in the form of technical affidavit deposed by deposed by Dr. Kerstin Pauli, a copy of which is

annexed with the statement as Annexure c

Furthermore, it is very important for a pharmaceutical product to always have the same constant properties to guarantee constant and reliable efficacy. There is a need to find the most stable form of a compound because only the most stable form can ensure that all properties and characteristics regarding stability, dissolution rate, shelf life, efficacy, and bioavailability remain constant during manufacturing, storage, and administration. The polymorphic form I of sorafenib tosylate of the present invention is surprisingly more stable than the other polymorphs found and ensures a constant and reliable efficacy, therapeutic or otherwise. In this regard the Applicant refers to and relies upon the evidence in the form of technical affidavit deposed by Dr. Britta Olenik, which is annexed with the statement as Annexure B.

60. Therefore, the present invention is patentable and none of the claims fall within the prohibition of Section 3(d). When the polymorphic form I of tosylate salt of sorafenib itself is patentable, its preparation ought to be patentable as well.

GROUND 9: U/s 25(1) (h), THE FAILURE TO DISCLOSE DETAILS OF CORRESPONDING FOREIGN APPLICATIONS;

Opponent I arguments & hearing submission

The patentee has failed to disclose to the Controller the information required under Section 8: It is submitted that the Applicant-Respondent has failed to disclose the details of corresponding foreign applications filed and on this ground alone the patent application should be rejected.

The applicant is required to provide all the information regarding the

prosecution of the equivalent applications till the grant of the Indian application to the Controller in writing from time to time and also within the prescribed time. The applicant has failed to furnish the details of National phase applications filed in USA, Europe etc, which are still under examination and not granted. Therefore the applicant has failed to comply with the requirements of the section 8 of the act and the opponent demands rejection on this ground also.

Opponent II arguments & hearing submission

Opponent II has not pressed this ground.

Applicants arguments & hearing submission to Opponent I

The averments made by the Opponent are wrong and denied in toto. It is submitted that the requirement under Section 8(1)was fulfilled by providing a list of corresponding foreign applications on Form-3 dated, March 14, 2007,August 9, 2012, February 15, 2013, August 12, 2013, March 04, 2014, and August 12, 2014. It is further submitted that the requirements under Section 8(2) were only requested by the learned Controller at the time of issuance of the First Examination Report (FER) dated September 16, 2013, which as per the provisions of the Patents Act was required to be complied with within six months from the date of request, i.e., March 17, 2014. The Section 8(2) details were submitted by the aforesaid deadline under cover of our letter dated March 04, 2014.

Without prejudice to the above, it is submitted that requirements under Section 8 need to be complied with until the grant of a patent and considering that the patent application is still pending, the said ground taken by the Opponent is pre-mature and ought not to be taken cognizance of. Therefore, the Applicant has complied with the information required under Section 8 of the Act, and the ground taken by the Opponent is wrong and frivolous **(Reference in this**

regard is -made to the page 12, paragraph 43 of the statement in support of the application).

It is submitted that in this regard, the Applicant refers to and relies upon the case titled *Sukesh Behl v. Koninklijke Philips Electronics* [FAO (OS) No.16 OF 2014] which is annexed hereto and marked as **Annexure-11.**

It is submitted to the Learned Controller that the requirements under Section 8 are mere procedural requirements and based on doctrine of duty of candour. As long as the Applicant is not trying to mislead the Learned Controller, the Learned Controller ought not to take into consideration the grounds of opposition based on Section 8.

In any case, since the Section 8(2) details were submitted within the prescribed time period, it is submitted that the ground taken by the Opponent is wrong and frivolous.

OTHER MISCELLANEOUS GROUNDS

REBUTTAL TO THE ARGUMENTS OF THE APPLICANT BY THE OPPONENT II:

(i) Rejection of Pre-grant Opposition as no evidence was filed.

The Applicant has argued that the pre-grant opposition has not been accompanied by any expert evidence and therefore, none of the arguments made by the Counsel should be considered. In this regard, it is submitted that:

(a) Filing of evidence is not mandatory:

As per Section 25(1) of the Patents Act, read with Rule 55(1), any person may file a representation accompanied by evidence, if any. The words "if any" in Rule 55 are very important and denote that the evidence may be filed, if required. Filing of evidence is not mandatory. The law must be

read only in this manner because the Patent Office and the Controller are specialized tribunals, empowered to adjudicate upon technical issues by themselves as they are experts in certain technical fields unlike a court of law, wherein the judges are by and large from a legal background.

In addition, if the grounds taken in Opposition are such as anticipation, non-compliance of Section 8 etc., the arguments advanced under these grounds are purely legal and factual. There is no requirement for any expert to intervene in these grounds and provide his expert opinion. Such expert evidence may at best be required to substantiate a ground of obviousness. Even for this ground if the arguments are fairly simplistic and the controller is fairly capable of adjudicating thereon without external aid, there is no need for any expert evidence. It must be borne in mind that the pre-grant opposition is a summary proceeding unlike a post-grant opposition.

RULING BY IPAB

In the case of Ajanta Pharma Limited Vs. Allergan inc. & Ors. The IPAB has held in paragraph 15 that if the novelty and inventive merit of an application can be destroyed by well published literature then, the evidence is superfluous.

(b) Evidence may be by way of documents or affidavit:

As per the Evidence Act, Section 3, evidence may be of two types – documents and affidavit, i.e. documentary evidence and evidence by way of affidavit. Documentary evidence is given when a person wants to rely on the contents of that document.

The document is relied upon for the content of that document and for such contents, only the author of the document can depose as to the veracity of that document and not any third party to the document including the opponent. Therefore, it is futile to demand an affidavit from this Opponent

in respect of the contents of a paper authored by a third person.

In any case, Evidence Act allows any person to rely on evidence which may be mere documents. In all court proceedings, or before tribunals, parties often rely on documents which may be extracts from dictionary, scientific papers, internet extracts and all of these are admissible under the category 'documentary evidence'.

Even otherwise, as per the Patents Act Section 129 read with rule 126, affidavit can only be given in respect of facts which are personal and which are known to the deponent. In the present case, the facts which emanate from the documents are set out in the pre-grant representation and this requirement of law is satisfied. The Opponent is relying on documentary evidence which satisfy the requirement of Rule 55(1).

(c) JUDGEMENTS RELIED UPON BY APPLICANT

The Applicant relied upon the judgments Molnlycke AB Vs. P&G (1994 R.P.C. 49), Stix Limited Vs. Maharaja Appliances Limited, Roche Vs. Cipla, Reynolds Vs. Herbet Smith and Co. in support of the proposition but evidence by way of affidavit must be provided.

None of these are applicable in the present case as none of these judgments relate to pre-grant proceedings. They are judgments rendered in the context of infringement proceedings in a court of law which does not include technical expert as judges.

In view of the above, the preliminary objection raised by the Applicant is not tenable in law and deserves to be rejected.

(ii) PROOF OF LACK OF INVENTIVE STEP IN PRE-GRANT PROCEEDING VERY HIGH, NOT MET BY OPPONENT.

The argument of the Applicant that the threshold of inventive step is pre-grant opposition is far higher than revocation of post-grant proceedings, is

without any merit. The use of the words "clearly does not involve inventive step" denotes clarity. The Opponent is required to prove his case clearly, without a doubt. That, certain does not mean that the proof of lack of inventive step is higher. No grades or degree of proof is prescribed in law and cannot be read into it. This argument of the Applicant must therefore, be rejected.

Applicant's contention to Opponent I

PRELIMINARY SUBMISSIONS

(A) Reliance placed by the Opponent on *Novartis AG v Union of India* & *Ors. (MANU/SC/0281/2013)*- Misplaced:

At the very outset, it is submitted that the reliance placed by the Opponent on case law titled *Novartis AG v Union of India* & *Ors. Civil Appeal nos.* 2706-2716 *of 2013* which is annexed hereto and marked as Annexure-I is misplaced. In this regard, the attention of the Learned Controller is drawn to paragraph 191 of the said judgment which is reproduced herein below for the Learned Controller's ease of reference:

We have held that the subject product, the beta crystalline form of imatinib Mesylate, does not qualify; the test of Section 3(d) of the Act but that is not to say that Section 3(d) bars patent protection for all incremental inventions of chemical and pharmaceutical substances. It will be a grave mistake to read this judgment to mean that section, 3(d) was amended with the intent to undo the fundamental change brought in the patent regime by deletion of section 5 from the Parent Act. That is not said in this judgment.

It is submitted that from the observation made by the Hon'ble Supreme Court of India, it is evident that the Hon'ble Court made it clear that the observations made therein were specific to the subject matter before it and as such, the said case law cannot be interpreted to mean that it bars patent

protection for all incremental inventions of chemical and pharmaceutical substances. Each case has to be decided on its own merits and therefore1 the observations made therein will not have the blanket application as has been the understanding of the Opponent. For the reasons detailed out herein below/ it is submitted that the said case law has no application, whatsoever, *to* adjudicate upon the issues involved in the matter.

(B) Grounds of Pre Grant the present representation are Frivolous:

2. The Applicant humbly submits that the grounds on which the present representation has been filed by the Opponent and the argument set forth therein are frivolous in that they have not fathomed and appreciated the Applicant's invention, as will be evident in the Applicant's corresponding submissions to the statement which are enumerated herein below for the Controller's just consideration.

3. At this stage, it is pertinent to draw the attention of the Learned Controller that the Opponent in the present has failed to annex the amended and/ or original set of claims on records. In absence of filing the claims under opposition, it can safely be concluded that the submissions made by the Opponent in the present representation are based on conjectures and surmises and are baseless. On this ground alone, the present representation ought to be rejected.

(C) No evidence filed by the Opponent to establish lack of inventive step:

4. It is submitted that Section 77 (1) (c) read with section 79 of the patents Act,1970 (hereinafter referred to as "the Patents Act") mandates that evidence before the Controller should be in the form of an affidavit. It is further submitted that the issue as to whether the subject patent application lacks inventive step' or not cannot be decided by making mere submissions which in e**ither event are based on conjectures &**

surmises in a manner as been made by the Opponent in the present representation.

5. Without prejudice to the above, it is submitted that it is a settled proposition of law that in order to assess obviousness, the Court would invariably require the assistance of expert evidence. In this regard the Applicant refers to and relies upon the case titled *M6lnlycke v Proctor* & *Gamble.* [1994] R.P.C. 49 at page 113 which is annexed hereto and marked as Annexure-2 and *Stix Limited v Maharaja Appliance Limited (l.A. No. 7441 of 2008 in CS (OS) No. 1206 of 2008* which is annexed hereto and marked as Annexure·3.

6. In the present case, the Opponent has failed to corroborate the submissions by placing cogent evidence in the form of an affidavit on record as mandated by Section 79 of the Patents Act and also being the settled proposition of law. In view of the above, the present representation ought to be outrightly rejected.

(D) Threshold of inventive step much higher in Opposition proceedings than in case of revocation proceedings:

7. It is submitted that the threshold of Inventive step is much higher in Opposition proceedings than in revocation proceedings.

In case, the Learned Controller has an iota of doubt regarding the inventive step, the Learned Controller should allow the grant leaving the question to be finally decided, when an occasion arises, by Intellectual Property Appellate Board (IPAB) and/ or the High Court. In "Patent Law" by P. Narayanan, Fourth edition, the author has at pages 403 and 213 (which is annexed hereto and marked as Annexure distinguished the inventive step requirement in case of an opposition proceeding and in case of a revocation proceeding as under:

"The words "clearly does not involve any inventive step" in Section 25(1)(e) would appear to indicate that in an opposition proceeding the evidence required to establish lack of inventive step would be more stringent."

"Under Section 64(1) (j) obviousness and lack of inventive step is also available as a ground of revocation of a patent by petition before the High Court. In opposition proceedings under Section 25(1) (e) and Section 25(2) (e) it must be shown that the invention "clearly" does not involve any inventive step while there is *no such qualification under Section 64(1)(}). This shows that if the matter is in doubt, the Controller may allow the grant leaving the question to be finally decided, when an occasion arises, by the High Court."*

(E) Scheme of the Patents Act- The Opponent ought to have put the best case forward:

It is submitted that before the Learned Controller adjudicates upon the present representation by way of an opposition filed by the Opponent against the grant of patent of the patent application, it is pertinent to draw the attention of the Learned Controller to the relevant provisions of the Patents Act which will provide an insight of the scheme of the Patents Act. It is submitted that prior to the January 1, 2005, there was no concept of post-grant opposition and Section 25 provided opposition to grant of patent. It is submitted that the Section 25(1) of the Patents Act read with Rule 55 of Patents Rules, 2003 (hereinafter referred to as "the Rules") contemplates representation by way of an opposition which is a diluted form of representation.

Rule 55 of the Rules provides the procedure for pre-grant Opposition under Section 25(1) of the Act. Rule 55(1) mandates the Opponent to file statement

and evidence, if any, in support of the representation. Rule 55(3) states that on consideration of the representation, if the Contro11er is of the opinion that the application for patent shall be refused or the complete specification requires amendment, 'he shall give notice to the Applicant to that effect along with a copy of such representation, whereupon, the Applicant, as per Rule 55(4), shall file his statement and evidence, if any, in support of his application within three months from the date of notice. In view of the above, it is evident, that what is contemplated for the Applicant under Rule 55 (4) of the rules is to file statement and evidence in support of his application and not reply statement (which is the case re post-grant opposition proceeding i.e., reply to written statement filed by the Opponent as contemplated under Rule 58 of the Rules re post-grant opposition proceeding). Accordingly, each of the parties is required to put **is** best case in support of its respective submissions.

It is further submitted that as the Rules are silent on filing of a rejoinder by the Opponent in response to the statement and evidence of the Applicant in support of the application and also on filing of the reply evidence by the Opponent as contemplated under Rule 59 of the Rules re post-grant opposition, the Opponent ought to put the best case forward, which, in the absence of any cogent evidence in the form of an affidavit, as mandated by Section 79 of the Act, the Opponent has miserably failed.

It is submitted that the submissions made in the patent application/ complete Specification are made on oath in as much as Form 1 mandates a declaration to be made by the Applicant therein. In view thereof, there can be no doubt on the credibility of the Applicant.

Without prejudice to the above, it is submitted that the patent application in question discloses and claims subject matter comprising type I polymorph of

sorafenib tosylate having higher thermodynamic stability, mechanical stability, and dissolution rate than sorafenib tosylate type II polymorph. The polymorph II crystals are meta-stable in nature. In general meta-stable polymorphs tend to react with surrounding molecules like carrier molecule, other constituents of pharmaceutical compositions, humidity and the like. For example, the meta- stable state of sorafe.nib tosylate tends to convert itself into more stable structure, which may eventually lead to change in physical characteristic like dissolution rate, solubility, absorbability and the like of sorafenib tosylate. That the change in physical characteristics of the molecule will affect the therapeutic efficacy of the molecule is well understood in art.

The tendencies of meta-stable compounds to convert into different structures by exhibiting polymorphism or otherwise, or to form different compounds by reaction with other compounds, are not desirable due to changes in the physical and chemical properties of the pharmaceutical compounds, which in turn determines the therapeutic properties of a drug. Therefore, compounds in their most stable form are required for efficacious and stable drug formulation.

It is submitted that the thermodynamic polymorphs of a compound are a solution to such meta-stability issues of a compound. However, the determination of stable structure and preparation of polymorphs itself takes considerable effort and intellectual investment. Furthermore, although polymorphism is well known phenomenon in art, the determination and formation of polymorphs that suits a particular pharmaceutical application is in itself a mammoth task and involves substantial intellectual and financial investment.

Opponent II rebuttal to Applicants preliminary submissions

I. Preliminary Submissions

(a) Amended set of claims

(b) Form of an Affidavit

(c) Expert evidence

(d) Threshold in opposition proceedings

(e) Onus discharged

(f) Opponent's submissions on Admissions made by the Applicant

(g) Opponent's submissions on Affidavits filed by the Applicant

The "Statement and Evidence in support of the application U/S 25(1) of the Patents Act, 1970 read with Rule 55(4) of the Patent Rules, 2003" submitted by the Applicant on January 19, 2015 is hereinafter referred as "Statement and Evidence" and the Representation U/S25 (1) read with rule 55 of the Act is hereinafter referred as "Representation".

(a) Amended set of claims:

It was submitted that there is no alteration to the scope of the current set of claims. Therefore, present representation automatically addresses the subject matter of the pending claims and there is no need to file a fresh or supplementary representation. The newly inserted claims 14-16 dependent on Claim 1 cover characteristic details of compound of claim 1 and merit no reply.

(b) Form of an affidavit

Applicant raised several questions under the principles of C.P.C on the admissibility of the affidavits filed by the Opponent.

It was submitted that at this juncture, we need to observe that the principles of C.P.C and the decisions given thereon may not always be applicable in a patent or trademark litigation, more particularly in a patent litigation. We may in civil litigation on the particular facts of the case refuse to receive the

evidence and documents, if they are belatedly or improperly produced before the Court.

But the same principle cannot be applied here. It may noted be that the 'any person' in opposing the grant or interested in revoking the grant had belatedly come across a prior art which squarely anticipates the patent or renders the patent obvious. The Controller cannot shut out the documents merely on the ground of delay.

Similarly, if affidavits submitted by the Opponents which squarely anticipate the application for patent finds some legal deficiencies, it cannot be rejected at its outset.

It was submitted that a patent is granted only for an invention, which is a new product or process involving inventive steps and capable of industrial application. If opposition is filed on one or more of the various grounds spelt out in S.25 which would include novelty, obviousness, lack of inventive steps, etc. and the documents or evidences are belatedly or improperly produced to support the case, the Controller cannot shut his eyes and allow an application merely because the documents have been produced improperly.

On the other hand, the Controller has a duty in law to make sure that an application should not be granted wrongly to the provisions of the Patents Act. Because, that which ought to be in public domain would be wrongfully be granted a monopoly and it is the duty of the Ld. Controller to bring it back to the public domain in public interest.

Opponent submitted that since question has been raised, Opponent intend to submit the supplementary affidavits meeting all the legal formalities.

(c) Expert evidence

Applicant argued that no expert testimony evidence in support of obviousness was provided by the Opponent.

Opponent's rebuttal:

It was submitted that:

- Subject matter in dispute is straight forward and the invention as well the prior art are clearly understood, the Ld. Controller which any way is a technical person can always act on the documentary evidence and decide the matter.

- There is no need of citing expert evidence in each and every case. Patent Office in each case before it has to examine the inventive step of an invention and by definition the aspect of obviousness has also to be taken into account.

- The examination of an application is carried out by a qualified technical examiner, being a technical person which are wholly guided by the prior art before them and the knowledge that they possess by way of qualification and experience and on making themselves familiar with the general common knowledge related to a specific area of knowledge relevant for a given case. Therefore, if the Law requires that obviousness cannot be established without expert testimony then the patent system itself will collapse because every applicant for patent will require the Controller to prove his objections on inventive step and obviousness with expert evidence.

- Also, when reference to a person of average skill is made it refers to the knowledge that a person who has understood the invention would derive from the prior art as well as the common general knowledge associated with such prior art.

- Therefore, on the basis of above it was submitted that, filing of expert evidence is not a *sine qua non* to make out a case of obviousness.

- Opponent relied upon following case laws for support which were handed-out during the hearing. The relevant paragraphs there from are set-out for ready reference:

POSITION IN EP:

- THE BOARD OF APPEAL OF THE EUROPEAN PATENT OFFICE IN T 0375/00 HELD:

Page 09, last lines of Para 1.2.2 under heading Unnamed Experts:

"In the opinion of the Board an expert is only then necessary when the Board does not consider itself in a position to decide upon a matter without technical assistance.

As the Board includes two technically qualified members such cases will be rare and will only occur in special circumstances. Such special circumstances do not occur in the present case which is a relatively simple mechanical case. Moreover, it was open to the appellant for himself to actively find the necessary evidence. The appellant has not done this. If the Board were to be active in seeking experts to help the case of a party then the Board could be open to an accusation of not acting impartially. It is therefore neither necessary nor desirable for the Board to obtain the evidence of an expert in this case."

BOARDS OF APPEAL OF THE EUROPEAN PATENT OFFICE IN T 1110/03 HELD:

Page 01, Second last paragraph, under "Headnote":

I. "When evaluating evidence it is necessary to distinguish between a document which is alleged to be part of the state of the art within the meaning of Article 54(2) EPC - in the sense that the document itself is alleged to represent an instance of what has been made available to the public before the priority date of the opposed patent - and a document which is not itself part of the state of the art, but which is submitted as evidence of the state of the art or in substantiation of any other allegation of fact relevant to issues of novelty and inventive step.

II. In the first situation, a document is direct evidence of the state of the art; its status as state of the art cannot normally be challenged except on authenticity. In the second situation, a document is also evidence albeit indirect; it provides a basis for an inference about, e.g. the state of the art, common general knowledge in the art, issues of interpretation or technical prejudice etc. - an inference which is subject to challenge as to its plausibility.

III. *Only a document of the first kind can be disregarded on the sole ground that it is post published; documents of the second kind do not stand or fall by their publication date even on issues of novelty and inventive step*."

POSITION IN THE USA:

- SAM HOUSTON V. THE POLYMER CORPORATION; 78-2714, 78-2860; UNITED STATES COURT OF APPEALS, NINTH CIRCUIT:

Last paragraph under heading "OBVIOUSNESS"

Section 103 of 35 U.S.C. establishes nonobviousness as one of three conditions of patentability. The ultimate question is one of law, but the legal conclusion is resolved against the background of three factual inquiries: (1) the scope and content of the prior art; (2) differences between the prior art and the claims in the suit; (3) the level of skill in the pertinent art. Graham v. John Deere Co., 383 U.S. 1, 17, 86 S.Ct. 684, 693, 15 L.Ed.2d 545 (1966).

STANDARD OF REVIEW

We begin with the proposition that: When Fed.R.Civ.P. 56 standards are met and the court, without the aid of expert testimony, can understand the prior art and patent claims, summary judgment may be proper.

- PHILIP W. WYERS AND WYERS PRODUCTS GROUP, INC. V. MASTER LOCK COMPANY; 2009-1412; UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT:

Page 14, last paragraph:

"The Court also made clear that expert testimony concerning motivation to combine may be unnecessary and, even if present, will not necessarily create a genuine issue of material fact.

See id. at 427. We had held that the district court erred in granting summary judgment, as the affidavits of Teleflex's two experts stating their opinion that the invention was nonobvious created a material issue of fact. We had noted that "[a]t the summary judgment stage of a proceeding, it is improper for a district court to make credibility determinations." Teleflex, 119 F App'x. at 290."

Page 16, Lines 7 onwards

"We furthermore concluded that no expert opinion was required to support the obviousness determination, because the technology was "easily understandable." Id. at 1329-30 (quoting Cen-tricut, LLC v. Esab Grosup, Inc., 390 F.3d 1361, 1369 (Fed. Cir. 2004)); see also Sundance, 550 F.3d at 1365.5....."

Page 16, Second paragraph

"Thus, in appropriate cases, the ultimate inference as to the existence of a motivation to combine references may boil down to a question of "common sense," appropriate for resolution on summary judgment or JMOL. See Perfect Web, 587 F.3d at 1330. Other recent cases have confirmed the appropriateness of this approach."

(d) Threshold in opposition proceedings

Opponent submits that pre-grant opposition can be filed by any person and need not to be a person interested. The reason for providing such a broader scope for challenging an application for patent before grant is express in itself that no unwarranted patent be allowed to grant. Because, that which ought to

be in public domain would wrongfully be granted a monopoly and it is the duty of the Controller to bring it back to the public domain. Opponent totally disagreed with the statements made in the "Statement and Evidence" that threshold in opposition proceedings is high. Opponent states that intentions of the legislature for creating porous filters like pre-grant opposition, post-grant opposition is express in itself that no frivolous invention should be allowed to grant in public interest.

(e) Onus not discharged

- Applicant states that Opponent failed to discharge the Onus.

It was submitted that there is no statutory presumption of validity even of a granted patent in the Act. In fact, there is Section 13 (4) which clearly says that the examination and investigations required U/S 12 and 13 shall not be deemed in any way to warrant the validity of the patent.

Therefore, once the Opponent produces his *prima facie* evidence regarding novelty, inventive steps and other grounds, the initial onus is discharged by the opponent and onus shifts to the patentee.

(f) Opponent's Submissions on Admissions made by the Applicant

- The Applicant has made several admissions in the "Statement and Evidence", and also during the oral proceedings namely:

(i) Applicant repeatedly admitted to overcome the insufficiency objections that, example 1 of the application results in Polymorph-1 of Sorafenib Tosylate directly.

Opponent's Submissions

Opponent submitted that example 1 of the impugned application forms the part of prior art, which is admitted by the Applicant too (see page 17, para 34, lines 04-05).

In this regard, Applicant place reliance on Section 58 of the Indian Evidence Act which states that "*Facts admitted need not be proved*"

Opponent submitted that this statement of Applicant is also supported by the Affidavits filed the Opponent. Therefore, as admitted by the Applicant and as shown by the Opponent Polymorph-1 of Sorafenib tosylate is merely a prior art, hence lacks novelty in view of D1 which discloses Sorafenib tosylate.

Applicant also challenged that, D1 does not refer to any particular parameters of the Sorafenib tosylate. In this regard Opponent submitted that, it is a well settled rule that inherent anticipation does not require disclosure of particular parameters.

In this regard Opponent relied upon Manual Of Patent Practice And Procedure 2008, pages 25 and 26, section 3.4.7 which states that "*a prior art experiment which, when performed, reliably produced a particular result "more than 99 percent of the occasions on which it is conducted" would be regarded for the purposes of disclosure as "inevitably" leading to the result in question. It follows that a claim which defines an invention by reference to parameters, for example, of a process or a product, is anticipated by a disclosure, which when put into practice would necessarily fall within the scope of the claim, even if the disclosure does not refer to these particular parameters"*

(ii) Applicant in the "Statement and Evidence" clearly states that contents of representation filed by the Opponent under paragraph 2 or more particularly under paragraphs 2.2a, 2.2b and 2.2c are misleading (see page 14-15, para 27-29 of the Applicant's Statement and Evidence filed U/S 25(1)).

Opponent submitted that all the statements made under paragraph 2 of the representation are referred from the impugned application only. Therefore, as admitted by the Applicant that these statements are misleading, application

should be rejected *prima facie* for making frivols or misleading statements in the application for patent.

(g) Opponent's Submissions on Affidavits Filed by the Applicant

- Applicant submitted Affidavit of Dr. Britta Olenic, annexed as Annexure B at page 42 of the "Statement and Evidence" to show that Polymorph-II of Sorafenib tosylate is much more sensible to mechanical stress compared to Polymorph-I.

Opponent submitted to the Ld. Controller that test was not conducted according to proper standards. It was submitted that there are many flaws in the test and do not find any place according to law as well as science.

- Opponent submitted that polymorph I was grinded only for 30 seconds, and question remains unanswered that what will happen if said polymorph would have been grinded for 1 minute to 5 minutes. Opponent submitted that there is no answer to such questions in the test data.
- Opponent submitted that 30 second time duration is a just a spark moment and should not be considered as a proper test.

- Opponent submitted that both the grinding test for polymorph-I and polymorph-II were conducted at two different dates. There is no answer as to why the test was not conducted on same date and by the same person.
- Opponent submitted that there is no reference to the source of polymorph-II in this Affidavit. The question remains unanswered as to how the polymorph-II was prepared (process details).
- There is no XRPD and DSC data of the grinded polymorph-I as well grinded polymorph-II of the Sorafenib tosylate in the affidavit of Dr. Olenic. There is only reference to untreated forms of Sorafenib tosylate at page 21 of the impugned application.

- No data (XPRD OR DSC) is provided to show partial conversion of form II to amorphous, as mentioned in the affidavit.

Based on above flaws, Opponent submitted that affidavit of Dr. Britta Olenic should be rejected *in-limine*.

- Additionally, Applicant submitted Affidavit of Dr. Kerstin Pauli, annexed as Annexure C at page 53 of the "Statement and Evidence" to show that dissolution of Polymorph-I of Sorafenib tosylate is higher than its free base.

Opponent submitted that affidavit does not provide any comparative data between Polymorph-I and Polymorph-II of Sorafenib tosylate. It is well settled rule that comparison should be between recent previous prior art and which D1 in this case which discloses Sorafenib tosylate. Therefore, affidavit of Dr. Pauli has no value in the instant case.

With regard to the averments made in the affidavit, for all one knows the higher solubility that is attributed to the polymorph-I of Sorafenib tosylate may actually be a property of Sorafenib tosylate itself. One does not have to be an expert in chemistry to know that salts normally have much better solubility than compounds in free base form.

Therefore, it was submitted that said affidavit does not fulfil any purpose in the instant case.

Applicant's submission preliminary issues

(A) Reliance placed *by* the Opponent on *Novartis AG v Union o{lndia* & *Ors. (MANU SC/0281/2013)* -Misplaced:

2. At the very outset, it is submitted that the reliance placed by the Opponent on case law titled *Novartis AG v Union of India* & *Ors. Civil Appeal nos. 2706-2716 of 2013* which is annexed hereto and marked as Annexure-1 is misplaced. In this regard, the attention of the Learned Controller is drawn to

paragraph 191 of the said judgement which is reproduced herein below for the Learned Controller's ease of reference:

We have held that the subject product, tire beta crystalline form of imatinib Mesylate, does not qualify; the test of Section 3(d) of the Act but that is not to say that Section 3(d) bars patent protection for all incremental inventions of chemical and pharmaceutical substances. It will be a grave mistake to read this judgment to mean that section 3(d) was amended with the intent to undo the fundamental change brought in the patent regime by deletion of section 5 from the Patent Act. This is not said in this judgment.

It is submitted that from the observation made *by* the Hon'ble Supreme Court of India, it is evident that the Hon'ble Court made it clear that the observations made therein were specific to the subject matter before it and as such, the said case law cannot be interpreted to mean that it bars patent protection for an incremental inventions of chemical and pharmaceutical substances. Each case has to be decided on its own merits and therefore, the observations made therein will not have the blanket application as has been the understanding of the Opponent. For the reasons detailed out herein below, it is submitted that the said case law has no application, whatsoever, to adjudicate upon the issues involved in the matter.

(B) Grounds of Pre-Grant in the present representation are Frivolous:

3. The Applicant humbly submits that the grounds on which the present representation has been filed by the Opponent and the argument set forth therein are frivolous in that they have not fathomed and appreciated the Applicant's invention, as will be evident in the Applicant's corresponding submissions to the statement which are enumerated herein below for the Controller's just consideration.

4. At this stage, it is pertinent to draw the attention of the Learned Controller that the Opponent in the present has failed to annex the amended and/ or original set of claims on records. In absence of filing the claims which are under opposition, it can safely be concluded that the submissions made by the Opponent in the present representation are based on conjectures and surmises and are baseless. On this ground alone, the present representation ought to be rejected.

(C) No evidence filed by the Opponent:

5. At the very outset, the Applicant strongly objects to the revised declarations which were handed over to the learned Controller with a copy to the Applicant at the time of hearing on February 5, 2015, to be taken on record. It is submitted that at this late juncture no document, whatsoever, can be taken on record. In fact, the learned Controller had also indicated in the letter intimating the hearing that arguments will be based on the submissions already made.

6. Without prejudice to what has been stated hereinabove it is submitted that the declarations (Exhibits 12 to 14), purported to be affidavits filed by the Opponent, by no stretch of imagination, can be treated as evidence in as much as they hold no sanctity in the eyes of law. It is a settle proposition of law that the importance of verification is to test the genuineness and authenticity of allegations and also to make the deponent responsible for allegations. In essence, verification is required to enable the court to find out as to whether it will be safe to act on such affidavit evidence. It is submitted that the declarations, original or revised, filed by the Opponent are devoid of any such verification clause. In this regard, the Applicant refers to and relies upon, Section 3(a), Section 35 of the Indian Stamps Act, 1899, Section 139 read with Order 19 Rule 3 of the Code of Civil Procedure, 1908 and De1hi High Court Rules, Chapter 12 (Oaths affirmations and Affidavits) Rule 10, Rule 11

and Rule 15 thereof which is annexed hereto and marked as Annexure*2 (colly). The Applicant in support of the settle proposition mentioned herein above refers to and relies upon case laws, *Amar Singh* v *Union of India* [2011] *7* SCC 69 at page 78-79, paragraphs 22-24, *State of Bombay v Purustwttam Jognayak* [1952} SCR 674 at paragraph 15, *Sundar Industries v General Engineer Works* [C.R.No. 1165 of 1981] at page 130, *Ramas/umker Pathak v* The *Controller, Central Excise, Allahabad and* Drs. (1970) SCConline All 276 at paragraph 19 which is annexed hereto and marked as Annexure-3 (colly).

In view of the settled proposition of law, it is evident that the purported affidavits are not only devoid of any evidentiary value, but also inadmissible as evidence. In view of the above, it is submitted that the learned Controller ought not to take cognizance of the said declarations.

7. It is further submitted that Section 77(1)(c) read with Section 79 of the Patents Act, 1970 (hereinafter referred to as "the Patents Act") mandates that evidence before the Controller should be in the form of an affidavit. It is also submitted that the issue as to whether the subject patent application lacks inventive step or not cannot be decided by making mere submissions which in either event are based on conjectures and surmises, in a manner as have been made by the Opponent in the present representation.

8. Without prejudice to the above, it is submitted that it is a settled proposition of law that in order to assess obviousness, the Court would invariably require the assistance of expert evidence. In this regard, the Applicant refers to and relies upon the case titled *Molnlycke v Proctor* & *Gamble.* [1994] R.P.C 49 at page 113 which is annexed hereto and marked as Annexure4 and *Strix Limited* P *Malmraja Appliance Limited (I.A. No. 7441 of 2008 in* CS *(OS) No. 1206 of 2008* which is annexed hereto and marked as Annexure-5.

9. In the present case, the Opponent has failed to corroborate the submissions by placing cogent evidence in the form of an affidavit on record as mandated by Section 79 of the Patents Act and also being the settled proposition of law.

10. It is submitted that it is a settled proposition of law that the onus as to the invalidity of a plaintiff's patent and the grounds of insufficiency of description, want of novelty, absence of inventive steps and want of utility was rightly placed on the defendants. In this regard, the Applicant refers to and relies upon the case titled *Raj Prakash v Mangat Ram Chowdhry* & *Ors (R.F.A. (05)* 2 *of1973)* which is annexed hereto and marked as Annexure--6. In view of the above, the present representation ought to be outrightly rejected.

(D) Threshold of inventive step much higher in Opposition proceedings than in case of revocation proceedings:

11. It is submitted that the threshold of inventive step is much higher in Opposition proceedings than in revocation proceedings. In case, the Learned Controller has an iota of doubt regarding the inventive step, the Learned Controller should allow the grant leaving the question to be finally decided, when an occasion arises, by Intellectual Property Appellate Board (IPAB) and/ or the High Court. In "Patent Law" by P. Narayanan, Fourth edition, the author has at pages 403 and 213 (which is annexed hereto and marked as Annexure-7) distinguished the inventive step requirement in case of an opposition proceeding and in case of a revocation proceeding as under:

"The words "clearly do not involve any inventive step" in Section 25(1)(e) would appear to indicate that in an opposition proceeding the evidence required to establish lack of inventive step would be more stringent."

"Under Section 64(1) (/) obviousness and lack of inventive step is also mailable as a ground of revocation of a patent by petition before the High Court. In opposition proceedings under Section 25(1)(e) and Section 25(2)(e)

it must be shown that the invention "clearly" does not involve any inventive step while there is no such qualification under Section 64(1)(). This shows that if the matter is in doubt, the Controller may allow the grant /earring tire question to be finally decided, when an occasion arises, by the High Court."

(E) Scheme of the Patents Act - The Opponent ought to have put the best case forward:

12. It is submitted that before the Learned Controller adjudicates upon the present representation by way of an opposition filed by the Opponent against the grant of patent of the patent application, it is pertinent to draw the attention of the Learned Controller to the relevant provisions of the Patents Act which will provide an insight of the scheme of the Patents Act. It is submitted that prior to the January 1, 2005, there was no concept of post-grant opposition and Section 25 provided opposition to grant of patent. It is submitted that Section 25(1) of the Patents Act read with Rule 55 of the Patents Rules, 2003 (hereinafter referred to as "the Rules") contemplates representation by way of an opposition which is a diluted form of representation.

13. Rule 55 of the Rules provides the procedure for pre-grant Opposition under Section 25(1) of the Act. Rule 55(1) mandates the Opponent to file statement and evidence, if any, in support of the representation. Rule 55(3) states that on consideration of the representation, if the Controller is of the opinion that the application for patent shall be refused or the complete specification requires amendment, he shall give notice to the Applicant to that effect along with a copy of such representation, whereupon, the Applicant, as per Rule 55(4), shall file his statement and evidence, if any, in support of his application within three months from the date of notice. In view of the above, it is evident, that what is contemplated for the Applicant under Rule 55 (4) of the Rules is to file statement and evidence in support of his application and not

reply statement (which is the case re post-grant opposition proceeding i.e., reply to written statement filed by the Opponent as contemplated under Rule 58 of the Rules re post-grant opposition proceeding). Accordingly, each of the parties is required to put its best case in support of its respective submissions.

14. It is further submitted that as the Rules are silent on filing of a rejoinder by the Opponent in response to the statement and evidence of the Applicant in support of the application and also on filing of the reply evidence by the Opponent as contemplated under Rule 59 of the Rules re post-grant opposition, the Opponent ought to put the best case forward, which, in the absence of any cogent evidence in the form of an affidavit, as mandated by Section 79 of the Act, the Opponent has miserably failed.

(F) *Ex post (acto* analysis- Not permissible:

15. It is submitted that it is a settled proposition that care must be taken not to construct an argument of obviousness based upon *ex post facto* analysis. Hindsight is not to be confused with foresight. Such analysis "is unfair to inventors". Obviousness is to be considered without knowledge of the invention otherwise that consideration amounts to impermissible *ex post facto* analysis. It is further submitted that obviousness has to be answered not by looking with the benefit of hindsight at what is known now and what was known at the priority date and asking whether the former flows naturally and obviously from latter, but by hypothesising what would have been obvious at the priority date to a person skilled in the art to which the patent in suit relates, who is assumed to have access to what was known of the art immediately before the priority date.

16. It is submitted that it is settled proposition of law that while finding an answer to the question of whether or not improvement made by the plaintiff is only a workshop improvement that is so obvious to a person skilled in the art,

one must cautiously remove the hindsight bias. In this regard, the Applicant refers to and relies upon the case titled *British Westinghouse* l' *Braulik* (1910) 27 R.P.C. 209 at 230 which is annexed hereto and marked as Annexure-8 and *M.* C. *Jayasingh v. Mishra Dhatu Nigam Limited(2014)* SCC Online Mad 163 which is annexed hereto and marked as Annexure-9.

(G) Inevitable Results must be strictly proved i.e., beyond reasonable doubt:

17. It is submitted that "inevitable results" must be strictly proved i.e., "must result" "necessarily result" in the claimed invention. It is submitted that it is a settled proposition that even though it was "overwhelmingly likely" that the prior art had formed a composition within the claims of the patent in suit, this was not enough for the purposes of anticipation. It is further submitted that inevitable result objection should only be raised where there "can be no reasonable doubt as to the practical effect of the prior teaching". In fact, it has been observed by the Courts that "likelihood, even overwhelming likelihood" does not suffice in this regard, the Applicant refers to and relies upon the case titled *Ferag l' Muller Martini* [2007] EWCA Civ 15 at paragraphs 7 to 9 which is annexed hereto and marked as Annexure-10.

(H}The Opponent has terribly failed to discharge the Onus:

It is submitted that it is a settled proposition of law that in the opposition proceedings, it is the Opponent, who at the first instance, must plead and prove that the invention claimed in the patent application does not come within the purview of "invention" and other criteria as laid down in the Patents Act. It is only thereafter, that the Applicant is required to counter it.

As evident from the pleadings, the Opponent has terribly failed to make out a case for refusal for grant of patent inasmuch as the pleadings are vague in addition to not being supported by evidence in the form of affidavits as required by the law. It is submitted that the Opponent has also failed to

discharge its onus. Accordingly, the present representation by way of opposition deserves to be dismissed at the threshold itself.

Conclusions:

From the above pleadings, it appears that both the opponents and the applicant have cited a number of grounds and case laws to establish their stand. Some of the points are irrelevant/superfluous and some of the points are relevant and worth discussing in the instant patent application under pre-grant opposition. As far as the time line and procedural part of the procedure as defined in the law are concerned, both the opponent and the applicant are well disciplined. However, the plethora of grounds, prior art documents and case laws put forth by both the parties are irrelevant in nature need not be addressed. Both the parties have unnecessarily over burdened the Controller in citing different case laws. However, I am concerned with the relevant documents, relevant grounds of opposition and relevant case laws. My decision is based on the outcome of invention disclosed, analysis of the relevant documents and case laws, and the argument made by both the opponents and applicant.

Having considered the detailed arguments of both the parties, the teachings of the various prior art documents on record, the affidavit (s) filed by both the parties, I shall now deal with each ground of the opposition as discussed during the hearing.

As far as Preliminary Issues are concerned, all the relevant issues are taken into consideration while deciding the case.

Regarding the applicants contention that the documents filed by the opponent cannot be considered as evidence since they have not been filed as an affidavit as mandated by section 79 of the Patent Act, it is a settled position that lack of novelty has to be judged only on the basis of prior publication and/ or use,

whereas inventive step has to be looked into on the basis of prior art in combination with the common general knowledge. Moreover, rule 57 of the Patents Act requires the filing of the written statement and the facts on which the opponent makes out his case. The requirement of evidence to be filed is optional. If the opponent is successful in proving obviousness on the basis of documents in combination with the common general knowledge, then additional evidence may not be required. The applicant has rightly pointed out that the affidavits filed by the opponent II were not in the manner as prescribed U/s 79 of the Patents Act. But an important fact that needs to be taken care of is that, as such patent cannot be granted on the grounds that the documents are belatedly or improperly produced before the Controller. At this point, it is to be noted that the opponent has submitted properly executed affidavits with verification clause in accordance with the procedure as prescribed U/s 79 of the Patents Act, along with hearing submissions. Considering the fact that patents grants monopoly rights to the applicants & this right cannot be merely given on the basis of failure to produce the evidence in the form of affidavits as required under Patents law. Affirming with the principles of natural justice & in public interest these affidavits are taken on record. **As such the affidavits filed are of not of much significance or relevance while deciding this matter.** IPAB order 173 of 2013 clearly requires that the opponent has to plead and prove his case. In this regard, the opponents have pleaded their case on the various documents relied upon by them in their written statement. Whether these documents relied upon by the opponent in combination with the common general knowledge will be adequate to establish their challenge on the ground of obviousness will be dealt with by me hereinafter.

GROUND 1: CLAIMS NOT PATENTABLE UNDER SECTION 3(c)

After going through the submissions of both the parties, it is clear that the application relates to a novel form, thermodynamically stable at room temperature of the tosylate salt of sorafenib which is different from sorafenib base itself. The document WO 00/42012 relates Sorafenib base & does not describe any polymorphic form of sorafenib tosylate salt. Though the documents WO 03/047579 and WO 03/068228 describe a tosylate salt of sorafenib but as such there is no mention of any polymorphic form. In absence of any evidence that any polymorphs described in the application were known & that the polymorph 1 would be inherently produced, it cannot be concluded that the inventions is a mere discovery of a scientific principle & thus does not fall under the ambit of Section 3(c) of the patents Act.

I conclude that such a ground of opposition is not validly established by the opponent I.

GROUND 2: SECTION 25(1) (g): INSUFFICIENT DISCLOSURE

That the complete specification does not sufficiently & clearly describe the invention or the method by which it is to be performed.

After going through the arguments & submissions of both the parties on the above mentioned ground where section 10(4) is in question, I am of the opinion that the complete specification of the patent application sufficiently and clearly describes the invention as well as the method by which it is to be performed. The polymorphic forms of sorafenib tosylate are sufficiently and clearly described in the description in tables 2 to 6 by X-ray diffractometry, IR spectroscopy, Raman spectroscopy, FIR spectroscopy and NIR spectroscopy. The polymorph of example 1, i.e., polymorph ll, is not part of the invention claimed in the patent application. The fact as pointed out by applicant that

over 40 patents have been granted on corresponding applications filed in various countries where the complete specification fulfilled the test of describing the invention sufficiently and the best mode of carrying out the invention further supports the fact that the complete specification clearly fulfils the requirement of Section 10(4) of the Patents Act by sufficiently & clearly defining the invention or the method by which it is performed.

I conclude that such a ground of opposition is not validly established by the opponents.

GROUND 3: INVENTION NOT PATENTABLE UNDER SECTION 3(i)

In view of deletion of claims 5 to 6 and 9 to 11, which were related to the use of the compound of claim **1** or a pharmaceutical composition thereof for the treatment of certain disorders or diseases during reply to First Examination Report dated 04th March, 2014.

The opposition ground is rendered moot.

GROUND 4: CLAIMS NOT PATENTABLE UNDER SECTION 3(e)

Section 3(e) the Patents Act, 1970 mandates that, for the claims relating to the composition or combination, the claims should define all the novel, inventive features in terms of its percentage or ratio of the constituents used to prepare the composition or combination clearly, ensuring that the composition or combination is not just a mere admixture but also a synergistic composition supported with working examples.

It is also a fact that, when the claims of a invention relates to any product or compound, it is the normal practice of the inventors to incorporate claims relating to composition or combination in order to broaden the scope of the claims, so no one infringes the product claims & in such a case there is as such no need to incorporate any working examples for preparation of such composition or combination in the patent application, subject to the condition that the product or compound qualifies for a invention under section 2(1)(j) of the Patents Act , 1970 i.e. the product is novel, inventive & has industrial applicability .

The question of Section 3(e) of the Patents Act, 1970, comes in picture only when the product or compound qualifies the test for an invention under section 2(1) (j) of the Patents Act, 1970

In the present case it the clear that though invention clears novelty & industrial applicability tests but fails to qualify for an invention under Inventive step.

Since the claims lack inventive step on the basis of cited documents, the composition or combination claims does not have any relevance & are not patentable under Section 3(e) of the Patents Act, 1970.

I conclude that such a ground of opposition is validly established by both the opponents.

GROUND 5: CLAIMS NOT PATENTABLE AS LACKING NOVELTY UNDER SECTION 25(1) (b)/(c)

After going through the submissions, the documents acknowledged in the specification & cited by the opponent I, it is clear that Document WO 00/42012 does not describe any polymorphic form of sorafenib tosylate salt. WO 03/047579 and WO 03/068228 describe a tosylate salt of sorafenib but without any specification of the polymorphic form. As regards Scott Wilhelm et al also narrates the use of the compound BA43-9006 in clinical settings- the same constitutes a specific use of the compound BA43-9006.

None of the document provide a more thermodynamically or mechanically stable polymorphic form of sorafenib tosylate salt. The opponents' argument that in absence of any data it must be presumed that the cited document disclosed the polymorph 1 of the applicant is not found to be persuasive

Also after going through the submissions, the documents acknowledged in the specification & cited by the opponent II.Though the experiments were carried out by the method as disclosed in the specification or from the known method it must be appreciated that it was the applicant who has carried out the at first

instance. The applicants explanation to the opponents assertion that the opponents could not reproduce the polymorph II while conducting the process of claim 1 in the affidavit (submitted with hearing submission) might be due to unintentional seeding as supported by the applicant in Annexure A cannot be denied. Also just relying upon the theory of disappearing polymorphs which exists or not & the mere assertion that polymorph–I must have formed in view Document D1 is not a concrete proof to establish novelty.

The opponents' reliance on document D3 that modification -3 of sorafenib tosylate was used in the clinical studies & D4 that a tablet formulation of sorafenib tosylate was used in clinical studies & according to the common knowledge that "***compounds in most stable form are required for efficacious and stable drug formulation*"** (refer to Page 12, para 21, line 05-06 of the "Statement and Evidence") & then drawing inference that a any composition of Sorafenib tosylate would certainly use stable form which is as per Applicant's statement is polymorph–I may be logic that may be acceptable but does not help in establishing novelty, thus claim 1 is novel.

Since claim 1 novel claims 5-7 & claims 10-13 are also novel.

At this juncture I would rely on the decision by ***Hon'ble IPAB, In OA/8/2009/PT/CH (250/2012)*** *rejected novelty ground "to defeat novelty, the appellant should show that an earlier document, disclosed all that the patentee is seeking to patent. And that each limitation of the claimed invention is found in a single prior art reference. The appellant has not done this. So the ground of novelty is rejected.* In the present case both the Opponents have relied on more than one document to bring out their case but were still unsuccessful.

I conclude that such a ground of opposition is not validly established by both the opponents.

GROUND 6: PRIOR USE (SECTION 25(1) (d)

Section 25(1) (d) mandates the opponent to show that the invention so far as claimed in any claim of the complete specification should have been publicly known or publicly used in India before the priority date of the claim. The explanation that follows to it clearly specifies

Explanation – For the purposes of this clause, an invention relating to a process for which a patent is claimed shall be deemed to have been publicly known or publicly used in India before the priority date of the claim if a product made by that process had already been imported into India before that date except where such importation has been for the purpose of reasonable trial or experiment only.

Opponent I asserts that the sorafenib tosylate is mentioned in WO 03/047579 and WO 03/068228, but the documents nowhere discloses any polymorphic form I of sorafenib tosylate. The other document relied i.e. Scott Wilhelm.et al. "Current Pharmaceutical Design 2002" [referred to as Annexure E in the Opponent's statement] discloses only the use of the compound BAY 43-9006 which is sorafenib itself & does disclose polymorph I of sorafenib tosylate. Thus the opponent I fail to provide any concrete evidence to support his claims that polymorphic form I of sorafenib was publicly known or publicly used in India before the priority date of the claim tosylate.

The opponent II relied on the post published documents D3 & D4.

D3 which is a scientific discussion of the pharmacological activity of sorafenib in treating cancer, published by the EMEA in 2006, i.e. after the filing date of the present patent application discloses reports on two clinical studies 100391 (phase II study) and 11213 (phase III study), allegedly using film-coated tablets containing 274 mg of sorafenib tosylate, microcrystalline cellulose,croscarmellose, hypromellose sodium lauryl sulphate, magnesium

stearate, water, titanium dioxide and red ferric oxide (03, page 2149, last paragraph).

Though D3 discloses that the active substance exhibits polymorphism and crystallizes in three different modifications (modification I II and III) (D3, page 3/49, first paragraph), but it fails to provide that which of the modifications have been used for the clinical studies (page 29/49, second paragraph and page 36/ 49).

Document D4 is an approval letter by FDA. It only discloses that the studies were carried out between September 25, 2002 and September 2006 (study 100391) and between November 19, 2003 and September 2006 (study 11213) (see e.g. D4, page 3, item 5).

It is clear that D4 mentions the date when the clinical studies started, but there is no clear cut evidence of the date of delivery of the sorafenib tosylate tablets & its use in public domain before the priority date of the present patent application.

Both the documents fails to disclose that sorafenib tosylate in the form of polymorphic form I has been used in the clinical trials. It is evident from the documents submitted that the clinical studies were not conducted in the public domain, but were subject to a specific confidentiality.

Thus it is clear from the arguments & submissions that the opponents rely only on the post published documents & confidential clinical trials which are not in public domain for free use.

None of the prior art mentions the use any polymorphic form of sorafenib tosylate, nor does any concrete evidence provided by the opponent for prior use of the polymorphic form I of sorafenib tosylate. Therefore the ground of opposition U/s 25(1) (d) is not sustained.

I conclude that such a ground of opposition is not validly established by both

the opponents.

GROUND 7: INVENTIVE STEP (SECTION 25(2) (e)

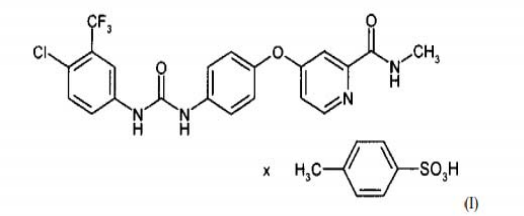
The applicant states that the present invention relates to a novel form, thermodynamically stable at room temperature, of the tosylate salt of 4-{4-[({[4-chloro-3-(trifluoromethyl) phenyl] amino} carbonyl) amino] phenoxy}-N-methylpyridine-2-carboxamide, to processes for its preparation, to medicaments comprising it and to its use in the control of disorders like cancer. The problem associated with the pharmaceutical products is to have always the same constant properties to guarantee constant and reliable efficacy. From the applicants' statement, it is clear that there is a need to find the most stable form of a compound because only the most stable form can ensure that all properties and characteristics regarding stability, dissolution rate, shelf life, efficacy, and bioavailability remain constant during manufacturing, storage, and administration. The applicant addresses the problem by providing a polymorphic form I of sorafenib tosylate which is surprisingly more stable than the other polymorphs found and ensures a constant & reliable efficacy, therapeutic or otherwise.

From all the documents cited & disclosures & evidences filed the teachings that flow from them is as follows,

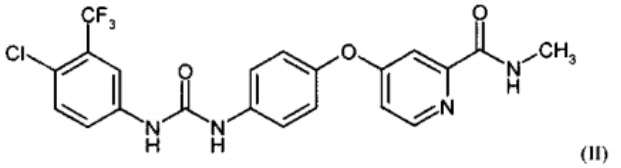
It is evident from the description and claims of the present invention relates to a novel form, thermodynamically stable at room temperature, of the tosylate salt of 4-{4-[({[4-chloro-3-(trifluoromethyl) phenyl] amino} carbonyl) amino] phenoxy}-N-methylpyridine-2-carboxamide, to processes for its preparation, to medicaments comprising it and to its use in the control of disorders like cancer.

The tosylate salt of 4-{4-[({[4-chloro-3-(trifluoromethyl) phenyl] amino}

carbonyl) amino] phenoxy}-N- methylpyridine-2-carboxamide is mentioned in WO 03/068228 and WO 03/047579 and corresponds to the compound of the formula (I):



The compound 4-{4-[({[4-chloro-3-(trifluoromethyl) phenyl] amino} carbonyl) amino] phenoxy}-N-methylpyridine-2-carboxamide is described in WO 00/42012 and corresponds to the compound of the formula (11):



The compounds and their salts, disclosed in WO 00/42012, for example tosylates, are described there as inhibitors of the enzyme Raf kinase and may be used for the treatment of disorders, for example cancer.

Conclusions for Opponent I

After careful consideration of the arguments of both the parties on the documents cited it is clear that **Annexure "A" i.e. WO 0042012** discloses the base Sorafenib. The compounds and their salts, disclosed in WO 00/42012, for example tosylates, are described there as inhibitors of the enzyme Raf kinase and may be used for the treatment of disorders, for example cancer.

Annexure "F" i.e.W0/1996/027592 discloses a process for the preparation of polymorphic B form of (E)-4- [[3-[2- (4-cyclobutyl-2-thiazolyl) ethenyl] phenyl] amino]-2, 2-diethyl-4-oxobutanoic acid by agitating Polymorphic Form A in a solvent and adding the seed crystals of Form B.

Annexure "G" i.e. W0/1999/001444 in example 23 discloses a process for the preparation of thermodynamically stable polymorphic form I of the tachykinin receptor antagonist 2-(r)-(1-(r) -(3,5-bis(trifluoromethyl) phenyl)ethoxy)-3-(s)-(4-fluoro) phenyl-4-(3-5 (-oxo-1hAh-1,2A,-triazolo) methylmorpholine by effecting the compound of Form II in methanol and seeded with crystals of Polymorphic form I.

Annexure "H" i.e. A chapter from the book "Advanced Pharmaceutical Solids" by Jens T. Carstensen, published by Marcel Dekker Inc, ©2001. It clearly discloses the various experimentation techniques to obtain polymorphs and to convert metastable polymorphs into stable polymorphs. Thus the process and methods used for making polymorphs or converting a metastable polymorph into a stable polymorph is well documented in literature.

The teachings that flow from the above cited prior arts is that one can easily convert one polymorphic form to other polymorphic form & is conversion is spontaneous. Also the use inert solvent & seeding technology is known from the prior art for the conversion one polymorphic form to another polymorphic form. Thus applying the same teachings the process as claimed in the claims 2-4 of the instant invention can be arrived.

Claims 2-4 and claims 8-9 of the impugned patent application deal with process for the preparation of polymorphic form I of sorafenib tosylate. Claims 8-9 deal with the process of converting from polymorph II to polymorph I.

Certainly combining the above teachings of the prior art for a skilled artisan, it is clear cut motivation to prepare stable polymorphic form of Sorafenib tosylate as claimed in the impugned patent with enhanced properties with reasonable success by combining the above teachings of any of the references as mentioned in the cited documents no inventive step resides in the same.

Conclusions for Opponent II

After going through the submissions of both the parties it is clear that Document D1 (WO 03/068228) as cited by the opponent 2, also disclosed in the impugned patent specification discloses tosylate salt of sorafenib and its use in the treatment of disorders in which angiogenesis plays an important role for example in tumor growth. The teaching that flows from this document is that tosylate salt of sorafenib is known.

D5 as cited by the opponent is research article published in Chemistry & industry, 1989, pages 527-529 is a general article which discloses the common general knowledge in the field of polymorphism surely discloses that ***"The thermodynamically stable polymorph needs to be identified. If the compound is enantiotropic, there will be two or more stable polymorphs and transition temperatures as well. These can be identified by simple techniques, for example by stirring or shaking excess solid with solid at different temperatures.*** "(See on page 528, column 02). The same article also on page 527, column 02 under section *"Crystals and Crystallisation", "The use of seed crystals can be helpful in obtaining a desired polymorph. Manufacturing processes seem to be worked out by trial and error aided by serendipity, and then adhered to rigidity.* "

The teaching that certainly flows from this article clearly suggests that stirring or shaking and seeding technology is very well known in the art prior can be used to prepare a thermodynamically stable polymorph.

Thus a person skilled in the art can easily combine the teachings D1& D5 to arrive at thermodynamically stable polymorph 1 of sorafenib tosylate. Therefore claim 1 lacks inventiveness.

Claims 2, 3, 4, 8 and 9 relates to the conversion of one polymorph to another thermodynamically stable polymorph, particularly a process for the

conversion of polymorph-II to polymorph-I.

The disclosure on page 15 & 16 on the specification of the impugned invention discloses the process for the conversion of polymorph-II to polymorph-I of Sorafenib tosylate; *"Preference is given to preparing the compound of the formula (I) in the polymorph I by effecting the compound of the formula (I) in the polymorph (1l) obtained as described in example 1, in methanol, ethanol, a mixture of both solvents or a mixture of both solvents with water, preferably a 1:1 mixture with water, and shaking or stirring at a temperature of from 50°C up to the reflux temperature of the*

Solvent, preferably at from 60 to 80°C, in the absence of crystals of a solvate of the compound of the formula (I), for example in the absence of crystals of the methanol solvate or the ethanol solvate of the compound of formula (I),for up to one day. The crystals are cooled to from -30°C to room temperature, preferably from -25 to 1 0°C, isolated and dried The compound of the formula (I) is thus obtained in the polymorph I Most preferably isopropanol, ethyl acetate or a mixture thereof is used as solvent.

"Preference is likewise given to preparing the compound of the formula (I) in the polymorph I by effecting the compound of the formula (I) in the polymorph II, obtained as described in example 1, in methanol, ethanol, a mixture of both solvents or a mixture of both solvents with water, and shaking or stirring at a temperature of from 1 0°C up to the reflux temperature of the solvent, preferably at room temperature, for up to 1 day. The mixture is subsequently seeded with crystals of the compound of the formula (I) in the polymorph I and stirred or shaken, for example at room temperature, for from 1 hour to 14 days, preferably from 2 hours to 7 days. The crystals are isolated and dried. The compound of the formula (1) is thus obtained in the polymorph I most preferably isopropanol, ethyl acetate or a mixture thereof is used as solvent"

Thus from the disclosures Dl in view of D5 it is clear that, polymorph-I of Sorafenib tosylate is obtained by heating the polymorph-II of Sorafenib tosylate in an inert solvent. Subsequently, it mentions that seeding is preferred for obtaining the polymorph-I of Sorafenib tosylate.

Also referring to the disclosure page 02, first paragraph of the impugned application & the admittance of the fact that Sorafenib tosylate of Dl exist in polymorph-II, starting from Dl conversion of a known compound to another thermodynamically stable polymorph certainly is obvious in view of D5. Therefore the process as claimed in the claims 2, 3, 4, 8 and 9 of impugned application involves no inventive step of any sort and does not satisfy the criteria of obviousness.

Document D6 relates to review article published Pharmaceutical Research, vol. 12, No. 7, pages 1995, 945-954 provides a review of strategic approaches to remove much of uncertainty by presenting concepts and ideas in the form of flow charts to control the crystal form (polymorph) of drug substance. D6 provides a review of strategic approaches to remove much of uncertainty by presenting concepts and ideas in the form of flow charts to control the crystal form (polymorph) of drug substance.

It outlines investigations of the formation of polymorphs and the controls needed to ensure the integrity of the drug substance containing either a single or mixture of polymorphs. D6 on page 946, under the heading; *"Formation of Polymorphs - Have Polymorphs Been Discovered?"The first step in the polymorph decision tree is to crystallize the substance from a number of different solvents in order to answer the question: Are polymorphs possible? Solvents should include those used in the final crystallization steps and those used during formulation and processing and may also include water, methanol, ethanol, propanal, isopropanol, acetone, acetonitrile, ethyl acetate,*

hexane and mixtures if appropriate. New crystal forms can often be obtained by cooling hot saturated solutions or partly evaporating clear saturated solutions. ..... "

The teaching that flow from this document D6 is the use of specific solvents during preparation of polymorphs & specifically mentions the use of solvents such as water, methanol, ethanol, propanal, isopropanol, acetone, acetonitrile, ethyl acetate, hexane and mixtures. Here I see that same solvents has been used by the applicants in preparing the polymorph I of Sorafenib tosylate in the working examples of the impugned application

Thus by combining teachings of D5 & D6, a skilled artisan it is practically possible to arrive at a process of converting one polymorph to another polymorph using the solvents mentioned in the D6. Thus process claims lack inventive merit.

In order to establish the ground of Inventive step as mandated under section 2(1) (j) of the Patent Act, the applicant had asserted that the polymorph possess unexpected properties. Even if the assertion is considered the claiming of a polymorph I from polymorph II by using the method which is inherently disclosed in the prior art does not necessarily make the claim inventive.

However it is crystal clear that the applicant has emphasized more on physical stability of the polymorph I during preparation, which alone cannot be considered as a sole factor for technical advancement of the present invention under section 2(1) (j) of the Patent Act. Thus from the above facts, it is clear that applicant have failed to establish any technical advancement or any economic significance of the Polymorph I of sorafenib tosylate over the disclosures of prior art.

Also the position itself is clear in the landmark judgment which has been aptly applied for judging Inventive step. I rely on the landmark judgment, which

goes as **In *Bishwanath Prasad Radhey Shyam Appellant v Hindustan Metal Industries*** the Supreme Court of India laid down the importance of assessing inventive step, as follows:

"*It is important 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 interrelation they produce a new process or improved result. Mere collection of more than one integers or things, not involving the exercise of any inventive faculty, does not qualify for the grant of a patent.*"

From the aforesaid, I am of the opinion that the compound Sorafenib base & tosylates salt of sorafenib are also known in the art. The requirement of finding the most stable form of a tosylate salt to ensure that all properties and characteristics regarding stability, dissolution rate, shelf life, efficacy, and bioavailability remain constant during manufacturing, storage, and administration can be easily achieved by using the above mention cited art and there is no inventive contribution of the applicant atleast in this arena. Now, taking up the question of whether identifying the suitable polymorph I from the known sorafenib tosylate having more stability what contribution it exerts, I see from the various documents that there is a disclosure of the tosylate salt also being stable. Now, while judging obviousness any factor that will lead to reasonable expectation of success is relevant and a person skilled in the art has a sound knowledge in this field and not completely ignorant. This being the opinion of the Hon'ble IPAB, I am convinced that having known the

therapeutic activity of sorafenib base & that of sorafenib tosylate, the requirement of identifying a stable polymorph having specific stability, dissolution rate, shelf life, efficacy, and bioavailability that remains constant during manufacturing, storage, and administration identifying the suitable form which will exhibit these characteristics will be routine experimentation and cannot be considered as inventive. The position of the applicant that non-analogous prior art is irrelevant while judging obviousness is incorrect since all knowledge before the priority date of the patent which is not specific to this field will be held to constitute common general knowledge. Regarding, the composition claim & combination claims as such the product & process claims not inventive, the same are obvious on the face of the prior art. Thus the claimed invention falls under the ambit of Section 2(1)(ja) in view of lack of inventive step in absence of any technical advancement over the prior art & also in the arena of economic significance or both and is obvious for a person skilled in the art. Thus the invention as claimed in the claim 1 & its dependent claims lack inventive step & is obvious to a person skilled in the art.

I conclude that such a ground of opposition is validly established by both the opponents.

GROUND 8: CLAIMS NOT PATENTABLE UNDER SECTION 3(d)

After going to the arguments of both the parties, I am of the opinion that for a polymorph to qualify for an invention under section 3(d) of the Indian Patents Act, has to show significant improvement of therapeutic efficacy as compared to known form. The impugned patent relates to a novel form, thermodynamically stable at room temperature, of the tosylate salt of sorafenib, to processes for its preparation, to medicaments comprising it and to its use in the control of disorders like cancer however there is no disclosure

in the specification as to enhancement in the therapeutic efficacy as compared to its structurally similar forms i.e. the tosylate salt of sorafenib mentioned in documents WO 03/068228 and WO 03/047579 & also admitted in the specification of the applicant. The specification of the impugned application focuses on physical attributes such as the properties and advantages of a thermodynamically stable form of Sorafenib tosylate salt. The inventive feature being claimed as the polymorphic form 1, which is stable enough and does not convert into another polymorphic form and prevents changes in solubility or bioavailability profile. There is however no mention in the entire specification that the polymorph 1 of Sorafenib tosylate salt exhibits better therapeutic efficacy and treats/contributes to an improvement in the treatment of cancer. No research data or clinical trials results are disclosed in the specification nor provided in any form to support therapeutic efficacy.

Further the applicant has relied on the technical affidavit deposed by Dr. Kerstin Pauli. However after going through it the data as submitted reveals that the efficacy of the tosylate salt of sorafenib in polymorphic form l is higher than its base sorafenib due to a higher dissolution in tablets containing both drugs each.

A simple comparative test for studying the dissolution rate has been conducted on the polymorph I of sorafenib tosylate & sorafenib base rather than sorafenib tosylate polymorph II being the closest prior art.

The other affidavit filed Dr. Olenik focuses on mechanical stress test & concludes that the polymorph I of sorafenib tosylate is more stable & technically advanced than the other polymorphs including polymorph II & ensures a constant & reliable efficacy.

Also the problem as addressed by the applicant is to provide a form of sorafenib tosylate which has superior properties regarding

manufacturing, storage, and administration & the solution proposed is in finding the most stable form of a compound because only the most stable form can ensure that all properties and characteristics regarding stability, dissolution rate, shelf life, and bioavailability remain constant during manufacturing, storage, and administration. Since these factors will have influence on the bioavailability of the drug rather than the therapeutic efficacy of the drug. The physical stability of the compound during formulation cannot be considered as a sole factor for improvement of therapeutic efficacy of the drug under as required under section 3 (d) of the Indian Patent Act, almost the same view was expressed in the landmark decision issued by Hon'ble Supreme court in Novartis case (referring to paragraphs 180-192) where the Supreme Court was concerned with the patentability of polymorphic form of imatinib mesylate. It was contented by the Applicant/Petitioner, Novartis before the Supreme Court that the crystal form has better physical properties including that it is thermodynamically more stable, less hydroscopic and has lower hygroscopicity (page 63, para 168). This was supported by expert evidence submitted by the Appellant-Novartis. Comparison was made of these physical properties of the crystal form with the base and it was contended that because the crystal form exhibits better solubility, the same should be taken as a measure of increased bioavailability and hence, improved therapeutic efficacy. It was contended that the crystal showed 30% improvement in bioavailability as compared to the free base (para 168-169, page 63). The Supreme Court considered these submissions in paragraphs 175-190 and at paragraph 180, especially paragraph 187 the Supreme Court has held that *"In whatever way therapeutic efficacy may be interpreted, this much absolutely clear that the physic-chemical properties of beta crystalline form of Imatinib Mesylate, namely (i) more*

beneficial flow properties, (ii) better thermodynamic stability, and (iii) lower hygroscopicity, may be otherwise beneficial but these properties cannot even be taken into account for the purpose of the test of Section 3(d) of the Act, since these properties have nothing to do with therapeutic efficacy". The Supreme Court has also held in paragraph 188 that *"Bioavailability falls outside the area of efficacy in case of a medicine…."* Further, in paragraph 189, the Court held that *"... the position that emerges is that just increased bioavailability alone may not necessarily lead to an enhancement of therapeutic efficacy…."* The Supreme Court has also held that *"... whether or not an increased in bioavailability leads to enhancement of therapeutic efficacy in any given case must be specifically claimed and established by research data…."*

Thus the Hon'ble Supreme Court outrightly rejected that the mere comparison of base with a claimed form as sufficient for establishing therapeutic efficacy and held that therapeutic efficacy must be established by submitting appropriate research and clinical data.

In the present context, even if the claim of the applicant is taken into consideration, it does not have a legal standing in view of absence of any clinical trials results demonstrating the fact that the newly formed polymorph 1 of sorafenib tosylate is more efficacious than polymorph II of sorafenib tosylate in terms of therapeutic effects.

Here, I see that all the data furnished by the applicant pertains to physical attributes such as storage, stability, bioavailability studies resulting in a thermodynamically stable at room temperature polymeric form of the tosylate salt of sorafenib, but the requirement of showing enhanced therapeutic efficacy still remains unaddressed.

The Hon'ble Supreme court has held in the Novartis case that Para *173. The*

aforesaid properties, (physical attributes according to Manley), would give the subject product improved processability and better and longer storability but, as we shall see presently, on the basis of those properties alone, the beta crystalline form of Imatinib Mesylate certainly cannot be said to possess enhanced efficacy over Imatinib Mesylate, the known substance immediately preceding it, within the meaning of section 3(d) of the Act.

Accordingly, I opine that the invention fails to demonstrate therapeutic efficacy and therefore fails to fulfill the requirement of a patentable invention u/s 3(d) of the patents Act.

I conclude that such a ground of opposition is validly established by both the opponents.

GROUND 9: U/s 25(1) (h), THE FAILURE TO DISCLOSE DETAILS OF CORRESPONDING FOREIGN APPLICATIONS;

Section 8(1) mandates the applicant to provide information and undertaking relating to foreign filings within the prescribed period. Rule 12 provides a period of six months to provide all the details of foreign filings. Section 8(2) also casts a duty on the applicant to provide information to the controller as and when required relating to the processing of the application in a country outside India.

The applicant has filed first form 3 on 14th March, 2007 disclosing only details of two countries. The applicant has then updated the details of foreign filings by filing another form 3 on 14th August, 2012, disclosing the details of foreign filings in almost 77 countries & that to not in prescribed manner. Consequently 3 form 3 giving updated details of foreign filings were filed details that also not in prescribed manner.

In the present case the agent of the applicant has filed second form 3 after a gap period of five years & only after the opponent one filed his opposition opposing it under section 8 i.e. after 14th October 2011.

After contesting the ground under Section 8 during hearing & after validly establishing the ground by opponent, the applicant filed a petition under rule 137 on 19th January, 2015 for obviating the irregularity citing the details were not available at the time filing. An important point is that ignorance of fact is an excuse but ignorance of law cannot be pleaded as an excuse. Here the petition under rule 137 is not taken on record as it is beyond the reasonable time i.e. after 7 years & is also detriment to the interest of opponent I, as it was one of the validly established grounds of opposition.

Also compliance under section 8(1) is a continuing one, that is, the applicant is required to disclose details at regular intervals so as to keep the Patent Office abreast in prescribed manner. The scheme of law requires that the Patent Office is kept aware of any foreign filing within six months of such filing. Hence, rule 12(2) dictates the six month period within which the Applicant-Patentee has to discharge its duty.

The Applicant has creatively attempted to escape liability under section 8(1) by furnishing the required details at the last moment & filing a petition for obviation of delay, thereby, diluting the express provision of law as well as the object of the law. Hence, one time stray filing cannot be held to have satisfied the requirement of section 8(1). Further, such a conduct of the applicant is not permitted so as to dilute the requirements under section 8.

I hereby rely on the orders of Hon'ble IPAB, which has in series of decisions issued strict guidance that the requirement under section 8 cannot be diluted by the Ld. Controller (*Ajanta Pharma v. Allergan Inc.*, Order 173/2013; *Tata Chemicals v. Hindustan Unilever*, Order 166/2012; *Fresenius Kabi Oncology*

v. Glaxo Group Order 161/2013).

In the present case the applicant has failed to discharges his duties miserably under section 8(1) of the Patents Act. Thus the opponent has successfully established the ground of opposition as contested under section 8.

I conclude that such a ground of opposition is validly established by the opponent I.

After having considered all the circumstance of this case, representation and expert evidence of opponents, reply of the applicants, expert evidence in support of the applicant, written submissions and arguments in the hearing made by both parties and also my discussion and findings as mention above, I am of the opinion that the opponents have succeeded in proving their grounds relied upon by them. **The application is refused on the ground of lack of Inventive step(Section 2(1)(ja), Section 3(d), Section 3(e) & finally Section 25(1)(h) of The Patents Act, 1970.** In view of the above, I accept the representation and refuse to proceed with the application for grant and therefore, there shall be no patent in pursuance of this application. There is no order as to costs.

Dated, the 24th day of February, 2015.

(Dr. Ajay S. Thakur)

Assistant Controller of Patents & Designs.

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