MANU/IC/0034/2009

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INTELLECTUAL PROPERTY APPELLATE BOARD, CHENNAI

M.P. Nos. 1 to 5/2007 in TA/1 to 5/2007/PT/CH and M.P. No. 33/2008 IN TA/1/2007/PT/CH and TA/1 to 5/2007/ PT/CH

Decided On: 26.06.2009

Appellants: **Novartis AG represented by its Power of Attorney holder Ms. Ranjna Mehta Dutt**
Vs.
Respondent: **Union of India (UOI) through the Secretary, Department of Industry, Ministry of Industry and Commerce and Ors.**

Hon'ble Judges/Coram:
Z.S. Negi Chairman and P.C. Chakraborti, Member (T)

Counsels:
For Appellant/Petitioner/Plaintiff: Shanti Bhushan, Sr. Adv.

For Respondents/Defendant: M. Ravindran, Addl. Solicitor General for R 1, 2 and 8 in TA/1 TO 5/2007/PT/CH, Anand Grover, Adv. for Respondent 3 in TA/1/2007/PT/CH, Sanjeev K. Tiwari and H. Rajeshwari, Advs. for Respondent No. 3 in TA/2/2007/PT/CH, S. Majumdar and S. Ramesh Kumar, Advs. for Respondent No. 3 in TA/3/2007/PT/CH, V. Lakshmi Kumaran and Parthasarathy, Advs. for Respondent No. 3 in TA/4/2007/PT/CH and V. Lakshmi Kumaran and Parthasarathy, Advs. for Respondent No. 3 in TA/5/2007/PT/CH

Subject: Intellectual Property Rights

Acts/Rules/Orders:
Patents Act, 1970 - Sections 2, 2(1), 3, 4, 8, 8A, 8(2), 10, 10(4), 24A, 25(1), 29 to 34, 59, 84, 92, 103, 115, 117B, 117G, 133 and 135; Patents (Amendment) Act, 2005; Patents Rules, 2003 - Rules 54(4) and 55; Patents (Amendment) Rules, 2006; Patents (Amendment) Act, 1999; Evidence Act, 1872 - Sections 1 and 45; Indian Patents and Designs Act, 1911 - Section 2(8); General Clauses Act, 1897 - Section 6; Patents (Amendment) Act, 2002; Trade Marks Act, 1999 - Section 92(1), 92(2); Intellectual Property Appellate Board (Procedure) Rules, 2003 - Rules 8(2), 12 and 26; Code of Civil Procedure (CPC) - Order 1, Rule 27; Constitution of India - Article 226

Cases Referred:
F. H & B Corporation v. Unichem Laboratories AIR 1969 BOM 225; Bayer AG (Baatz's) Appln 1982, RPC (12) 321; Apotex Inc. v. Sanofi - Synthelabo Canada Inc. 2008 SCC 61; Pfizer Canada Inc. v. The Minister of Health and Ratiopharm Inc 2006 FCA 214; E.I. Du Pont De Nemours & Co (Witsiepe's) Application 1982 FCR 303; I.G. FarbeinIndustrie A.G.'s Patents 1930 (Vol 47) RPC 289; Merrel Dow Pharmaceuticals Inc v. H.N. Norton & Co. Ltd. (1996) R P C 76; Schering Corporation v. Geneva Pharmaceutical 339 F 3d 1373; Bristol - Meyers Squibb Co v. Ben Venue Labs. Inc. 246 F-32 1368, 1378; Atlantic Works v. Brady 107 US (1883); Takeda Chemical Industries and anr. v. Alphapharrn Pty and Anr.; Eli Lilly & Co. v. Bd. Of Regents of Univ. of Wash. 334 F. 3d 1264, 1270; Pfizer, Inc. v. Apotex, Inc. 480 F.3d 1348, 1371 (Fed. Cir. 2007); Synthon B.V. v. Smithkline Beecham (2006) 1 Reports 685 : (2005) UKHL 59; Brooks v. Steel & Currie (1897) 14 RPC 46; Agouron Pharmaceuticals Inc. v. Controller of Patents AID No. 2 of 2001; Quantel v. Spaceward 1990 RPC 83; Van der Lely N.V. v. Bamfords [1963] RPC 61 ; Bugges Insecticide v. Herbon [1972] RPC 197; General Tire Rubber Co. v. Fire Stone Tyre and Rubber Co. Ltd. [1972] RPC 457; Martin & Biro Swan v. H. Millwood [1956] RPC 125; Smithkline Beecham Corporation v. Apotex 403 F.3d 1331(2005); Novartis AG v. Union of India and Ors. (2007) 4 MLJ 1153

Supreme Court Status:
Judgment challenged *vide* MANU/SC/0281/2013 dated: 01.04.2013

Citing Reference:

Discussed	17
Distinguished	3
Mentioned	11

Case Note:
Intellectual Property Rights - Patent - Pre-grant oppositions — Priority date - Section 25(1), 133 of

Patent Act, 1970 - Appellant filed an application for patent for an invention titled "Crystal Modification of a N-phenyl-2-pyrimidineamine derivative, processes for its manufacture and its use" - Assistant Controller of Patents and Designs refused to proceed with the application for patent on the grounds of non patentability, non obviousness, novelty, anticipated by prior provision, selection patent and Section 3(d) - Hence, present appeal - Whether issue of priority could be taken as ground for rejection of a patent application in pre-grant opposition since it was not covered under Section 25(1) - Appellant contented that when the application is examined and patentability is considered under the patent law as amended to provide the provision of product patents in the amended patent law, the provision of priority date would also have to be considered on the same law as amended which is in force from 1st January, 2005 - Held, issue of convention priority is one of the grounds of that opposition and could, therefore, be a ground for rejection of a patent also - Law debarred the examination of all 'mail box' applications including the one of the impugned application of the Appellant filed before 1st January, 2005 - When the examination report on patentability is based on the amended patent law effective from 1st January, 2005, then convention priority date would not have to be decided according to the old or unamended law - Appellant fully justified and entitled to get the convention priority date, 18th July, 1997 under the amended Section 133 of the Act - Appeal disposed of

Intellectual Property Rights - Patent - Pre-grant opposition — Novelty/Anticipation - Inherent anticipation - Assistant Controller of Patents and Designs alleged that invention was anticipated — Whether Appellant's invention was anticipated and lacked novelty — Whether there was inherent anticipation of Appellants patent - Held, if the invention is anticipated it shall be held not to be novel - As per judicial pronouncements to establish anticipation based on what was known before the priority date of the claim it must be shown that in some prior publication there is information about the alleged invention equal to the purposes of practical utility to that given in suit — Information given in the prior document must be sufficient to enable the instructed reader at once to perceive and understand and be able practically to apply the discovery without the necessity of making further experiments - In the present case, a person skilled in the art cannot predict the polymorphism and prepare the subject compound from the available disclosure - Therefore, it is not right to take prior publications for consideration and cannot be held that documents anticipate the Appellant's subject compound - Hence, a case of anticipation against the Appellant's impugned application is not made out - With regard to inherent anticipation it was held that inherent anticipation fails when there are possibilities of formation of multiple forms - In the present case, existence of multiple polymorphs was not known before the priority date of the impugned application - When there are existence of multiple polymorphic forms of imatinib mesylate, question of the burden of disproving the inherency by the Appellate does not arise - Appeal disposed of

Intellectual Property Rights - Patent - Pre-grant opposition — Inventive step/Non-obviousness - Respondents alleged that Appellant's alleged invention is obvious for the reason of prior publication - Appellant has contradicted the same and advanced twofold inventive steps formula as well as selection patent argument for the purpose - Held, as per Section 2(1)(ja) inventive step means a feature of an invention that involves technical advance as compared to the existing knowledge or having economic significance or both and that makes the invention not obvious to a person skilled in the art — In the present case, Appellant has made a technical advance as compared to the existing knowledge by way of demonstration of polymorphism, isolation, characterisation of beta (and alpha) crystal forms of imatinib mesylate, identifying suitable properties in the beta crystal form usable in the making of oral solid drug formulation for curing cancer - Hence, the argument that imatinib mesylate always exists in crystal form now named as beta form and that impugned invention lacks inventive step cannot be accepted — Appeal disposed of

Intellectual Property Rights - Patent - Pre-grant opposition — Selection patent - Appellant has projected that it is entitled to a patent protection as a selection patent by way of an inventive selection as a surprising discovery of a crystal form named as beta crystal form under certain conditions in the mesylate salt of imatinib - Held, in case of selection patent, the essence of the inventive step, is to be defined in clear terms the nature of the characteristics which he alleges to be possessed by the selection for which he claims a monopoly - In chemical patents the concept of "selection patent" where the inventive step is demonstrated by way of an inventive selection of even a new, unexpected or unpredictable single member having surprisingly advantageous properties previously not known from a known series of a family disclosed in the art can be accepted - In the present case, Appellant after a painstaking research has identified this particular salt imatinib mesylate and within it, it has surprisingly found a crystalline form named as beta form which is also surprisingly discovered to possess, very advantageous properties as disclosed in the specification - crystalline form (the beta form) is not known or disclosed or published anywhere though the use of salt imatinib mesylate was known before - Isolation of this new form, its characterization by physico-chemical methods and particular utility as a cancer curing solid dosage

formulation with good storage capacities and advantageous properties are all surprising, unexpected or unpredictable and can not be termed as mere verification - Beta crystalline form is a new form of imatinib mesylate only as a substance, so covered by the originating patent, the 1993 patent - Thus, Appellant's impugned application satisfies all the minimum requirements or conditions for determining a case of selection patent — Appeal disposed of

Intellectual Property Rights - Patent - Pre-grant opposition — Inventions not patentable - Section 3 (d) of the Patents Act, 1970 — Respondents contented that Appellant's alleged invention claims only a new form of a known substance without having any significant improvement of efficacy and therefore not patentable under Section 3(d) of the Act - Appellant contented that its invention of beta crystalline form of imatinib mesylate is not a mere discovery of a new form of a known substance but an invention with inventive steps involving human intervention and therefore satisfying the definition of invention and provisions of Section 3(d) do not apply - Held, for determining patentability of pharmaceutical substances mere meeting of novelty and inventive step (and industrial applicability) criteria does not entitle one to get a product patent - It has to satisfy the requirement of section 3(d) of the Act which says that a new salt forms, polymorphs etc. or derivatives of a known substance is not patentable unless this form demonstrates significant enhancement of properties with regard to efficacy - Efficiency means therapeutic efficacy - In the present case, eventhough Appellant's alleged invention consisting of claims for the product, beta crystalline form of imatinib mesylate, pharmaceutical composition containing the same and process for preparing beta crystalline form of imatinib mesylate is novel and possesses inventive step and is additionally satisfied by way of "inventive selection" as a selection patent they did not satisfy the requirement of section 3(d) - Imatinib mesylate as such and its beta form are therapeutically same substances and also beta form of imatinib mesylate and imatinib are same substances with regard to efficacy — Appellant has failed on account of efficacy requirement for its beta crystalline form of imatinib mesylate under Section 3(d) of the Act - Hence, by not satisfying Section 3(d) of the Act would mean that a claim for beta crystalline form of imatinib mesylate and a pharmaceutical composition containing the same as products are not patentable under Section 3(e) of the Act because these are all termed as same known substances - However, process for preparing the subject compound beta crystalline form of imatinib mesylate is not affected by the said provisions of Section 3(d) of the Act - Hence, a patent on the said process cannot be denied to the Appellant — Appeal disposed of

Ratio Decidendi:

"Issue of convention priority is one of the grounds of patent opposition and could, therefore, be a ground for rejection of a patent also." "Inherent anticipation fails when there are possibilities of formation of multiple forms."

"In chemical patents the concept of "selection patent" where the inventive step is demonstrated by way of an inventive selection of even a new, unexpected or unpredictable single member having surprisingly advantageous properties previously not known from a known series of a family disclosed in the art can be accepted."

"For determining patentability of pharmaceutical substances, mere meeting of novelty and inventive step and industrial applicability criteria does not entitle one to get a product patent."

ORDER

P.C. Chakraborti, Member (T)

1. By this order we dispose of five appeal Nos. TA/1 to 5/2007/PT/CH and miscellaneous petition Nos. 1 to 5/2007 in TA/1 to 5/2007/PT/CH filed by the appellant seeking stay of operation of the impugned orders and miscellaneous petition No. 33/2008 in TA/1/2007/PT/CH filed by the respondent No. 3. This common order is being passed because the above five appeals are preferred by a single Appellant against the five almost identical orders passed by the Assistant Controller of Patents and Designs deciding five pre-grant oppositions to the grant of a patent to the Appellant and in all the five appeals the issues are almost identical and the appeals were heard together.

2. **BACKGROUND**

The Appellant, a Swiss pharmaceutical company engaged in the manufacture and sale of pharmaceutical and medicinal products including anti-cancer drugs, filed an application for patent on 17.7.1998 claiming Switzerland priority date of 18.7.1997 for an invention titled "Crystal Modification of a N- Phenyl-2-Pyrimidineamine derivative, processes for its manufacture and its use" and the same was allotted the application No. 1602/MAS/1998. Thereupon M/s Cancer Patients Aid Association, India, M/s Natco Pharma Limited, M/s Cipla Limited, M/s Ranbaxy Laboratories Limited, India and M/s Hetro Drugs Limited, India (hereinafter referred to as R 3, R 4, R 5, R 6 and R 7, respectively) filed representations by way of

oppositions under Section 25(1) of the Patents Act, 1970 as amended by the Patents (Amendment) Act, 2005 (hereinafter referred to as the Act) with request for hearing under Rule 55 of the Patents Rules, 2003 as amended by the Patents (Amendment) Rules, 2006 (hereinafter referred to as the Rules) After hearing on different dates, the Assistant Controller of Patents and Designs (hereinafter referred to as R 8) passed five orders, all dated 25.01.2006, refusing to proceed with the application for patent for the reasons specified in the respective orders. Aggrieved by the aforesaid orders, the Appellant herein filed Writ Petitions Nos. 24754 to 24758 of 2006 before the High Court of Madras and the High Court by its order dated 23.2.2007 converted the said writ petitions into appeals. During the pendency of the writ petitions, the Central Government brought into force the provisions relating to appeals to the Intellectual Property Appellate Board under the Act from the 2nd day of April, 2007. The Central Government appointed the then Controller General of Patents, Designs and Trade Marks as Technical Member (Patents) in the Intellectual Property Appellate Board and he assumed the charge of said post on 2.4.2007 and the Central Government by notification S.O. 514 (E) dated 3.4.2007 appointed, under Section 117G of the Act 1970, the 2nd day of April, 2007 as the date on which all cases of appeals against any order or decision of the Controller and all cases pertaining to revocation of patent other than on a counter-claim in a suit for infringement and rectification of register pending before any High Court, shall stand transferred to the Appellate Board. As a consequence to the said notification, Section 117G of the Act became operational and pursuant thereto the Madras High Court by order dated 4.4.2007 transferred the said writ petitions to this Appellate Board and the same were re-numbered as TA/1 to 5/2007/PT/CH. Since the Technical Member (Patents) has held the post of Controller General, immediately before his appointment as such Member, the Appellant filed M.P. Nos. 6 to 10/2007 praying amongst others that the Technical Member (Patents) be directed to cease acting as Technical Member to hear the appeals. The matter was heard and by order dated July 20, 2007, this Appellate Board dismissed the said miscellaneous petitions relying on the doctrine of necessity and ordered that the appeals shall be heard by the same Bench i.e. constituting the Chairman and the Technical Member (Shri S. Chandrasekaran). Aggrieved by the said order, the Appellant filed a Writ Petition under Article 226 of the Constitution before the Hon'ble High Court of Madras seeking for quashing the said order and to direct the Intellectual Property Appellate Board (IPAB) to stop the Technical Member (Patents) from acting as such to hear the said appeals and to direct the Central Government to appoint another Technical Member (Patents) in lieu of the existing Technical Member (Patents). The High Court of Madras by order dated November 13, 2007 directed the IPAB to constitute special Bench consisting of the Chairman and the Vice-Chairman to hear the appeals. The said Bench would be open for seeking assistance of a Scientific Adviser under Section 115 of the Act 1970 if they thought fit. Aggrieved by the order of the Madras High Court, R 4 filed a SLP before the Hon'ble Supreme Court of India for a direction for the appointment of a new Technical Member in the IPAB to hear the instant pending appeals because of the involvement of high technology in the matter and also for statutory requirement under the Act for the presence of a Technical Member in the Board having a specified qualification. Vide their Order dated October 1, 2008 in Civil Appeal Nos. 6004-6019 of 2008 [arising out of SLP (C) No. 1323-1337/2008] the Hon'ble Supreme Court directed that IPAB duly reconstituted under their orders, which would include Dr. P.C. Chakraborti, Deputy Controller of Patents and Designs, as a Technical Member, would hear and decide the said pending appeals with hearing starting from November 3, 2008 onwards on a day to day basis. The Appellant and the Respondents were heard by the Appellate Board having Dr. P.C. Chakraborti as the Technical Member with effect from November 3, 2008 as per the orders of the Supreme Court. However, there were some intermittent adjournments at the requests, convenience and mutual agreement of all the parties concerned. Initially, two weeks' time was granted to the parties to prepare the paper book as requested by the parties concerned to get the documents transferred from the High Court of Madras. Actual hearing started on November 17th and continued on November 18 to 21, 24 to 26, December 3, 4, 10, 11, 2008 and finally concluded on December 24, 2008. The Appellant and the Respondents were given full opportunity to present their respective cases orally and liberty was given to submit written arguments and counter-arguments which they availed.

3 **Appellant's patent application**

The Appellant's patent application No. 1602/MAS/1998 as referred to in the above para 2 relates to a particular crystal form of methanesulfonic acid addition salt of 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-(4-pyridin- 3-yl) pyrimidin-2-ylamino) phenyl] benzamide, processes for the preparation, pharmaceutical compositions containing the said crystal form and their use in diagnostic methods. In the patent specification the Appellant discloses that it had surprisingly found a crystal form which is described as beta form under certain conditions be found in the methanesulfonate salt of the said compound to have very advantageous properties.

As a background to the invention it states that the preparation of the said compound (for the sake of convenience hereinafter referred to as "imatinib" as the compound is known), and use thereof, especially as an anti-tumour agent, were described in Example 21 of EP - A - 0564409 published on 6th October, 1993 and in equivalent applications in numerous other countries. Imatinib was exemplified in these publications only in free form (not as a salt). The said specification discusses the physical properties such as X-ray diffraction characteristics, hygroscopicity, flow properties (processibillity) melting points, crystal shapes and relative thermodynamic stability of two different forms viz. alpha-form and the beta-form of the said methanesulfonic acid addition salt of imatinib (hereinafter referred to as imatinib mesylate as the salt is known). The specification also discloses the processes for the preparation of both the alpha and beta forms of imatinib

mesylate. It further discloses the different pharmacological properties of imatinib mesylate preferably used in the beta crystal form. It is stated that beta crystal form of imatinib mesylate is non-needle shaped, having better flow properties, thus better processible, less hygroscopic and more theremodynamically stable, thus better storable than its needle shaped, alpha crystal form, characterized by their differences in the melting points and the X-ray diffraction diagrams. Because of the advantageous properties, beta-crystal form is superior to the alpha form with respect to the manufacture of pharmaceutical preparations in solid dosages. Different disease curing/preventing properties of preferably beta crystal form of imatinib mesylate have also been disclosed. However, it is also mentioned that inhibitory and pharmacological effects of imatinib mesylate preferably in the beta crystal form are also found with the free base imatinib.

The specification also mentions antiproliferative, especially anti tumour activity of imatinib mesylate in vivo, described for the treatment of abl - dependent tumours in Nature Med. 2, 561 - 6 (1996).

The examples give different processes for the preparation for the beta crystal form and also the starting alfa-crystal from and the processes for the preparation of tablets and capsules containing beta crystal form of imatinib mesylate as the active substance.

The claims contained in the application are reproduced as under:

1. A form of the methanesulfonic acid addition salt of a compound of formula 1, comprising crystals of the ß-modification

(Editor: The text of the vernacular matter has not been reproduced. Please write to contact@manupatra.com if the vernacular matter is required.)

2. A crystalline form of the methanesulfonic acid addition salt of a compound of formula 1 according to claim 1, which remains dry at 93% relative humidity and 25°C.

3. A crystalline form of the methanesulfonic acid addition salt of a compound of formula 1 according to claim 1 and 2 in essentially pure form.

4. The ß-crystal form of the methanesulfonic acid addition salt of a compound of formula 1 according to claim 1, which has a melting point below 225°C.

5. The ß-crystal form of the methanesulfonic acid addition salt of a compound of formula 1 according to claim 1, which has a melting point of less than 217°C, defined as the start of melting in the differential scanning calorimetry thermogram.

6. The ß-crystal form of the methanesulfonic acid addition salt of a compound of formula 1 according to claim 1, which shows on X-ray diffraction a peak at an angle of refraction 2theta of 20°, said peak having a relative line intensity of 65, i.e. the peak marked (5) in Fig. 2/3.

7. The ß-crystal form of the methanesulfonic acid addition salt of a compound of formula 1 according to claim 1, which shows in a X-ray diffraction diagram lines having a relative line intensity of 20 or more at the following angles of refraction 2theta (relative line intensities given in parentheses): 9.7° (40), 13.9°(26), 14.7° (23), 17.5° (57), 18.2° (90), 20.0° (65), 20.6° (76), 21.1° (100), 22.1°(89),22.7° (38),23.8° (44), 29.8° (23) and 30.8° (20) essentially as in Fig. 2/3.

8. The ß-crystal form of the methanesulfonic acid addition salt of a compound of formula 1 according to claim 1, which has a melting point of 217°C, defined as the start of melting in the differential scanning calorimetry diagram, and which shows an X-ray diffraction diagram essentially as in Fig. 2/3.

9. The ß-crystal form of the methanesulfonic acid addition salt of a compound of formula 1 according to any one of the claims 3 to 8, which is present in essentially pure form.

10. The form of the methanesulfonic acid addition salt of a compound of formula 1 according to any one of the claims 1 to 9 for use in a process for diagnostic or therapeutic treatment of the human or animal body.

11. A pharmaceutical composition, comprising a form of the methanesulfonic acid addition salt of a compound of formula 1 according to any one of the claims 1 to 9, and a carrier.

12. Use of a form of the methanesulfonic acid addition salt of a compound of formula 1 according to any one of the claims 1 to 9, for the preparation of a pharmacological agent for the treatment of a tumour disease

13. Processes for the preparation of the ß-crystal form of the methanesulfonic acid addition salt of a compound of formula 1 according to claim 1, characterized by

a) digesting another crystal form or an amorphous starting material of the

methanesulfonic acid addition salt of a compound of formula 1 with a suitable polar solvent in suspension at a temperature between 20 and 50°C, or.

b) dissolving another crystal form or an amorphous staring material of the methanesulfonic acid addition salt of a compound or formula 1 in a polar solvent at a suitable temperature of 25°C up to the reflux temperature of the reaction mixture, and then initiating crystallisation by adding a small amount of the ß-crystal form as seed crystal at a temperature between 20 and 70°C.

14. A form of the methanesulfonic acid addition salt of a compound, substantially as described, with reference to the accompanying drawings.

15. A pharmaceutical composition, substantially as herein described, with reference to the accompanying drawings.

16. Use of a form of the methanesulfonic acid addition salt of a compound, substantially as herein described, with reference to the accompanying drawings.

17. Processes for the preparation of the ß-crystal form of the methanesulfonic acid addition salt of a compound, substantially as herein described, with reference to the accompanying drawings.

The patent application of the Appellant was kept under "Mail Box" which meant that the application would not to be taken up for examination before 01.01.2005 under the law.

The Appellant had also filed an application for Exclusive Marketing right (EMR) No. EMR/01/2002 dated 27.03.2002 corresponding to the above patent application No. 1602/MAS/1998 before the Patent Office and the EMR, was granted on 10.11.2003

The Appellant's above patent application was also examined and the first examination report dated 17th March, 2005 contained the following objections:

1. Novelty of this invention is anticipated by prior publication refer US 5521184 & AU3569493.

2. Subject matter of claims does not constitute an invention under Section 2(1)(j) of the Patents Act, as it lacks inventive step, see for instance, EP-A-0564409.

3. Claim 13 define a plurality of distinct inventions.

4. Claims 11 & 15 fall within the scope of Sub-clause (e) of Section 3 of the Patents Act, 1970.

5. The question of unity of the invention will be considered after the specification has been amended to avoid the objections pointed out above.

6. Claims do not sufficiently define the invention.

7. Claim 17 is not sufficiently definitive in the absence of explicit statement of invention.

8. Claim 13 is not clearly worded.

9. Title is not precise.

10. The question of novelty will be considered after the objections above have been complied with.

11. Since 'Switzerland' was not a convention country on the date of filing this application in India, conventional status cannot be allowed for this application. You may convert this application into an ordinary application by filing Form 13.

12 Application number shall be mentioned in Form 6.

13. You may furnish information relating to objections, particularly novelty and inventiveness of invention, of the applications filed in Brazil, South Korea, and USA within 3 months from the date of this letter as required under Section 8(2) of the Patents Act, 1970.

14. Pages of complete specification shall be serially numbered at the bottom of each page.

15. Blank space in complete specification shall be scored out.

16 Your request on Form 13 is allowed.

17. You are requested to quote Reference No. and Date of FER (this) letter for all future correspondence.

manupatra 4 **Pre-grant oppositions against the Appellant's patent application including the grounds taken in general**

The five pre-grant oppositions against the Appellant's above patent application were filed during May - July 2005 by the R 3 to R 7. The main grounds were:

1. Claims particularly 1 to 11: not an invention within the meaning of the Act or not patentable under Section 3(d) [ground under Section 25(1)(f)].

2. Claims particularly 1 to 10: lack novelty (prior publication or prior public knowledge) and inventive step and not patentable under Section 2(1)(j) and 2(1)(ja) [ground under Section 25(1)(b)-(e)].

3. Claim 11 : not an invention within the meaning of the Act and not patentable under Section 3(e) [(ground under Section 25(1)(f)].

4. Claim 12 : not an invention within the meaning of the Act and not patentable under Section 3(d) and 3(i) [ground under Section 25(1)(f)].

5. Claim 13: not patentable under Section 2(1)(j) [ground under Section 25(1)(b) to (e)].

6. Claim 14 - 17: omnibus claims not patentable for the reasons stated in para 1 to 5 above.

7. Application not made within 12 months from the date of protection made in the convention country [ground under Section 25(1)(i)].

8. The complete specification does not sufficiently and clearly describe the invention or the method by which it is to be performed [ground under Section 25(1)(g)] - [only raised by R 3].

9. Commercial exploitation of the invention that causes serious prejudice to human health - not patentable under Section 3(b) [ground under Section 25(1)(f) -- [only raised by R 3].

10. The claims are not definitive [only raised by R 5, R 6 and R 7].

5. **The findings of the R 8 in the impugned orders on the Pre-grant oppositions**

(i) The invention is anticipated by prior publications of US Patent No. 5521184 of 1993 (1993 Patent), "Nature Medicine" of May 1996 and the Patent term extension certificate for the 1993 patent issued by the USPTO which specifically mentions imatinib mesylate (Gleevec^{R}) as the product. Moreover, NATCO (R 4 herein) has satisfactorily proved that the salt normally exists in the beta form which is the most thermodynamically stable product.

(ii) The invention is obvious for the reasons of prior publication as above.

(iii) Not patentable under Section 3(d) of the Patents Act, 1970 as amended by the patents (Amendment) Act, 2005.

The patent application claims only a new form of a known substance without having any significant improvement of efficacy. Even the affidavit submitted on behalf of the applicant fails to prove enhanced efficacy of the beta isomer over the known substance.

(iv) Claiming wrong priority

Switzerland was not a convention country at the time of making the application.

R 8 refused to proceed with the application (1602/MAS/1998) in view of the above findings.

6. **The main grounds taken in the appeals (originally writ petitions)**

Section 3(d) of the Act:

R 8 had erred in concluding that the subject matter of the application was not patentable under Section 3(d) of the Act. Section 3(d) did not apply to the present case. The invention of beta crystalline form of imatinib mesylate was not a mere discovery of a new form of a known substance but an invention with inventive step involving human intervention. The subject compound was at two steps removed from the prior art i) the imatinib free base chemically changed into methanesulphonic acid salt form and ii) converting the salt to a particular crystal form of this salt, the beta crystal form. Since the subject compound fulfilled the criterion of being an "invention" because of human intervention and an informed/deliberate exercise to achieve an end result there was no occasion for R 8 to

apply provision of Section 3(d). Even assuming without admitting that the subject compound was a mere discovery of a new form of a known substance, it was still patentable, as it had resulted in the enhancement of known efficacy of the known substance i.e. imatinib free base, thereby making the subject compound more efficacious. R 8 ought to have appreciated the tests/clinical trials conducted by the applicant (Appellant) which showed 30% enhancement of bio-availability over the said known substance. In the field of pharmacology, any substance which had a variance of 20-25% bio-availability (either more or less) was not considered bio-equivalent with the other compound under comparison and therefore could not be termed "same substance". Absence of definition of efficacy and the constituents thereof and precedents from other jurisdictions, R 8 ought to have held 30% enhancement of bio-availability as a significant improvement with regard to efficacy. R 8 also had not cited any legal or factual reason/justification as to why 30% enhancement of bio-availability was not a significant improvement. R 8 also ignored the affidavit placed on record by the Applicant (Appellant). That apart, from having more bio-availability, the subject compound was far more suitable for the preparation and formation of drugs usable for the treatment of BCR-abl positive cancer and tumours such as leukaemias (especially chronic myeloid leukaemia) compared to the free base. This fact should have been taken into consideration while deciding on the efficacy of the subject compound. R 8 also failed to take all the materials/submissions of the Applicant(Appellant) into consideration and dispose of them specifically. In view of this, the orders were bad in law and against the principles of natural justice.

Anticipation/ not an invention:

The subject compound imatinib mesylate ought to have been considered to be novel on the date of filing of the present patent application as long as there was no specific and enabling disclosure in the prior Article

Reference of "Gleevec" in the extension certificate of Appellant for US Pat No. 5521184 of 1993 (Zimmerman Patent), which cited imatinib mesylate under trade mark "Gleevec" did not disclose more than what was disclosed in the Zimmerman patent for Imatinib free base. Specific disclosure of a drug in a patent was no pre-condition for the issuance of a patent term extension certificate by the USPTO. The certificate was inadmissible and did not contribute in clarifying the question whether the claimed subject was anticipated by prior Article There was no mention of beta crystalline form of imatinib mesylate in the extension certificate which remained novel and inventive and had not been disclosed in any patent, document or publication. The subject specification in the beginning itself cited the compound in the 1993 patent as did the granted patents for beta crystalline form of imatinib mesylate in other jurisdictions. 1993 patent disclosed imatinib and a list of suitable pharmaceutically acceptable salts including mesylate. There was no example disclosing the preparation of imatinib mesylate or mention of Imatinib mesylate at all. No procedure was described how to prepare the salt, what conditions to apply and what physical properties the obtained salt might have. Thus, the beta form of imatinib mesylate, the subject compound was novel over the 1993 patent. Consequently, both the 1993 patent and the patent for beta crystalline form of imatinib mesylate were subsisting on the Register in those jurisdictions without any conflict. There was a difference between disclosure and claim scope. A subject matter which was merely embraced by patent claimed, but not specifically disclosed in the prior art could still be validly claimed in a patent as a selection patent/invention. R 8 had erred in ignoring the contention of the Petitioner/(Appellant) that in absence of R 4 producing test results to prove that they had practised any claim/example of the 1993 patent to produce the subject compound, as was required by law, the challenge to the subject application on the ground of inherency or inevitability lost its base.

Further, R 8 was erroneous in placing reliance on reports submitted by IICT [Indian Institute of Chemical Technology (Hyderabad)] and IIT [Indian Institute of Technology, (Delhi)] and coming to the conclusion that R 4 had satisfactorily proved that the salt was inevitably obtained in the beta form which was the most thermodynamically stable product. Tests conducted by IICT and IIT could not be relied upon as the beta seed crystal was present in the starting material before various solvents were added to the free base suspension. If such seed crystals were present, formation for beta crystalline form would invariably follow. It was pertinent to point out that the tests showed that the end products were achieved by practising the methods described in the subject application and not through the prior art of the 1993 patent or otherwise. Further, citation of "Nature Medicine" paper by R 4 mentioned imatinib mesylate but did not disclose any procedure how to prepare imatinib mesylate. In other words, the said paper did not enable the manufacture of the mesylate. Therefore, this salt was novel and not anticipated by any of the cited documents. Further R 4 had failed to give any explanation to the contention of the Appellant that if the methane sulphonic acid addition salt when produced existed only "inherently" as a beta form and was naturally occurring stable form, then why and how had the Respondent R 4 had managed to obtain marketing approval for the alpha form from the Drug Controller General of India. The present claims were drawn to the beta crystal form of imatinib mesylate. As disclosed in the present specification, imatinib mesylate existed in alpha & beta crystal forms. The beta crystal form was thermodynamically more stable at room temperature. Once the beta crystal form was

invented, the isolation of the less stable alpha form required working under condition of highest purity. As soon as the seeds of the more stable beta crystal form were present, the alpha form could hardly be obtained. Before the stable beta form was invented by the Appellant in 1997, it was possible to obtain the salt in less stable (meta stable) form, such as the alpha form. If suitable purity, conditions were met, the alpha form could also be obtained today.

R 8 also failed to appreciate that other crystal forms of imatinib mesylate were described in WO 2004/106326 (published on 09.12.04) by R 7) of (so called H1 form and amorphous hydrate). That document showed that the crystalline form of imatinib mesylate that was obtained depended on the conditions chosen for the manufacture of the salt. Obtaining the beta crystal form was by no means inevitable as concluded by R 8. As distinct forms of imatinib mesylate existed including the alpha, alpha 2, beta and H1 forms, R 8 had erred in concluding that obtaining the beta crystal form was inevitable, when the impugned patent specification itself disclosed two distinct forms, the alpha and beta forms. It is a settled proposition of law that any information as to the alleged invention given by any prior publication must be for the purpose of practical utility, equal to that given by the subsequent patent. The latter invention must be described in the earlier publication that was held to anticipate it in order to sustain the defence of anticipation. It was not enough to prove that an apparatus described in an earlier specification could have been used to produce this or that result. It must also be shown that the specifications contained clear and unmistakable directions so as to use it. It must be shown that the public had been so presented with the invention that it was out of the power of any subsequent person to claim the invention as his own.

With regard to sufficiency of knowledge, the courts held that the earlier publication must give the requisite knowledge clearly, and it was not enough that it merely gave the means of attaining such knowledge. It must give sufficient information to a worksman skilled in the particular art or craft in order to enable him to carry out the invention. The courts had gone to the extent of observing that even when the prior document and the subsequent specification were identical or nearly identical in language, it did not necessarily follow that the court must conclude that the first was an anticipation of the second.

Further, R 8 had erred in ignoring the contention of the petitioner (Appellant) that the present case did come within the definition of an "invention" in as much as the claimed compound was novel, involved an inventive step and was capable of industrial application. In view of the above provision of Section 2(1)(j) of the Patents Act, 1970 was fully applicable to the present case.

Obviousness:

> R 8 also failed to take into consideration of the fact that one could never predict that a specific beta crystal form existed. Specifically, there was no general teaching or suggestion in the prior art that would have allowed one to predict how to make the beta crystal form which could be achieved only by human intervention and ingenuity. As mentioned earlier, imatinib mesylate existed in several forms including the alpha, alpha 2, beta and H1 form. No teaching or suggestion existed in any prior art document to identify and to anticipate the favourable properties or characteristics of the beta crystal form of imatinib mesylate prior to its being invented. Furthermore, when averring that the beta crystal form was inherently formed upon working the 1993 patent, R 8 had confused the concepts of novelty and obviousness. Inherent formation of the beta crystal form might be an argument against novelty but not against an inventive step. It was submitted that the 1993 patent only disclosed the free base imatinib and did not disclose any salt thereof. Further, R 8 ought to have appreciated the contention of the Petitioner (Appellant) that the free base compound in the 1993 patent did not and could not exhibit polymorphism to yield the beta crystal form. Human intervention had to be present in order to produce the subject compound, imatinib mesylate, let alone the beta crystal form.

Priority

R 8 also erred in rejecting the application on the ground that the subject application wrongly claimed priority. The issue of priority could not be taken as a ground for rejection of an application in pre-grant opposition since it was not covered by Section 25(1) of the Act. R 8 ought to have appreciated the contention of the Petitioner (Appellant) that priority date was a legal fiction designed to let the applicant claim a date from the basic/first filed application in a convention country so as to avoid anticipation by publication of the invention between the priority date and the filing date in India. In the present case, the novelty of present invention remained intact since there had been no prior publication anywhere in the world and the Swiss application was not published until 2003 i.e. until the patent was granted in that country.

Other grounds

> (i) R 8 ought to have exercised his powers under Section 77(i)(a) of the Act for cross-examining the concerned personnel of IICT and IIT, especially when the said reports/ tests were controverted by the Applicant (Appellant) in cogent terms.

(ii) R 8 on the principle of comity failed to give due weight to the fact that in 35 countries with strict and advanced regulatory regimes, patent had been granted for the subject compound.

(iii) R 8 erred in ignoring the contention of the Applicant (Appellant) that no other manufacturer, including R 4 could make the subject compound from the 1993 patent and the other companies had to wait for the commercial embodiment of the Petitioner's (Appellant's) product in 2002, sold under the trade mark GLIVEC/GLEEVEC before they could launch their products in the market in 2003. In view of the above, R 8 was erroneous in rejecting subject application on the basis of anticipation and/or obviousness.

(iv) Amendments in the Indian Patent Law relating to product patent were contrary to what had been envisaged in 1995 when filing of "black box" application commenced. It was legitimately expected that the provisions of TRIPS would be implemented in their letter and spirit and uniform patent regime would be established also in India. However, there had been an uneven playing field wherein Indian applicants could file patent applications (and enforce patents) for subject matter which was presently forbidden in India or was subject to conditions outside of Article 27 of TRIPS. The Petitioner's (Appellant's) subject application and indeed all other black box applications carried great economic worth and were vital to sustain the research and development in the industry so that innovative drugs could continue to be invented.

(v) R 8 failed to take all the materials/submissions of the Applicant (Appellant) into consideration and disposed of them specifically. In view of this the orders were bad in law and against the principles of natural justice.

7. **Arguments/counter arguments at the hearing**

The Learned Counsel for the Appellant and the Respondents advanced lengthy arguments at the hearing taking us to various documents/case decisions/technical literature from the huge volumes of records submitted and relied on by the parties pertaining to the case followed by written submissions, Appellant's replies thereto, supplementary arguments on behalf of R 4, R 6 and R 7 and supplementary replies thereto by the Appellant to the said arguments of R 4, R 6 and R 7.

Gists of all these arguments are given in the following sub-paragraphs:

(1) Arguments of the Appellant:

Shri Shanti Bhushan, learned senior counsel appearing on behalf of the Appellant initiated his argument at the hearing with the background of the appeals, which are directed against the impugned orders of R 8 on the pre-grant oppositions by the Respondents whereby the Appellant's impugned patent application No. 1602/MAS/1998 dated 17.07.1998 with Swiss convention priority of 18.07.1997 was rejected. Drawing our attention to the said patent application, he claimed that the Appellant, NOVARTIS AG, a world leader in making innovative drugs, had invented and filed the above patent application related to beta crystalline form of methanesulfonic acid addition salt of a base compound, 4-[4-methyl piperazin-1ylmethyl]-N-[4-methyl-3-(4-pyridin-3yl) pyrimidin-2-yl amino) phenyl] benzamide, known as imatinib, processes for its preparation pharmaceutical compositions containing the said crystalline form and their use in diagnostic methods or therapeutic treatment of warm-blooded animals, especially humans. The beta crystalline form of the methanesulfonic acid addition salt of imatinib or imatinib mesylate invented by the Appellant had specific cancer curing property. This drug was being marketed by the Appellant in several countries, including USA and European Union in the brand name of GLEEVEC/GLIVEC. It had been running a philanthropic programme known as Glivec International Patient Assistance Programme (GIPAP) in 83 countries including India since 2001 to provide the subject drug at no cost to patients meeting certain criteria. In fact the Appellant used to distribute 99% of this drug free of cost. He informed that patents had been secured on the drug in at least 35 different countries of the world including USA and European Union. He emphasized that if a patent was not granted on genuine inventions such as the one here by the Appellant, there would be no incentive for R & D or any investment particularly for invention of new drugs. He also informed that on an application by the Appellant before the Patent Office in India, after an exhaustive scrutiny and satisfying on all grounds Exclusive Marketing Rights were granted to it on the same drug on 10.11.2003 based on

the prevailing law, [Section 24A of the Patents Act, 1970 as amended by the The Patents (Amendment) Act, 1999]. The said certificate granted an exclusive right to sell or distribute the beta-crystalline form of imatinib mesylate and its dosage forms to the Appellant. This right is not available to the Appellant post January, 25, 2006, because of the rejection of the said Patent application. He said that the said orders of the R 8 were erroneous as stated in the appeals and claimed that under the Indian law, the Appellant was entitled to get a patent. He also brought to our attention the various provisions of the Indian Patent law before and after amendment vis-à-vis TRIPS Agreement and argued that the Appellant's invention satisfied the definition of invention under Section 2(1)(j) with novelty and inventive step [Section 2(1),(ja)] and industrial application; new invention under Section 2(1)(l) read with Sections 29-34 and was also not attracted by any of the provisions of Section 3 particularly, Section 3(d) Act, 1970. He also informed that corresponding patent application in US was initially not granted by the Examiner. The appellate authority then reviewed the matter and reversed the Examiner's decision. He also brought to our attention the different remarks in the decision of the said appellate authority. He stated that the same equally applied to India also as the patent laws post TRIPS in the different countries including India were almost the same. Referring to the impugned patent application Shri Shanti Bhushan stated that the said base compound, imatinib and the use thereof especially as an anti-tumour agent were described in Example 21 of EP - A-0-564 409 which was published on 6th October, 1993 (1993 patent) and equivalent applications in numerous other countries. This compound was exemplified in these publications only in free form (not as a salt). The invented beta crystalline form of the methanesulfonic acid addition salt of imatinib i.e. imatinib mesylate in the impugned application was surprisingly found to have very advantageous properties over the alpha form also disclosed in the specification. The alpha form was needle shaped, meta stable at room temperature and hygroscopic and not particularly well suited to pharmaceutical formulations as solid dosage forms because of its flow characteristics were unfavourable, whereas the beta crystalline form was not needle shaped, thermodynamically more stable at temperature below 140°C, less hygroscopic with better flow properties than that of the alpha crystal form thus beta form was having better storage properties and easier processability. The alpha and beta forms had the different melting points with marked differences in X-ray diffraction diagrams as given in the specification.

Referring to the comparison of hygroscopicity of the alpha crystal form and the beta crystal form of imatinib mesylate, in the application with the help of a Table in the specification he showed that at 93% relative humidity, the water content in the alpha crystal form was 40% while that in the beta crystal form was only 0.15%. This showed that beta crystal form of imatinib mesylate would remain less hygroscopic as compared to the alpha form.

With reference to the prior 1993 patent given in the specification as background of the invention he explained that this specification claimed different pyrimidine derivatives including imatinib and pharmaceutically acceptable salts thereof which had anti-cancer properties. It gave a list of different salt forming groups or radicals having basic or acidic properties to form the salts of the bases including of imatinib. In all these salts, the active ingredient was imatinib and therefore, all of them would have therapeutic effect on cancer. What 1993 patent disclosed was the possibility of making various salt forms of the imatinib free base which could run into hundreds. At that particular point of time, it could not have been concluded by any stretch of imagination that the particular beta crystalline form of imatinib mesylate would have advantageous properties which would be efficacious in the treatment of cancer. It was only after years of painstaking and expensive research that imatinib mesylate salt in a particular crystal form namely the beta crystalline form with special properties was discovered by the Appellant. Thus, the Appellant's invention was two steps improvement over the said 1993 patent as prior art, namely, i) preparation of imatinib mesylate from imatinib, and ii) preparation of the beta crystal form of imatinib mesylate from imatinib mesylate.

Challenging the refusal of the application under Section 3(d) of the Act, Shri Bhushan argued that the Appellant with human intervention and ingenuity in research had selected methanesulfonic acid addition salt of imatinib in a particular form, namely, the beta-crystalline form with advantageous properties from the host of different possible salts of imatinib which were not prepared before. The principle of selection patent was adopted by courts which also was found mentioned under Section 3(d) Act. He referred to, and read out some relevant paragraphs of an article by Julian Jeffs published in 1988 in the European Intellectual Property Review in relation to the principle of selection patent [E.I.P.R. 1988, 10 (10) 291-296]. Highlights of some of

the important passages of the article relied on by him are given below:

(i) "The concept of selection patent is that it is a patent granted for making an inventive selection from a field, that is, in general terms, already known. It is a concept that is of interest both to the scientist and to the lawyer, for much research lies in investigating selectively materials that scientists are already aware of in principle - for instance by selectively substituting known groups in known organic compounds and assessing the pharmaceutical or physical consequences of such a substitution; and such research (which can be painstaking, difficult and expensive) would be futile in economic terms, and therefore, not worth doing in a commercial laboratory, unless the lawyers can protect the fruits of it by securing the grant and enforcement of a valid patent."

(ii) "In the context of a selection patent, the inventive step will generally lie in making the discovery that what has been selected provides a genuine advantage over the generality from which it is selected, the advantage being one that could not be predicted."

(iii) " A mere selection among possible alternatives is not subject matter. A selection to be patentable must be a selection in order to secure some advantage or avoid some disadvantage. It must be an adaptation of means to ends impossible without exercise of the inventive faculty. It follows that in describing and ascertaining the nature of the invention consisting in the selection between possible alternatives the advantages to be gained, or the disadvantages to be avoided, ought to be referred to."

(iv) "In a sense it is still true to say that there is no prevision in chemistry. Any one of the millions of dyestuffs in question might be found to possess some unexpected and distinct properties, either of colour or fastness, or to have some other incidental advantage. There is no short cut to knowledge of this kind. A laborious and systematic investigation of a long series of combinations becomes necessary."

(v) "Three general propositions may be asserted, as true. First, selection patent to be valid must be based on some substantial advantage to be secured by the use of the selected members. (The phrase will be understood to include the case of a substantial disadvantage to be thereby avoided.) Secondly, the whole of the selected members must possess the advantage in question. Thirdly, the selection must be in respect of a quality of a special character which can fairly be said to be peculiar to the selected group."

(vi) "The conclusion arrived at is that in a selection patent, the inventive step lies in the selection for a useful property or characteristic adequately defined; and this is the proposition which has to be kept in mind in considering the application to amend and the petition for revocation."

He also argued that the principle of selection patent was followed in different countries including India and referred to the Bombay High Court Judgment, **F. H & B Corporation v. Unichem Laboratories** reported in AIR 1969 BOM 225 and read the extract from the same which is extracted below:

Even where an invention consists of the production of further members of a known series whose useful attributes have already been described or predicted, it may possess sufficient subject matter to support a valid patent provided the somewhat stringent conditions prescribed by Maugham. J., as he then was, in I.G. Farbenindustrie A.G.'s Patents (1930) 47 RPC 289 *as essential to the validity of a selection patent are satisfied, i.e. the patent must be based on some substantial advance to be gained from the use of the selected members of the known series or family of substances, the whole (or substantially the whole) of the selected members must possess this advantage, and this advantage must be peculiar (or substantially peculiar) to the selected group.*

He submitted, that the Appellant's application was a good case for selection patent as per the said article and the above judgment and other following judgments relied upon by the Appellant:

1982, RPC (12) 321 **Bayer AG (Baatz's) Appln**; 2008 SCC 61 **Apotex Inc. v. Sanofi - Synthelabo Canada Inc.**; 2006 FCA 214 **Pfizer Canada Inc. v. The Minister of Health and Ratiopharm Inc**; 1982 FCR 303 **E.I. Du Pont De Nemours & Co (Witsiepe's) Application**; 1930 (Vol 47) RPC 289 **I.G. FarbeinIndustrie A.G.'s Patents**.

With further reference to Section 3(d) he argued that the known substance for the purpose of Section 3(d) would have to be treated as imatinib free base which had in fact been prepared and tested in preclinical studies including tests demonstrating the inhibition of the growth of human bladder carcinoma cells in isolation and in mice as described in the 1993 patent. That patent merely suggested the possibility of its being converted into various kinds of salts, which had neither been prepared nor tested for their qualities.

If imatinib must be considered to be the known substance for the purpose of Section 3(d),then the beta crystalline form of a salt, namely, imatinib mesylate could not at all be treated as mere discovery of a new form of a known substance namely imatinib. He also brought our attention to the affidavit filed on behalf of the Appellant, by one Dr. Paul William Manley specifically to the following paragraphs:

> *8 The physical properties of the Free Base and imatinib mesylate differ in that the Free Base is only very slightly soluble in water (0.001g/100 ml) while imatinib mesylate is very soluble in water (beta crystalline form : 130 g/100 ml). Other physical characteristics of the subject compound are described at pages 2-3 of the specification. The attendant advantages because of these properties are also simultaneously described therein. These characteristics and hence the attendant properties/advantages are not shared by the Free Base. Furthermore, the beta form significantly differs from the alpha form.*
>
> Physical attributes:
>
> (a) The beta crystal form has substantially more beneficial flow properties and thus results in better processability than the alpha crystal form.
>
> (b) The beta-crystal form is the thermodynamically more stable at room temperature. Greater stability is thus expected.
>
> (c) The beta crystal form is less hygroscopic than the alpha-crystal form of the methanesulfonic acid addition salt of a compound of formula I.
>
> (d) The lower hygroscopicity is a further advantage for processing and storing the acid addition salt in the beta crystal form.

9. The preparation of the beta crystalline form of imatinib mesylate was not spontaneous and required human intervention. It is also well known that once a new stable crystalline was found, it may be impossible to again manufacture the less stable crystalline form due to the presence of seeds crystals of the more stable form. The method for preparing the beta crystalline form is described at page 7 of the description. It bears emphasizing that no other entity in the world was able to make the beta crystalline form of imatinib mesylate (and manufacture and market it as a commercial embodiment) prior to the launch of my company's beta crystalline form of imatinib mesylate under the brand name GLEEVEC/GLIVEC.

A salt such as imatinib mesylate differs significantly from the Free Base in properties with regard to efficacy.

> (a) The methanesulfonic acid addition salt is far more suitable for the preparation and formulation of drugs usable for the treatment of BCR-abl-positive cancer and tumour diseases such as leukaemias (especially chronic myeloid leukaemia and acute lympho-blastic leukaemia or GIST), compared to the Free Base.
>
> (b) Compared to the Free Base the methanesulfonic acid addition salt has higher solubility in general leading to a higher bio-availability and, an improved efficacy.

He also brought our attention to the affidavit of Dr. Massimini also sworn in on behalf of the Appellant particularly at paragraph 9 which reads thus:

> *9. A study conducted in rats provided statistical evidence for a difference in the relative bio-availability of the Free Base and Imatinib mesylate in the beta crystalline form. In such study, a mean AUC(0-48h)value of 264000 h*mg/ml was found for the Free Base compared with a mean AUC(0-48h) value of 344000 h*mg/ml for imatinib mesylate having the beta crystal form. In other words, an about 30% improvement of bio-availability was observed for the beta crystalline form of imatinib mesylate compared to the free Base.*

Referring further to that affidavit and copies of purportedly Novartis' findings of RAT PK Parameters (wiegand H. Pacard F. DMPK No. 500547, 2005) with relative bio-availability of free base and mesylate salt (ß-form) and imatinib; PK/PD Relationship in CML Patients (B.Peng et al. J. of Clin, Oncology (2004) Vol 22: 935 - 942); pharmacodynamic Parameters of Imatinib (Table 4 of B Peng et al. J. of Clin. Oncology (2004) Vol 22: 935-942) and footnotes therein (Appellant's compilation) p-305-307 (vol B), he argued that the said study conducted on rats highlighted 30% lower bio-availability for free base of imatinib than its mesylate salt meaning thereby that 400 mg dose, the recommended startup dose, would deliver only 70% of the total 400 mg dose strength (280 mg). This would certainly have significant clinical implication. It was well known that in a cancer drug, bio-availability was a very important feature of the drug because if in a particular form the bio-availability of the drug could be enhanced, it was possible to give lower doses of the drug which could not be equally effective so far as the disease to which the present patent application was concerned and yet the lower doses would reduce the adverse effects of that drug to a very significant extent. Thus, reducing the adverse effect by reducing the dose should be taken as enhanced efficacy. He also referred to a published

article "Blood" Vol. 99, Number 6, dated 15 March, 2002. That article showed that an increase in the dose of the drug, though imatinib was generally well tolerated induced an increase in the number of adverse events which could ultimately result in the discontinuation of the treatment. With reference to different text books he also argued that enhanced bio-availability led to enhanced efficacy. Since the beta crystalline form of imatinib was better bio-availabile as compared with the free base imatinib, the known substance, the subject compound in the present application would be more efficacious. He informed that the Appellant had filed Writ petition (No. 24759 and 24760) challenging the constitutional validity of amended Section 3(d) before the Madras High Court. He also referred to the decision dated 6th August, 2007, in that case by Hon'ble Mr. R. Balasubramanian J. and Mrs. Prabha Sridevan J. [Novartis A.G. and Anr. v. Union of India and Ors.] which upheld the validity of said Section 3(d) and further, the meaning of the term "efficacy" had been clarified as therapeutic effect or healing of disease (para 13). He argued that increased bio-availability, improved stability, non-hygroscopicity and better flow properties of the beta crystalline form of imatinib mesylate as compared to the imatinib base made the subject compound more effective or efficacious as a cancer curing drug. Thus, it satisfies the requirement of Section 3(d) fully.

Rebutting the R 8's rejection on the ground of lack of novelty and inventive step Shri Shanti Bhushan submitted that there was no prior art citation made by the examiner or the Respondents which could anticipate the Appellant's claims in the impugned application on the date of priority namely 18.07.1997, the date of filing the basic application in Switzerland for making the invention obvious. Only prior art was the disclosure in the 1993 patent (corresponding US Pat No. 5521184). The said 1993 patent disclosed inter-alia, imatinib as free base and possibility of making various salt forms of imatinib including imatinib mesylate. But no reference was there for any specific choice of salt as the cancer curing drug. The preparation of Imatinib mesylate let alone the beta form thereof was not disclosed in any prior art document. Without the disclosure of the specific preparation of imatinib mesylate the material was not readily available to a person skilled in the art, in particular in view of the fact that the free base could react with more than one unit of added acid to get di-or try - acidic salt. It was the Appellant's invention that selected the mesylate salt and also its discovery of different polymorphic forms namely the alpha and beta forms of imatinib mesylate, preparing and identifying the beta crystalline form having very advantageous properties which would be efficacious in the treatment of cancer. Such discovery could not have been possible by any stretch of imagination by any person skilled in the art on the date of priority thus fully satisfying the requirement of novelty and inventive step. He also referred in this connection to the International Preliminary Examination Report (IPER) under the PCT by EPO on the Appellant's patent application in EPO on the beta crystalline form of imatinib mesylate. Quoting the said IPER he argued that the Appellant's invention was also established as novel and having inventive step and industrial application. The Appellant's application under the PCT was substantially on the same invention as had been made in India. In the said IPER prior art taken was the US-A - 5521184 as D1 which was almost the same as the EP application No. EP-A-0-564409 referred to as the prior art given correspondingly, by the Appellant in its impugned application. The said IPER observed that there was no mention of any crystalline form of the monomethanesulfonic acid addition salt in the D 1. Thereby novelty of the claims had been acknowledged. Further, regarding the inventive step, the said Report stated "....The problem underlying the present application therefore appears to crystal form of the above mentioned salt disclosed in D1 possessing unexpected properties with respect to other forms of said salt (cf. description, P1 3rd paragraph). The applicant has shown that the ß-crystal form of said salt has a significantly lower hygroscopicity at high humidity levels (> 93%, see Table p 8) than the alpha crystal form of the same compound. Since the prior art D1 gives no indication of the existence of a particular crystalline salt with superior storage properties at high humidity levels an inventive step can be acknowledged for the crystalline form of the salt as claimed in claims 1-9, and compositions, uses and syntheses thereof (claims 10-12)". Shri Shanti Bhushan also referred to the decision of the USPTO Board of Patent Appeals and interferences in the USPTO which reversed the Examiner's order, deciding in favour of granting a patent to the inventor in the USA (mentioned supra) establishing novelty and inventive step.

On the question of establishment of the priority date of the Appellant's impugned application Shri Shanti Bhushan claimed that the Appellant was entitled to get the Swiss convention priority under Section 133 of the Act. If the application for the grant of patent had to be considered according to the law as it stood on 01.01.2005, when the law of product patent was applicable to India, the provision of priority date would also have to be considered on the position of law on or after 01.01.2005. He also referred to different case laws relied upon by the Appellant, copies of which were included in Vol. A, B & C of the Appellant as additional typed set of documents.

He finally requested for setting aside the impugned orders passed by the R 8 and for directing him to grant a patent on the impugned application to the Appellant.

(2) Counter-arguments on behalf of R 4

Shri Sanjeev Kumar Tiwari, learned Counsel for R 4 began his arguments with certain preliminary objections as given below:

(I) Appellant had introduced freshly

(i) Footnote to the bar chart (Rat PK PARAMETERS) PAGE 305 (Vol B) (of

Appellant's compilation)

(ii) chart/graph on p 306-307 (Vol. B) of Appellant's compilation in which footnote is incorporated.

(iii) Affidavits of Dr Bertrand Sutter and Prof. Christopher Frampton (page 389 & 364 respectively, Vol B).

(iv) IPER, (pp 59-65 Vol C), Appeal filed at the USPTO and the decision thereon by the USPTO (p 67-120, Vol. C of the Appellant's additional documents) and the Ld. Controller (R 8) could not be assailed on the basis of documents that were never before him. These documents being not part of the original records could not be considered in appeal unless made part of the appeal proceedings in a manner known to law. Additionally Dr. Sutter's affidavit was a part of a withdrawn suit No. 261/2004 filed by Novartis before the Hon'ble High Court of Bombay, also deemed withdrawn, without any interlocutory petition and leave of this Appellate Board, the same could not be considered and taken on record.

(II) Evidence of the Appellant (by way of affidavits) should be disregarded because,-

(a) these were affidavits of employees of the Appellant and not independent experts and were supposed to protect the interests of their employer (the Appellant herein) and therefore, could be biased, partisan and unreliable;

(b) contained false and misleading averments as Dr. Manley and Dr Massimini stated on oath that 1993 patent disclosed only the imatinib base and not the salt. This was a false deposition as the IPER relied on imatinib mesylate salt the prior art in the 1993 patent. The Appellant's argument relating to a selection patent was a categorical admission that salts of imatinib were disclosed in the 1993 patent; Disclosure in 1996 Nature Article (ref. in specification) also proved that salt was disclosed in the 1993 patent and the Novartis application before FDA (pg 12-23 of list of documents of Natco), named imatinib mesylate;

(c) the impugned patent application contained comparison of certain physical properties (not bio-availability) of the alpha crystal and beta crystal but there was no comparison between the free base and beta crystal on the claimed solubility; The impugned specification categorically stated that all the inhibitory and pharmacological effects of the free base could be found in the salt. In the teeth of such a statement, Dr. Massimini stated that the salt exhibited higher bio-availability, thus diluting his creditworthiness;

(d) Dr. Manley and Dr. Massimini as well as other affidavits also made deposition to the effect that the base was never tested before, while the 1993 patent clearly and categorically taught the use and correct dose to be administered. This showed that the base was actually tested and thus all the properties were known to the Appellant;

(e) Dr. Manley in his affidavit never deposed at all whether any independent study/experiment was carried out by him personally for the purpose of his expert opinion or whether he supervised such a study. Even for the results deposed no details of such experiments conducted in terms of the protocol followed, the instruments used, etc. Thus, the conclusion that could be drawn was that the deposition was without any experimental basis and was a mere camouflage. Further, there was no mention of beta crystal, Higher bio-availability was inferred only with regard to salt, not the beta crystal, an improved form of salt, as claimed by the Appellant;

(f) the affidavit of Dr. Massimini made averments in support of alleged bio-availability. However, the said deposition was based upon certain study conducted by some third person, certainly not by him. Though, the test results had been annexed as Annexure 'A' to the affidavit, details and protocols of such tests had not been disclosed;

(g) affidavit of Prof. Frampton was prepared after reading the impugned orders of R 8 rejecting the application. A perusal of para 10 thereof would make it clear that the said affidavit was drafted with mala-fide intention, nothing to do with the scientific aspect of the application and could not be said to be an expert evidence. The said affidavit in para 12 also made a deliberate departure from the other affidavits stating that though the 1993 patent disclosed the salt, did not disclose a method of how to prepare imatinib mesylate whereas the other deponents stated that the salt was not disclosed in the prior Article Appellant's projection of this case as a selection patent

deemed it to have admitted that imatinib mesylate was disclosed in the 1993 patent, otherwise, the Appellant could not have "selected" imatinib mesylate confirming that the said deposition of Prof. Frampton at para 12 is false. Further, from para 13 to 18 of this affidavit had commented about reports of IICT and IIT and speculated about possible seeding. But no concrete experiments/tests had been conducted nor any scientific reasoning given to dilute the said expert reports. In the experiments of IICT & IIT starting material taken was only the base. Accordingly, theory of possible seeding propounded was on the basis of mere assumptions and must be disregarded. Further, this affidavit was filed before this Appellate Board without any interlocutory application. Even otherwise, as per Rule 55(4) of the Rules, the Appellant was supposed to file his reply statement alongwith evidence and there was no provision for entertaining further evidence. Shri Tiwari also referred to the standards to which expert evidence should, conform, their duties and responsibilities etc. set out in the book of P. Narayanan on 'Patent Law', 4th Edition under "Evidence" (Chapter 18, paras 118 to 123). In the light of the above, these affidavits according to him were manipulated, tutored, misleading, speculative and also did not comply with the mandate of Section 45 of the Indian Evidence Act 1872.

On the subject of "Selection Patent" Shri Tiwari argued that doctrine of "selection patent" was evolved by foreign countries based on the provisions of law available with those countries but such provisions were not available in India or embodied under the Act 1970 and therefore, could not be imported into Indian law. Reliance on the High Court judgment AIR 1969 BOM 225 was ill-founded as the case was decided on old Indian patent law. The plea of selection patent was never placed before the Ld. Controller, never pleaded in the grounds of appeal and exposed for the first time during the oral arguments before this Appellate Board. He submitted that various judgments relied upon by the Appellant would show that a case of selection patent had to be asserted first in the specification and the patentee had to plead only as a case of selection patent. There was no such assertion, at all, in the Appellant's complete specification. He also referred to the Article by Julian Jeffs on selection patent which was also relied on by the Appellant on the drafting of specification in a case of selection patent in page 5 para 4 and 5 which read as follows:

> I must add a word on the subject of the drafting of the specification of such a patent. It should be obvious, after what I have said as to the essence of the inventive step, that it is necessary for the patentee to define in clear terms the nature of the characteristics which he alleges to be possessed by the selection for which he claims a monopoly. He has in truth disclosed no invention whatever if he merely says that the selected group possesses advantage. Apart altogether from the question of what is called sufficiency, he must disclose an invention; he fails to do this in the case of a selection for special characteristics, if he does not adequately define them. The cautions repeatedly expressed in the House of Lords as regards ambiguity, have, I think, special weight in relation to selection patent.
>
> I will summarize the conclusions at which I have arrived by saying that in a selection patent the inventive step lies in the selection for a useful and special property or characteristic adequately defined; and this is the proposition which has to be kept in mind in considering the application to amend the petition for revocation.

He also referred to the decision of the Justice Maugham in the matter of IG Farbenindustrie AG's patents (line 29 to 39, p92 of the compilation of judgments filed by the Appellant) and para 11 of Pfizer Canada Inc. v. The Minister of Health: 2006 FCA 214(page 3) also relied on by the Appellant and argued that according to those authorities, the patentee must define in clear term the specific characteristic properties which he alleged to be the basis for the selection for which he could claim a monopoly. In case of selection patent inventive step lay in the finding that an already disclosed product or process possessed advantageous properties/characteristics. The specification of impugned patent application totally lacked any details on this count. Referring to the grant of patents in 35 different countries including USA and EPO, he stated that the Appellant had relied upon some orders passed in the proceedings in other countries in relation to grant of the impugned invention as well as the report of the examiner. None of the said applications/proceedings/judgments/examiner's report showed that the application was allowed as an application for selection patent. Further, the Appellant never pleaded a case of selection patent for its impugned application before the Ld. Controller(R 8). Rather, it had urgued that its invention involved two inventive steps- preparation of imatinib mesylate salt and preparation of beta crystal form of the salt from imatinib mesylate. Accordingly, in the absence of proper pleadings in the opposition reply, appeal, memo, etc. the Appellant at this stage during oral arguments could not plead/urge a case of selection patent. He added that even if the Appellant had made out a case of selection patent, even then, it had to be filtered through various tests as laid down under the Act including that of novelty, obviousness, anticipation and Section 3.

Ms. Rajeswari, learned Counsel also appearing on behalf of R 4 in her argument gave a general information about Gleevec and flow chart about drug discovery as an introduction. She submitted that grant of patents in 35 other countries had no persuasive value for the grant of patent in India as the patents granted there were as per the provisions of law in those respective countries. The present application was not patentable in India as the same was also attracted by an unique provision of Section 3(d) in the Indian patent law. The claims,

particularly claim 1, preferred before the other countries were also significantly different than that before the Indian Patent Office. Further, it was not the case of the Appellant that the patents granted by these countries were as selection patent. Here, the Appellant had exposed its case only on the basis of selection patent.

She further argued that the Appellant while relying on the IPER had admitted that salt was present in the 1993 patent. The said report further stated that isolation of the crystalline form of salt could not be regarded as inventive since it fell within customery practice. Thus, the beta crystal was a new form of the known substance - the imatinib mesylate salt. There was no disclosure in the impugned specification of any enhanced efficacy of the beta crystalline form of imatinib mesylate over the known substance imatinib mesylate thus attracting the provision of Section 3(d) of the Act. However, an attempt was made by the Appellant to create an impression that the efficacy to be shown was vis-à-vis imatinib base, which it contended as the known substance. Still, the Appellant's claim could not stand the test of Section 3(d) - the enhanced efficacy by way of 30% enhanced bio-availability, thermodynamic stability and less hygroscopicity as no comparative data on that count was provided in the specification between the beta crystal and the base. In fact, the specification was totally silent about the aspect of bio-availability of beta crystal per se, much less any comparative data. Material, if any, on record was to the contrary that the base and the salt in beta form had the same efficacy. Even the stated 30% enhanced bio-availability for the beta crystalline form of imatinib mesylate over the base imatinib known by the affidavit of Dr. Massimini could not be accepted as correct as Dr. Massimini had not conducted the test/experiment himself, required protocol was missing. Further, the data at pages 306 and 307 of Vol. B (of Appellant) did not form part of the Annexure A referred to in that affidavit and also the footnote at p-305 (Vol. B). The document from which the data were extracted was not placed before the ld. Controller nor this Appellate Board. Even if a case of 30% bio-availability was accepted prima-facie, the Appellant in support of its case of selection patent should have compared other salts or crystals of the 93 Zimmerman Patent and then shown that only the claimed beta form had the alleged surprising properties. All of these were totally absent in the specification and record. The expression 'efficacy' had to mean therapeutic effect i.e. healing effect as per the decision of the Madras High Court on Section 3(d). The said judgment was final and binding in law. There was no demonstration of enhanced therapeutic effect of the beta crystal form of the salt over the base. There was also no evidence that reduced hygroscopicity and enhanced thermodynamic stability could contribute to therapeutic efficacy. On the Appellant's arguments that enhanced bio-availability meant enhanced thereapeutic effect by referring some text books were also not acceptable as none of the text books categorically stated that bio-availability automatically translated to therapeutic efficacy. Further, each of the articles were based on separate clinical studies, wherein bio-availability and therapeutic efficacy had been individually proven, which was not the case here. Thus, the Appellant had miserably failed to prove any enhanced efficacy, the only requirement of Section 3(d) of the Act.

On the ground of anticipation she argued that the Appellant's subject compound beta crystalline form of imatinib mesylate was anticipated by the 1993 patent as the mesylate salt disclosed in the 1993 patent in the description as well as in claim 23 (of USP 5521184) always inherently and spontaneously existed in the beta crystal form as the alpha form being unstable had no real existence. The same also had been established by the expert evidence of Indian Institute of Chemical Technology (Hyderabad) and IIT (Delhi). She added that these two institutes were independent autonomous bodies and for years regarded as the super specialist institutes all over the world. No one would doubt the veracity of experiments conducted by these institutes. There was nothing to impeach the sanctity and impeccable character of these two evidences. In this connection she brought our attention to the copies of test reports of these two institutes wherein it was shown that in the process of preparing imatinib mesylate from the free base imatinib using different process conditions only the beta form of the salt was invariably produced verified by its physicochemical data including of X ray diffraction data. In addition, Appellant's own documents to US drug authority and US certificate extending patent term (p 476 Vol B), the Appellant had given a commercial name GLIVEC to this beta crystalline form also found in their own pleading, (para 4, page 488, Vol B)__ "It is pertinent to mention that no other manufacturer including the opponent could make the beta crystalline form of imatinib mesylate from the 1993 Zimmerman patent and the other companies had to wait for the commercial embodiment of the Appellant's product in 2002 sold under the trade mark GLIVEC/GLEEVEC before they could launch their product in the market in 2002". GLIVEC, admittedly being the beta crystal form of imatinib mesylate for which the impugned application was filed, the same was fully anticipated by the 1993 patent. She also disputed the Appellant's pleading before R 8 as well as the ground of appeal that the 1993 patent only embraced mesylate without any enabling disclosure thereof. The plea of enabling disclosure was totally erroneous and unknown in the context of Indian Patents Act. The doctrine of 'enabling disclosure' was introduced in the amended UK Act of 1977 (and European countries) whereby definition of novelty (Section 2(2) of the UK Act, 1977) to include and mean "all matter" which was not there before the amendment. Referring to the judgment in **Merrel Dow Pharmaceuticals Inc v. H.N. Norton & Co. Ltd.** (1996) R P C 76 where the old law was discussed, where the requirement of "all matter" was not there in case of anticipation. It categorically stated that under the old Act, the patent could have been invalidated where the requirement of enabling disclosure was absent. Indian provisions could only be compared with the unamended old UK Patents Act and certainly not the new UK Patents Act, 1977. Thus, the doctrine of "enabling disclosure" could not be read into the Indian Act.

On the ground of lack of inventive step/obviousness, she argued that the Appellant pleaded and claimed for two inventive steps namely in reaching from base to salt in alpha crystal form and from alpha crystal form to beta crystal form. The plea of inventive step had been argued by the Appellant only in selecting beta crystal

salt from the 1993 patent. Even by adopting the plea of selection patent, the claim of inventive steps was totally defeated because for a case of selection patent, the beta crystal salt must form a part of the 1993 patent otherwise it failed. However, Appellant's claim for two fold inventive steps was totally missing in the specification/claims. The specification rather asserted a mere discovery of beta crystal form. She also submitted that from the "Nature" document of 1996 referred to in the impugned specification and the 1993 patent it was clear that the salt had been described and disclosed. The method of preparation was also disclosed which included customery method as well. Documents on record would clearly show that such salt always existed in crystal form only which now named by the Appellant as beta crystal. A skilled person having regard to the state of the art existing at the time of the impugned 1998 application could easily prepare the beta crystal form from imatinib base. There was no requirement of any inventive skill to prepare the beta crystal from the method disclosed in the 1993 patent.

On the ground of protection of priority date, she submitted that Switzerland was not a convention country on the date of filing the impugned application and, therefore, the Appellant was not entitled to get the desired convention priority. She finally submitted that as the Appellant failed in all the above grounds, the decision of R 8 should be upheld. [R 4 had made some further arguments which are given as a supplementary arguments under sub-para (12)]

(3) Counter-arguments on behalf of R 6 and R 7:

Shri V. Lakshmi Kumaran. learned Counsel, appearing on behalf of R 6 and R 7 initiated his arguments with the reference of different allotropic forms of carbon as a comparative example to the different polymorphic forms of imatinib mesylate. On the ground of anticipation, he submitted that beta form of imatinib mesylate was disclosed and enabled prior to the Appellant's Indian application. He referred to the Appellant's argument that original US Patent No. 5521184 (Zimmerman Patent) equivalent to 1993 patent disclosed imatinib free base and pharmaceutically acceptable salts of imatinib but not enabled in any of the prior arts. But on page 17, Col 3, line 21 of the 'Novartis Vol A' compilation, Zimmerman Patent provided for the formation of imatinib mesylate salt by reaction with "aliphatic sulfonic acids, such as methane -, ethane - or - 2-hydroxy ethane -sulfonic acid." Further, on page 25, Col. 19, line 33 of above 'Novartis Vol A' Compilation, Zimmerman Patent clearly stated that salts of the compound of formula I which included imatinib could be obtained in customery manner and the pharmaceutically acceptable salts also claimed in the Zimmerman Patent clearly provided for the making of the same salt by customery manner. Imatinib mesylate was enabled since the patent law of the United States clearly provided that only that subject matter was enabled could be claimed (35 USC Section 112). In the present case, pharmaceutically acceptable salts including imatinib mesylate were claimed and therefore were disclosed and enabled in the Zimmerman Patent. Also, the Appellant, in its application for patent term extension due to regulatory review of Zimmerman Patent clearly pointed out that the claims of the patent covered the approved product, imatinib mesylate (vide Novartis' letter on p-38 of Ranbaxy's compilation). Further, the Appellant in its reply affidavit to the common counter Affidavit filed by R 1, R 2 & R 8 admitted that imatinib mesylate was disclosed and enabled in the Zimmerman Patent (equivalent to the 1993 Patent) with the following statement "whereas the 1993 patent enables a person skilled in the art to prepare Imatinib mesylate, it does not disclose such monomethane sulfonic acid addition salt". Accordingly, the Appellant admitted that imatinib mesylate was disclosed and enabled in the Zimmerman Patent. Citing the publications viz., "Cancer Research" by Buchdunger et al, dated January 1, 1996 titled "Inhibition of the Abl Protein-Tyrosine Kinase in Vitro and in Vivo by a 2-phenylaminopyrimidine Derivative", "Blood" by Carroll et al, dated December 15, 1997 titled " CGP57148, a Tyrosine Kinase inhibitor, inhibits the Growth of Cells Expressing BCR - ABL, TEL-ABL and TEL - PDGFR Fusion Proteins " and "Blood" by Deininger et al dated November 1, 1997 titled The Tyrosine Kinase Inhibitor CGP57148B selectively inhibits the growth of BCR - ABL - Positive Cells" he also stated that imatinib mesylate was disclosed as CGP 57148 B, prior to the priority date of the 1998 of impugned application of the Appellant. The priority date for that application was July 17, 1998, as Switzerland was not a convention country in 1997 and convention priority date of 1997 was not admissible to the Appellant. Further, in the International Preliminary Examination Report, the Examiner also considered D-1 (Zimmerman Patent) as the most relevant state of the art disclosing methanesulfonic acid addition salts of the present compound of formula 1 which included imatinib mesylate. All these established that the 1993 patent disclosed and enabled imatinib mesylate salt. He also argued that as admitted by the Appellant only the beta crystalline form - Gleevec was commercialized and the patent term extension (before the US Authority) was for the said form as stated to be covered by the 1993 patent, it was clear that beta crystalline form of

imatinib mesylate was anticipated. Citing further, the statement in the affidavit of Dr. Sutter, the expert of the Appellant, that beta form of imatinib mesylate was the most thermo-dynamically stable form and once beta form of imatinib mesylate was obtained, other forms of the same got converted into this form (vanishing polymorph theory) he submitted that imatinib mesylate in solid form would automatically get converted into beta form (by contamination with beta seed crystals) and no other solid crystal form of imatinib mesylate could be obtained. This was a case of inherent anticipation as the court in **Schering Corporation v. Geneva Pharmaceutical** 339 F 3d 1373 was confronted with a similar problem. In this case, Schering Corporation had first patent on anti-histamine loratidine, the active component of CLARITIN. Subsequently, Schering filed a second patent on metabolite of loratidine called DCL. This compound was automatically formed when a patient was ingested with loratidine. The court in this case found the second patent was inherently anticipated by the first patent and espoused this concept in the manner that This Court sees no reason to modify the general rule for inherent anticipation in a case where inherency supplies the entire anticipatory subject matter. The patent law principle "that which would literally infringe if later in time anticipates if earlier"; **Bristol - Meyers Squibb Co v. Ben Venue Labs. Inc.** 246 F-32 1368, 1378 (Fed, Cir 2001) bolsters this conclusion. Similarly, "if granting patent protection on the disputed claim would allow the patentee to exclude the public from practicing the prior art, then that claim is anticipated." Atlas powder 190F. 3d at 1346. "The public remains free to make, use, or sell prior art compositions or processes, regardless of whether or not they understand their complete make up or the underlying scientific principles which allow them to operate. The doctrine of anticipation by inherency, among other doctrines, enforces that basic principle." Id at 1348. Thus, inherency operates to anticipate entire inventions as well as single limitations within an invention.

In the present case, he argued, that due to the seeding (espoused by the Appellant), no other form of imatinib mesylate could be formed. Therefore, a patent on beta form of imatinib mesylate would necessarily exclude others from making imatinib mesylate that was available as prior Article Therefore, the beta form of imatinib mesylate was inherently anticipated by the prior 1993 patent.

On the ground of inventive step/non obviousness, Shri Lakshmi Kumaran argued that the beta crystal form of imatinib mesylate was obvious over 1993 patent and other prior art references. He disputed the contention of the Appellant that the beta crystal form was not obvious because, it was two steps removed from imatinib, the subject of 1993 patent and tremendous amount of research and development took place to achieve the same with the product displaying three unexpected special properties, namely, higher bio-availability, lower hygroscopicity and higher stability which made the subject compound non-obvious over imatinib base. He submitted that while imatinib required substantial investment, the subsequent salt and the beta crystalline form were obvious next steps after obtaining the free base. With the help of an article titled "pharmaceutical salts" in the Journal of Pharmaceutical Sciences by Berge et al, published in January, 1977 where the authors studied different types of salts including mesylate approved by FDA that were made from the active substance and computing the relative frequency of the use of these salt forms in different pharmaceutical products he explained that the salt forms of active substance were chosen as they influenced number of physicochemical properties including dissolution rate, solubility, stability and hygroscopicity. In the said study, though the salt form mesylate showed only 2% relative frequency of use it could be concluded that a person skilled in the art would have at least tried this salt form of the active ingredient with a reasonable chance of success to achieve the very properties that the Appellant contended to be unexpected. Citing the case of **Pfizer Inc v. Apotex Inc.** 480 F. 3d 1348 (Federal Circuit 2007) where Pfizer had a first patent (USP4572909) over amlodipine and its pharmaceutically acceptable acid addition salts (referred to therein as '909 patent) and its claim for the besylate salt of amlodipine based on the unexpected properties of non-stickiness of this salt compared to another salt of amlodipine namely amlodipine mesylate was found to be obvious over the '909 patent in view of above Berge article. In the said judgment the court noted that the pharmaceutically active ingredients were frequently converted into their salt forms to improve the bio-availability and benzene sulfonate salt (besylate) was used in 0.25% of all the surveyed products according to the Berge article. However, the Court found that "the outcome of this case need not rest heavily on the size of the genus of pharmaceutically acceptable anions disclosed by Berge because clear and convincing evidence establishes that, out of the list of 53 anions, one of ordinary skill in the art would have favourably considered benzene sulphonate because of its known acid strength, solubility, and other known chemical characteristics as reported in several other publications Pfizer has admitted as prior Article" Quoting this finding of the Court Shri. Lakshmi Kumaran argued that according to the Berge article mesylate was used in 2% of all the cases and thus it became a far more likely to be a candidate for a salt form of imatinib and hence was likely to be tried more automatically. Quoting further the said Court's another finding that "upon making a new acid addition salt, it was routine in the art to verify the expected physicochemical characteristics of each salt, including solubility, pH, stability, hygroscopicity and stickiness, and Pfizer's scientists used standard techniques to do so. These types of experiments used by Pfizer's scientists to verify the physicochemical

characteristics of each salt are not equivalent to the trial and error procedures often employed to discover a new compound where the prior art gave no motivation or suggestion to make the new compound nor a reasonable expectation of success. This is not to say that the length, expense, and difficulty of the techniques used are dispositive since many techniques that require extensive time, money, and effort to carry out may nevertheless be arguably "routine" to one of ordinary skill in the art," he submitted that making a new acid addition salt and verifying them for expected properties cited by the Appellant were expected and it would be automatic for a person skilled in the art to make the salts to obtain these very same "unexpected" properties. He further submitted that the present case was similar to said Pfizer v. Apotex case. The Appellant's contention that beta crystalline form of imatinib mesylate had better bio-availability compared to imatinib free base was expected as salts increased solubility and consequently increased bio-availability. Similarly, with regard to hygroscopicity, it was a requirement that pharmaceutical tablets to have less hygroscopicity. Thus, finding new forms of imatinib mesylate salt would be to the routine process of finding a suitable salt that Pfizer v Apotex found as obvious.

On the ground of Section 3(d) Shri Lakshmi Kumaran referring back to his arguments on the ground of anticipation submitted that the discovery of beta crystalline form of imatinib mesylate was a mere discovery and was, therefore, could not be a regarded as an invention under Section 3(d). The 1993 patent disclosed and enabled imatinib mesylate and it was established that imatinib mesylate was a known substance. Therefore, Section 3(d) would apply to the present application. In order for the Appellant to satisfy Section 3(d), it should prove that beta crystalline form of imatinib mesylate exhibited enhanced efficacy over the known substance namely imatinib mesylate salt and not over the free base. In order to apply Section 3(d) to the impugned application it was required to know the meaning of the term "efficacy" as provided in Section 3(d). Since the instant invention related to the medical science, the term 'efficacy' must be given a meaning as understood under that field. Since the patent was a technical document and it was directed to a person skilled in the art, the terms used must be understood as these would be understood in the relevant technical area. The relevant field in the present case was pharmacology and medical science. Referring to Dorland's Illustrated Medical Dictionary the term "efficacy" was defined as "Efficacy in pharmacology, the ability of a drug to produce the desired therapeutic effect, it is independent of potency, which expresses the amount of the drug necessary to achieve the desired effect." Further, the 'Oncology Clinical Trials Glossary of Novartis defined 'efficacy' as "Efficacy: (of a drug or treatment) The maximum ability of a drug or treatment to produce a result regardless of dosage. A drug passes efficacy trials if it is effective at the dose tested against the illness for which it is prescribed." The meaning of "Bioavailability" by the Dorland's illustrated Medical Dictionary was given as "Bio-availability : the degree to which a drug or other substance becomes available to the target tissue after administration." The Goodman and Gilman's "The Pharmacological Basis of Therapeutics (8^{th} Ed.)" explained the difference between "efficacy" and "dose". With the help of Fig 2-6 (A-F) from that book (page 18 of 'Ranbaxy - 6' compilation) he argued that if dosage or potency of a drug was crudely equated with the availability of active ingredient to the target tissue, the Fig E clearly showed that efficacy could be independent of such dosage. Therefore, bio-availability, which could be loosely related to dosage, was independent of efficacy. Accordingly, he submitted that mere increase in bio-availability did not transform into enhanced efficacy. The drug action process in the body was explained by Shri Parthasarathy, learned Counsel appearing also on behalf of R 6 & R 7. Shri Parthasarathy explained that the drug action process which broadly be divided into three categories - absorption, binding and response. The absorption related to the amount of active ingredient that had been absorbed by the body. However, this absorption did not automatically translate into therapeutic response. After the active ingredient was absorbed by the body, for it to act, it must bind with the relevant reception of the target cell. This binding was the crucial step that determined effect, where there were less number of receptor sites, increased availability of the active ingredient did not produce any therapeutic response. Therefore, binding and not absorption was the key to healing the disease. Subsequently, after the receptor- drug binding occurs, the subsequent response could be measured. The response was typically in the form of increase or decrease of some parameter (in this case the white blood cell count). Bio-availability was related to the absorption and not the binding stage of the drug action and therefore was not a measure of the efficacy of drug. He also argued that the Hon'ble High Court on the issue of constitutional validity of Section 3(d) of the Act filed by the Appellant accepted this definition of efficacy and added "the dictionary meaning of 'therapeutic', as healing of disease - having a good effect on the body. Going by the above meaning for the word 'efficacy' and 'therapeutic' what the patent applicant was expected to show was, how effective the new discovery made, would be in healing a disease/having good effect on the body. So, it was necessary for the patent applicant to place on record what was the therapeutic effect/efficacy of a known substance and what was the enhancement in that known efficacy of the new substance in its application. This argument demolished the Appellant's contention that the beta form of imatinib mesylate had higher efficacy because it showed higher bio-availability. The impugned application must, therefore, be rejected for not satisfying Section 3(d). The burden of proof was heavily on the Appellant to prove directly with clear, unassailable evidence that beta crystalline form of imatinib mesylate had enhanced efficacy over the known substance, namely imatinib mesylate (say alpha or other forms) which the Appellant had failed miserably to discharge this burden. He further submitted that without prejudice to the above, even if, bio-availability was equated with 'efficacy' the Appellant had also failed to show that beta form of imatinib mesylate exhibited enhanced efficacy over the known substance imatinib mesylate salt. He added that the evidence in vivo data of the administration of beta form of imatinib mesylate to rats as proof that beta form showed enhanced efficacy as compared to imatinib free base did not include the protocol that the rats were fed with capsules of the drug or the drug in a solution. Typically, such experiments were conducted

using solution and that must be assumed to be the case here in absence of other evidence. In solution, the salt would lose its crystalline form and exist as the salt in liquid (melt or solution) or gaseous state where polymorphic differences would disappear because the structure of the solid state would no longer exist. Therefore, the evidence adduced by the Appellant related only to imatinib mesylate and not to beta form thereof. Since, the evidence failed to show enhanced efficacy of the new form of imatinib mesylate, the impugned application should be rejected for failing to satisfy the requirement of Section 3(d) of the Act.

On the issue of selection patent, he submitted that for a compound to be considered for selection patent, it must be first claimed as a group in an earlier patent and then compared to other members of the group to identify unexpected properties. Since the 1993 patent did not recognize crystalline forms of imatinib salts as part of the group of disclosed compounds, the same could not be selected from the 1993 patent and therefore, the beta form of imtainib mesylate was ineligible for a selection patent. He also submitted that without prejudice to the above, regardless of eligibility of the impugned application as a selection patent, the compound must satisfy Section 3(d) which did not distinguish between selection patent and normal patents and required certain incremental invention to be present as given in the said section. In the present case, the same was missing and thus failed in this requirement.

He finally submitted that the order of R 8 be upheld and grant of patent to the Appellant be denied.

[R 6 & R 7 had made some further arguments which are dealt with in the supplementary arguments under sub-paragraph (13)]

(4) Counter-arguments on behalf of R 3:

> Shri Anand Grover, learned Counsel appearing on behalf of R 3 referred to the Misc. Petition No. 33 of 2008 dated 13th November, 2008 filed by R 3 in TA/1/2007/PT/CH seeking introduction of additional evidence in the present appeal by way of adding few documents published between 1996 and 1997 (before the priority date of the application) as exhibits A to D which specifically disclosed the existence of methane sulfonate salt of imatinib. The said documents are given below:
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> > A) Buchdunger, et al "inhibition of the Abl-Protein-Tyrosine Kinase in Vitro and in Vivo by a 2-Phenylaminopyrimidine derivative", Cancer Research 56, 1 January 1996, 100-104;
> >
> > B) C. Gambacorti-Passerini, et al, "Inibition of the ABL Kinase Activity Blocks the Proliferation of BCR/ABL + Leukemic Cells and Induces Apoptosis". Blood Cells, Molecules and Diseases (1997) 23 (19) Oct 15:380-394;
> >
> > C) Deninger, et al, "The Tyrosine Kinase Inhibitor CGP57148B Selectively Inhibits the growth of BCR-ABL-positive Cells", blood, vol 90, No. 9, 1 November 1997, pp 3691-3698; and
> >
> > D) Carroll, et al, "CGP 57148, a Tyrosine Kinase Inhibitor, inhibits the growth of cells expressing BCR-ABL, TEL-ABL, and TEL-PDGFR Fusion Proteins", Blood, vol 90, No. 12, 15 December 1997. pp 4947-4952.

He requested that in the interest of justice these additional documents should be taken on record. However, he had taken note of the fact that the said documents were already on record and relied upon by other respondents.

In his argument he submitted that R 3 was a charitable organisation providing holistic and total management of cancer patients, including awareness, prevention, treatment and rehabilitation of them. It provided total management to about more than 1000 patients per year suffering from cancer. As a part of its services, R 3 provided treatment to cancer patients at subsidized rates. The R 3 was, therefore, concerned about patent applications relating to drugs used to treat cancer, such as imatinib mesylate, the subject matter of the impugned patent application. He added that the IPAB ought to strictly interpret the patentability criteria under the Indian law. India, being a signatory to the Trade Related Aspect of Intellectual Property Rights (TRIPS) was obliged to amend its patent law to confer a twenty year patent protection to pharmaceutical products and processes by 1st January, 2005 However, given the implication of TRIPS on affordability and accessibility of medicines, the Doha Ministerial conference adopted the Doha Declaration on the TRIPS Agreement and Public Health, shortly termed as 'Doha Declaration' in 2001. In paragraph 4 of the same, the relevant part stated "we affirm that the (TRIPS) Agreement can and should be interpreted and implemented in a manner supportive of WTO members' right to protect public health and, in particular, to promote access to medicines for all' (emphasis added), The Doha Declaration was made a part of the TRIPS Agreement and was binding on all the member states. Referring to the Article 27.1 of the TRIPS he argued that the said Article dealing with the criteria of patentable subject matter had left the terms "new", "inventive" and "capable of industrial application" undefined leaving each member country to define these terms according to its own needs in their territory. A flexibility was, therefore, inherent in Article 27.1 itself. India was thus free to set stricter standards

of patentability. Cognisant of the public health concern and the Doha Declaration, Indian Parliament introduced certain provisions, while passing the Act of 2005 to ensure that patents were granted only for genuine inventions and to prevent "ever greening", i.e. extension of patent terms by obtaining follow-on patents for trivial modifications.

The Hon'ble Madras High Court, in **Novartis AG v. Union of India and Ors.** MANU/TN/1263/2007, in upholding Section 3(d) against a constitutional challenge by the Appellant, stated, "we have borne in mind the object which the amending Act wanted to achieve namely, to prevent ever greening; to provide easy access to the citizens of this country to life saving drugs and to discharge their constitutional obligation of providing good health care to its citizens..." (in para 19). Thus, the amended Act should be interpreted in the light of all the relevant circumstances surrounding the amending Act. He submitted that the Indian Patent office was not bound to follow the practices of patent offices in other jurisdictions. Granting patents in other countries was thus irrelevant to the current proceedings. Referring to the Article 4 bis of the Paris Convention for the Protection of Industrial Property, to which India was a signatory, which stated "patents applied for in various countries of the Union by nationals of countries of the Union shall be independent of patents obtained for the same invention in other countries whether members of the Union or not" he submitted that there was an implicit recognition that patentability standards would differ from jurisdiction to jurisdiction and thus while interpreting Section 3(d) as well as the basic standards of patentability as embodied in Section 2(1)(j) and 2(1)(ja) of the Act, the granting authority ought to give these concepts the strictest possible interpretation in order to fully carry out the objectives of the amending Act. Giving a background history of the current appeals he submitted that before proceeding on the merits of the appeal it was important to deal with the issue as to whether the Appellant was entitled to submit additional evidence before the Appellate Board. Following principles analogous to those contained in the Code of Civil Procedure, 1908 for introducing additional evidence before the Appellate Board, the party sought to introduce such new evidence for which an application must be made to this effect and satisfy the Appellate Board of the reason for its inability to file the additional evidence earlier so that the other side could meet the case and the Appellate Board was able to pass an order thereon On the Appellant's submission of its entitlement of the patent for the alleged invention because it had expended a huge amount of time and money, he submitted that painstaking research or expenditure of time and money were not patentability criteria under the Indian law. Citing documents on record he submitted that the Appellant only contributed 10% of the money required for the research carried out [Ref: A note on Dr. Brian Druker's Involvement in the Research and Development of Gleevec". Pages 599-603 of Vol 3 of R 3]. Further, he cited the article "Novartis Outlays on R & D for Glivec: Evidence suggests outlays are substantially below average costs estimated by Tufts University Study" by James Love (Sept. 22, 2003) by which it was revealed that how the Appellant was benefited from the US Government and other non-profit support for pre-clinical work and a fast track clinical trial due to the designation of Gleevec as an orphan drug [Ref. pages 604-605 of Vol. 3 of R 3]. He submitted that the Appellant's claims of expenditure of huge time and money should, therefore, be disregarded.

Shri Grover put before us the state of the art in the field. In that direction, he submitted that Zimmerman patent (1993) disclosed the imatinib free base and also imatinib mesylate. As of 1998, it was well known in the pharmaceutical field that the conversion of a lead molecule into a pharmaceutically acceptable salt could result in numerous advantages, including improved dissolution rate and bio-availability. Examples were given of Morris et al, "An integrated approach to the selection of optimal salt form for a new drug candidate", International Journal of Pharmaceutics 105 (1994) 209-217 which disclosed a systematic and expeditious procedure for selecting the optimal salt that could be adopted in the drug development programme [pp. 458-466 of Vol. 2 of R 3] and Gould, et al "Salt selection for basic drugs" in International Journal of Pharmaceutics 33 (1986) 201-217 [pp. 467-483 of Vol. 2 of R 3] which showed the importance of converting a drug candidate into a salt for improved solubility and bio-availability. Thus, one ordinarily skilled in the art would have been well aware of the potential benefits of converting the free base imatinib into a pharmaceutically acceptable salt. Further, the use of methanesulfonic acid to obtain a pharmaceutically acceptable salt from a free base was known in the industry. Examples, were given of Engel et al "salt form selection and characterization of LY333531 mesylate monohydrate", Intl. J. of Pharm, 198 (2000) 239-247 [pp. 485-493 of Vol. 2 of R 3] which revealed that of the new chemical entities approved by the US Food and Drug Administration (US FDA) from the period 1995 - 1999 that had associated anionic salts, nearly 20% were reported to be mesylate salts. This study by Engel also adopted the salt selection process described by Morris (supra) and identified mesylate salt as the optimal salt form of another molecule (LY33531). Thus, he argued, assuming without admitting that Zimmerman patent did not specifically disclose imatinib mesylate, a person skilled in the art would have ample knowledge of the preparation of imatinib mesylate from the disclosures contained in the said Zimmerman patent alone, especially where, as here, methanesulfonic acid was specifically disclosed in the patent as a candidate acid. He also referred to the new documents introduced with the Miscellaneous petition by R 3 (supra) before the IPAB as the other prior art documents as evidence to show the specific existence of imatinib mesylate before the impugned application. Referring to the said documents he submitted that imatinib mesylate (CGP57148B) was explicitly disclosed in these documents published between 1996 - 1997.

On the ground of novelty/anticipation he submitted that the Appellant's impugned invention was not novel in view of the state of the art disclosed in the aforesaid documents. In further support thereof, he referred to the House of Lords decision in Synthon B.V. v. Smithkline Beecham Plc [2005] UK HL 59 wherein Lord Hoffman clarified that "even where a disclosure in a prior art reference is, by itself, not sufficient to produce the claimed

invention, it is nonetheless anticipating if all that is required are ordinary methods of trial and error which involve no inventive step and are generally necessary in applying any discovery to produce a practical result." Thus, the Zimmerman Patent (1993) disclosing imatinib free base along with specific identification of methanesulfonic acid as a candidate to form a pharmaceutically acceptable salt and other relevant prior art mentioned above, that patent provided ample information for one skilled in the art to produce imatinib mesylate. He also submitted that the Appellant's impugned invention was inherently anticipated in view of the studies conducted by IIT (Delhi) and IICT (Hyderabad) as submitted by R 4 which showed that using a variety of methods in preparing imatinib mesylate from imatinib only beta-crystalline form of imatinib mesylate was invariably produced. The Patent Controller had sufficient evidence before him to conclude that at least in certain conditions, the beta-crystaline form was inherently formed from practicing conventional methods of producing the mesylate salt. There was no need to show that the beta-crystalline form was always produced, or that alpha-form could not be formed. As long as the beta crystalline form was formed inherently from practising the mesylate salt, then this was a sufficient ground for inherent anticipation. He also referred to the US Court of Appeals for the Federal Circuit, in Smithkline Beecham Corporation v. Apotex 403 F.3d 1331(2005) which applied the doctrine of inherency, held that "where there are multiple polymorphs of a given compound, and the method described in the first patent for a specific form inevitably and inherently results in the production of even trace amounts of the later polymorphic form, the later polymorph is deemed to be inherently anticipated". In his further argument he submitted that in proceedings before the Board of Appeals and Interferences of the USPTO, the Board held that the burden would shift to the Applicant upon the presentation, of some scientific evidence to show inherency [pages 178-179 of Vol. A of Appellant's compilation]. The IIT and IICT studies submitted by R 4 were sufficient to shift the burden to the Appellant. However, it had not sufficiently discharged the burden of disproving the inherency.

Justifying the R 8's decision on the ground of inventive step he submitted that under Section 2(1)(ja) of the Act, "inventive step" is defined as "a feature of an invention that involved technical advance as compared to the existing knowledge, and that makes the invention not obvious to a person skilled in the art". Assuming, without admitting, that the mesylate salt form was not anticipated, given the mesylate obvious benefits of converting the free base into a pharmaceutically acceptable salt, the limited universe of acids with which to create such a salt, the prior art teachings that lay out a systematic and expeditious manner in which to select the optimal salt, and the knowledge of methane sulfonic acid as a known acid with which to create such an optimal salt, the alleged improvement from the free base to imatinib mesylate was obvious and did not involve the requisite inventive step as required under the Act. He added that US Court of Appeals for the Federal Circuit, in **Pfizer v. Apotex** (2007) (R 4's doc. P 181-185-195) had held that salt selection was obvious. Any property that was neither "surprising" nor "unexpected" was obvious. Improved solubility and stability were expected properties of a salt form. The beta crystalline form was, therefore, obvious to a person skilled in the Article It was expected that different polymorphic forms would have different physical properties, such as flow properties, hygroscopicity, etc. It was, therefore, obvious for a person skilled in the art to evaluate the crystal structure and changes in crystal structure and look for different forms with differing physical properties (ref: Morris et al; supra). Further, the beta crystalline form of imatinib mesylate did not represent a technical advance. Thus, for the foregoing reasons, the impugned application lacked inventive step.

On the question of patentability of the impugned invention under Section 3(d), Shri Grover submitted that from the prior art documents (supra) imatinib mesylate was a known substance at least in 1996 which was also admitted by the learned Counsel for the Appellant during arguments. Assuming, without admitting, that the beta crystalline form of imatinib mesylate was not inherently anticipated, the beta crystalline form of imatinib mesylate was a polymorph of the known substance imatinib mesylate. In order to overcome Section 3(d), the Appellant must show that the beta crystalline form of imatinib mesylate, the subject of impugned invention, exhibited enhanced efficacy as compared to imatinib mesylate. The Hon'ble Madras High Court in **Novartis AG v. Union of India and Ors.** MANU/TN/1263/2007 (supra) at para 13 held that "efficacy" was to be interpreted as "therapeutic efficacy", i.e. "the ability of a drug to produce the desired therapeutic effect." The Appellant had merely sought to show an increase in bio-availability, that too in rats, to show an increase in therapeutic efficacy. The concepts of efficacy and bio-availability were two distinct concepts in the pharmaceutical field. An increase in bio-availability could not be said to result in an increase in therapeutic efficacy in every case. The Appellant had relied on some extracts and abstracts of publications to show that an increased bio-availability resulted in an increased efficacy. It ought to produce the full text of the published articles before they could be relied upon to advance its proposition. Further, it ought to have shown by way of evidence to R 8 that alleged increased bio-availability in the present case led to an increase in therapeutic efficacy of the alleged invention. The burden of proof on the Appellant to show that there was enhanced efficacy [vide para 13 of Novartis AG v. Union of India and Ors. (supra)] had not been discharged by the Appellant. The Appellant's impugned patent specification only dealt with alpha and beta crystalline forms of imatinib mesylate. It made no mention of the advantageous properties of the beta crystal form of imatinib mesylate over the mesylate salt and did not take the mesylate as already known. Instead, the Appellant chose to compare the free base with the beta crystalline form of imatinib mesylate in showing an alleged 30% increase in bio-availability. Even, assuming that increase in bio-availability could be sufficient to show enhanced efficacy, it was insufficient to show enhanced efficacy under Section 3(d) as the Appellant chose the wrong base line. Buchdunger et al, [in the R 3's Misc. Petition, (Supra)] specifically stated that there was no difference in efficacy between mesylate and the free base.

The Appellant was aware that the increase in bio-availability was due to higher solubility of the salt (imatinib

mesylate) and had nothing to do with the specific crystalline form vide Annexure A to the affidavit of Dr. Massimini. The Appellant's specification only stated alleged improvements in hygroscopicity, stability and flow properties between the beta and alpha crystalline forms. No mention was made of any alleged improvement of bio-availability between the beta crystalline form over the alpha crystalline form or any other form of imatinib mesylate. If indeed there was an advantage, it should have been listed in the specification. Properties such as hygroscopicity, stability and flow properties could not be considered an enhancement in efficacy. These properties were not even considered relevant for the purposes of determining "sameness" of a drug while approving different polymorphic forms of a drug [Ref: USFDA Guidance on ANDAs at pp. 494-506 of Vol. 2 of R 3 and Raw, et al, "Regulatory considerations of pharmaceutical solid polymorphism in abbreviated new drug applications (ANDAs)" at pages 507-524 of Vol. 2 of R 3]. Further, the data on increased bio-availability could not be relied upon as it was not statistically significant. The Controller General of Patents, Designs and Trade Marks (hereinafter referred to as R 2) in his common counter-affidavit had stated that the increased bio-availability "may or may not be statistically significant". Since the Appellant had not provided any raw data of the subject rats it was not possible to accurately calculate the statistical significance of the data. Further, the data provided by the Appellant (vide Annexure A to the affidavit of Dr. Massimini) was not statistically significant with respect to Cmax (p= 0.3851). Also, the study set out at Annexure A to Dr. Massimini's affidavit suffered from other defects such as non-description of the protocol in detail and non-description of the cell lines used. The Appellant had also sought to introduce its own conclusion for proving therapeutic efficacy to the data on the bio-availability study by introducing footnotes to the table at p-305 of Vol. B of Novartis' compilation which again was also not supported by an affidavit. The footnotes should, therefore, be disregarded. Further, the data on pages 306 - 307 in Vol. B of Appellant's compilation was also not before R 8 and was not supported by any affidavit. This should therefore, be also disregarded. Thus, the Appellant had failed to discharge its burden of proving a significant enhancement in therapeutic efficacy over imatinib mesylate because;

a) it did not demonstrate that increased bio-availability led to increased therapeutic efficacy;

b) it compared the beta-crystalline form of imatinib mesylate with imatinib free base instead of imatinib mesylate; and

c) The data provided was not statistically significant and, therefore, its alleged invention was not an invention within the meaning of Section 3(d) of the Act.

On the Appellant's argument of its eligibility to get a patent under the doctrine of selection patent Shri Grover submitted that the doctrine of selection patent was a common law doctrine which was no longer applicable in India. The Indian Patents and Designs Act, 1911 incorporated the definition of invention from the Patents and Design Act, 1907 (UK). Section 93 of the Patents and Designs Act 1907 (UK) defined an invention as any manner of new manufacture, the subject of letters patent and grant of privilege and includes an alleged invention'. Section 2(8) of the Indian Patents and Design Act, 1911 defined an invention as "any manner of new manufacture and includes, an improvement and an alleged invention". It did not define novelty, inventive step or industrial application. This provision remained in force in India till 1972 when the Patents Act, 1970 was brought into force. The English Courts then developed the doctrine of selection patent against this definition of an "invention". In the Matter of **I.G. Farbenindustrie A.G's Patents** (1930) 47 RPC 283, the Bombay High Court, in deciding F.H. & B Corporation v. Unichem Laboratories MANU/MH/0064/1969 applied the English common law doctrine of selection patent to the case there at hand.

Under the unamended 1970 Act, the term "invention" was defined by Section 2(1)(j) as "any new and useful i) art, process, method or manner of manufacture; ii) machine, apparatus or other article; iii) substance produced by manufacture". Section 3 set out what were not inventions and Sub-section (d) excluded from patentability "the mere discovery of any new property or new use for a known substance....". In 2002 amendment of the 1970 Act, the definition of invention was amended to read as "invention means a new product or process involving an inventive step and capable of industrial application." In the 2005 amendment, the definition of inventive step was added by Section 2(1)(ja) which read as "inventive step means a feature of an invention that involves a technical advance as compared to the existing knowledge or having economic significance or both and that makes the invention not obvious to a person skilled in the art". He submitted that Sections 2(1)(ja) and 3(d) in fact excluded and overruled the common law doctrine of selection patent. He added that mere showing of an added advantage or avoidance of a disadvantage was not sufficient to meet the requirement of inventive step in India. Assuming, without admitting that such advantage or avoidance of disadvantage constituted technical advance, an applicant would have to satisfy that the alleged invention was not obvious to a person skilled in the Article Further, Section 3(d) excluded the patenting of discovery of a new property or a new use of a known substance. This clearly statutorily excluded the concept of selection patent. In any event, the Appellant's argument of a two step improvement, i.e. from the free base to the mesylate and from the mesylate to the beta crystal form was fatal to the argument of selection patent. If the Appellant's argument was to be accepted that the Zimmerman patent (1993) disclosed only imatinib free base and suggested various possible salt candidates, then applying the doctrine of selection patent to this argument, the Appellant only arrived at imatinib mesylate from the various possible salt candidates. On the other hand, if the said Zimmerman patent was held to disclose even imatinib mesylate, it did not disclose the possibility of existence of imatinib mesylate in various polymorphic forms, from which the selection of the beta crystalline form could be made. In fact, the Bombay High Court's judgment, cited by the Appellant in support of its case

on selection patent in F.H. & B. Corporation v. Unichem Laboratories, (supra) supported the position that imatinib mesylate lacked novelty. The court made it clear that the finding of novelty was based on the fact that it was not known that one of the subject compounds "could have anti-diabetic properties if they were activated by certain radicals" and thus "in that state of knowledge, it was not possible for skilled chemist to predict that the combining of the two starting materials mentioned in the plaintiff's patent would produce compounds, which would have hypoglycemic properties. In contrast, in the present case, the anti-tumoral properties of the free base were well known as were the expected benefits of increased solubility and bio-availability, in converting the free base into a pharmaceutically acceptable salt. Thus, unlike in the above case, a skilled chemist could have readily predicted the properties inherent in the combination of the free base with methanesulfonic acid. Even, the E.I. Du Pont De Nemours & Co case (supra), cited by the Appellant in support of its case on selection patent, further strengthened the argument that the 1993 patent anticipated imatinib mesylate. The subject invention in that case involved the discovery of a new use of a specific compound in a field unrelated to that involved in the prior art reference. The court noted, "If an ordinary uninventive man would not be likely to look for the advantages he desires to produce in the area occupied by the prior invention, a decision to do so may well amount to the beginning of an inventive step". Again, the advantages to be gained in solubility and bio-availability in converting the free base to a salt were well known in the field, and thus there was no novelty or inventive step involved in doing so. Thus, the impugned invention could not succeed as a selection patent.

On the priority issue, Shri Grover submitted that Switzerland was notified as a convention country only in December, 1998 and therefore, the Appellant's claiming priority of July, 1997 was not allowable. The argument of the Appellant that with the amendment of Section 133 in 2005, Switzerland automatically became a convention country and that the amendment would apply retrospectively to the present application was untenable as amendments to a law could not have retrospective effect unless they had been specifically made to apply retrospectively, as the proposition is amplified by Section 6 of the General Clauses Act, 1897. Therefore, the present application could not claim priority from Swiss application.

He finally prayed for the appeal to be rejected as the Appellant failed to satisfy any of the above grounds.

(5) Counter-arguments on behalf R 5:

> Shri S. Majumdar, learned Counsel appearing on behalf of R 5 submitted, that the arguments of R 5 was based on the facts of the pre-grant opposition made by it before the Patent Authorities on the matter. The opposition should be treated as a part and parcel of his submissions. There were several oppositions against the Appellant's impugned patent application and the findings therein were based on the facts and the circumstances of each case. Accordingly, the arguments of R 5 were purely based on its own case and had nothing to do with the facts of other oppositions by other respondents. R 5 argued in the said opposition that prior art disclosed imatinib mesylate and that there was no ingenuity or human intervention in the beta crystal form of imatinib mesylate. It did not stress on the ground of anticipation on the basis of the said prior art documents though R 8 had upheld anticipation in some other oppositions based on other documents relied upon by them. When a question was posed to the learned Counsel by the Board whether R 5 accepted that the claimed compound was novel, he admitted that R 5 had never pressed the ground of anticipation because none of the documents relied upon by R5 disclosed beta form of Imatinib mesylate and therefore, the novelty of the same was not disputed. He also clarified that whether the grounds of opposition were well taken or not would depend on a specific case and that did not and could not have any binding effect on all the oppositions against the same application.

On the ground of lack of inventive step/obviousness, he cited some articles published before the impugned application which defined the expression "polymorph". From the first article "polymorphism in binary mixtures as exemplified by nimodipine" by A. Grunenberg et al, in the Interntional Journal of Pharmaceutics 118 (1995) 11-21, he drew our attention to the introduction part which inter-alia stated "Like inorganic compounds and elements, organic compounds can crystallize in more than one crystal form. The ability of a substance to exist in several different forms is known as polymorphs. The polymorphs of a compound are chemically identical, but they differ in respect to their physical properties, such as density, crystal habit, spectra, melting point, solubility etc. (Burger 1990) --" and another portion at page 12 of the same article stating that "polymorphism of drug substance has been the subject to intensive research for many years (Borka and Haleblian, 1990). The solubility of a drug substance in aqueous media may have a crucial bearing in its bio-availability. The modifications of a drug substance may also differ in respect of important pharmaceutical properties such as tabletting characteristics, stability of suspension during storage, and millability. Therefore, knowleddge of the physical properties and polymorphism of the drug substance is essential for the successful development of a new medicine". He also drew our attention to the second article "polymorphic transitions of cimetidine during manufacture of solid dosage forms" by A. Bauer-Brandl in the International Journal of Pharmaceutics 140 (1996) 195 - 206, to the introduction part which inter-alia stated "Drug polymorphism, however, may not only cause confusion in analytics but also affect the chemical stability of the

drug substance itself as well as the physical stability of the dosage forms" (for a review on pharmaceutical aspects see Haleblian and Mc Crone, 1969). Furthermore, the crystal structure is crucial for the dissolution behaviour and therapeutic effectiveness of drugs and dosage forms. As a rule, the metastable i.e thermodynamically instable modifications show best solubilities, fastest dissolution rates and highest bio-availabilities. On the other hand, it can be expected that the metastable modifications in particular give rise to stability problems by transforming to more stable modifications during processing and storage, as was found for example for caffeine (Chan and Doelker, 1985; Pirttimaki et al., 1993). Referring to the above said matters in the articles he argued that it was clear that while both stable and metastable polymorphs demonstrated bio-availability with metastable showing higher bio-availability but the metastable had problems with regard to stability.

From the above arguments when referred to the Appellant's specification it would become clear that the alpha crystal form of imatinib mesylate was not suited to pharmaceutical formulation as solid form because of poor physical properties. On the other hand, beta crystal form of imatinib mesylate was less hygroscopic than the alpha form and thus had better storage stability and better suited to pharmaceutical formulation because of its physical properties. He submitted that both alpha and beta crystal forms of imatinib mesylate were made together and the comparative studies of these two forms showed that beta was suitable and the alpha was unsuitable because the alpha form was metastable at room temperature while beta form was thermodynamically stable at room temperature "greater stability is thus to be expected" (p 44 para 2, Vol. A of Appellant's compilation). Therefore, the Appellant admittedly knew that with the thermodynamic stability of the beta crystal form of imatinib mesylate there was reasonable expectation of success to solve the problem of stability which was the "surprising finding" of the Appellant. The alleged invention of the Appellant was to be seen and understood from the specification and nowhere in the specification there was any indication that the Appellant was trying to solve any problem relating to bio-availability. It would be clear beyond doubt that the considerations of the alleged invention were better processing and storing attributes (vide para 2 page 45 of Vol. A of the Appellant's compilation) and the Appellant was wholly aware of the fact that greater stability was to be expected with the beta crystal form of imatinib mesylate because of its thermodynamic stability at room temperature. He then relied on the judgment of US Courts of Appeals for the **Federal Circuit in Case No. 2006-1261 (Pfizer v. Apotex)** wherein the Appeal Court upset the findings of the District court which had found that "the skilled artisan would have had no expectation in success in making of besylate salt of amlodipine, because there is no reliable way to predict the influence of a particular salt species on the active part of the compound'. On the contrary, in the present case there was no possibility of the Respondent authorities of being driven to such a faulty finding for the reason that the admitted position of the Appellant was that "greater stability is to be expected'. If greater stability was to be expected then there would not have been any inventive step in merely finding that the beta crystal form of imatinib mesylate had higher stability. This was particularly true in view of the earlier cited portion in the article by A. Bauer - Brandl on "polymorphic transitions of cimetidine during manufacture of solid dosage forms" in Intl.J of Pharmaceutics 140 (1996) 195-206 (supra). With the aforesaid knowledge all that the Appellant had to do was to verify as to what was the characteristics of the alpha and beta crystal form of imatinib mesylate and which one had better stability and whether such stability met the requirement of the Appellant. Therefore, on the basis of the prior knowledge and the admissions in the specification, the Appellant was bound to try various crystal forms of imatinib mesylate and saw which one had higher stability. The aforesaid journal teachings also clearly indicated at improved bio-availability of the crystal forms of products and evidence produced by the Appellant in the present proceedings also claimed increased bio-availability which was to the order of about 30%.

Referring further to the passages in Pfizer v. Apotex (supra) 'First, this is not the case where there are "numerous parameters" to try. Rather, the only parameter to be varied is the anion with which to make the amlodipine acid addition salt. Although we recognize some degree of unpredictability of salt formation, see, e.g., sanofi - synthelabo v. Apotex Inc., 470 F. 3d 1368 (Fed. Cir. 2006), the mere possibility that some salts may not form does not demand a conclusion that those that do are necessarily non-obvious. This is especially true here, where (1) as noted above, the skilled artisan had a reasonable (although not guaranteed) expectation that amlodipine besylate would form', he argued that in the present case also there was no involvement of numerous parameters and the Appellant had to verify that which of the polymorphs of the compound imatinib mesylate would give the acceptable stability and it found that the beta form was superior to the alpha form and possibly other undisclosed forms tried during experimentation. Further, while the higher stability of one of many polymorphs was highly probable having regard to the knowledge available to prior literature and also as admitted by the Appellant, it was obvious to try different crystal modifications as to its stability and by such process the beta polymorph was discovered. He also added that it could have been possible that none of the polymorphs of imatinib mesylate gave the desired stability because result was not guaranteed and merely that the beta form showed higher stability which was not at all unexpected the Apellant's alleged invention of resorting to the beta form of the known compound imatinib mesylate could not be the subject matter of an invention.

He also alleged that the Appellant had cleverly suppressed the existence of the compound imatinib mesylate by stating that the same was not exemplified in the 1993 patent thereby avoiding wholly the 1993 patent so as to avoid the comparison of stability and other attributes of imatinib mesylate and the beta crystal form of imatinib mesylate. For the purpose of testing obviousness it was well settled that the comparative position of the alleged invention and the closest prior art had to be taken into consideration but the Appellant clearly did not do that. Citing again the judgment in Pfizer v. Apotex case (supra) which recognized the comparison with

the closest prior art as found in a few passages therein particularly at page 37 where the Appeal Court clearly found that the District Court had erred by not taking into account the closest prior art by stating "While we agree that the teaching of a prior art patent is not limited to its preferred embodiment, see Merck, 874 F.2d at 807 ["*the fact that a specific (embodiment) is taught to be preferred is not controlling, since all disclosures of the prior art, including unpreferred embodiments, must be considered, the other amlodipine salts of which Apotex complains (i.e. amlodipine tosylate and amlodipine mesylate)] were not expressly recited in the '909 patent or elsewhere in the prior Article Thus, the district court's obligation to consider the entire range of prior art compounds would have been satisfied here by its comparison of the closest prior art compound to amlodipine besylate*" he submitted that for the same reason in order to demonstrate inventive step/non obviousness the Appellant ought to have compared the allegedly inventive attributes with respect to the closest prior art, namely, imatinib mesylate. On the contrary, the Appellant had been mischievous and dishonest in trying to misguide the Tribunal by categorically stating in its pleadings that imatinib mesylate was not taught or disclosed in the 1993 patent. In support of the basic requirement of inventive step Shri Majumdar also placed reliance upon an old judgment of the US Supreme Court in the case of **Atlantic Works v. Brady** 107 US (1883) wherein the court held "*The design of the patent laws is to reward those who make some substantial discovery or invention which adds to our knowledge and makes a step in advance in the useful arts. Such inventors are worthy of all favor. It was never the object of those laws to grant a monopoly for every trifling device, every shadow of a shade of an idea, which would naturally and spontaneously occur to any skilled mechanic or operator in the ordinary progress of manufactures. Such an indiscriminate creating of exclusive privileges tends rather to obstruct than to stimulate invention. It creates a class of speculative schemers who make it their business to watch the advancing wave of improvement and gather its form in the form of patented monopolies which enable them to lay a heavy tax upon the industry of the country without contributing anything to the real advancement of the Article It embarrasses the honest pursuit of business with fears and apprehensions of concealed liens and unknown liabilities of law suits and vexatious accountings for profits made in good faith*". Citing the same he emphasized that the aforesaid observations squarely applied to the present case also which was no more than a shadow or shade of an idea of the 1993 patent which taught imatinib mesylate and based on the teachings of the prior art the Appellant created the alleged invention being the beta crystal form of imatinib mesylate, which did not involve any technical advancement. He also relied upon a judgment of the US Court of Appeals for Federal Circuit (06-1329) in the case of Takeda Chemical Industries and anr. v. Alphapharrn Pty and Anr. decided in June 2007 where the Appeal Court observed "*We disagree. The KSR Court recognized that "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 has good reason to pursue the known options within his or her technical grasp." KSR 127 S.Ct. at 1732. In such circumstances, "the fact that a combination was obvious to try might show that it was obvious under $ 103." ld. That is not the case here. Rather than identify predictable solutions for antidiabetic treatment, the prior art disclosed a broad selection of compounds any one of which could have been selected as a lead compound for further investigation. Significantly, the closest prior art compound (compound b, the 6-methyl) exhibited negative properties that would have directed one of ordinary skill in the art away from that compound. Thus, this case fails to present the type of situation contemplated by the Court when it stated that an invention may be deemed obvious if it was "obvious to try." The evidence showed that it was not obvious to try*.

Similarly, Alphapharm's reliance on Pfizer (discussed above) fares no better "Quoting the same he stated that upholding the doctrine of "obvious to try" and the comparison with the closest prior art highlighted in the decision were equally applicable in the present case. Further, quoting the same judgment in the latter portion where the court held *All of the compounds claimed in claims 1, 2 and 5 were included in generic claims in the prior art US Patent No. 4,287,200 ("200 patent"), unfortunately our law concerning when a species is patentable over genus claimed in the prior art is less than clear. It is of course well established that a claim to a genus does not necessarily render invalid a later claim to a species within that genus. See Eli Lilly & Co. v. Bd. Of Regents of Univ. of Wash.* 334 F. 3d 1264, 1270 (Fd. Cir. 2003). *In my view, a species should be patentable over a genus claimed in the prior art only if unexpected results have been established. Our case law recognizes the vital importance of a finding of unexpected results, both in this context and in the closely related context where a prior art patent discloses a numerical range and the patentee seeks to claim a subset of that range. See Application of Petering* 301F.2d 676, 683 (C.C.P.A. 1962) *(species found patentable when genus claimed in prior art because unexpected properties of the species were shown); see also Pfizer, Inc. v. Apotex, Inc.* 480 F.3d 1348, 1371 (Fed. Cir. 2007) (relying on lack of unexpected results in determining that species claim was obvious in view of prior art genus claim); In re Woodruff 919 F. 2d 1575, 1578 (Fed. Cir 1990) (When applicant claims a subset of a range disclosed in a prior art patent, the applicant must generally show that "the claimed range achieves unexpected results relative to the prior art range.") he submitted that the beta crystal form of imatinib mesylate was merely a species of imatinib mesylate. The property of higher stability of the polymorph of the beta crystal form of imatinib mesylate was not an unexpected or surprising effect having regard to the prior art with respect to polymorphism and the impugned claimed invention was wholly without merit being devoid of inventive step. Referring to the affidavits of Dr. Manley and Dr. Massimini he stated that both the affidavits were wholly evasive with respect to the compound imatinib mesylate taught in 1993 patent and were sought to focus on bio-availability of beta crystal form of imatinib mesylate vis-à-vis Imtinib base and not imatinib mesylate, the known closest prior Article The Appellant's attempt to establish inventive step by showing efficacy by the enhanced bio-availability was only an after thought on the face of Section 3(d) and if at all bio-availability had to be demonstrated it had to be done with respect to the imatinib

mesylate and not the imatinib base. The enhanced bio-availability even for the sake of an argument of an inventive step could not pass the test of the doctrine of "obvious to try" where even if something obvious to try resulted in unexpected effects was not treated as inventive enough to be granted a monopoly.

On the Appellant's argument of selection patent he submitted that the same was never the case of the Appellant and it was only now attempting to twist the case as a selection patent. Further, he argued that if the beta form of imatinib mesylate was claimed to be novel and not disclosed in the 1993 patent as argued by the Appellant, question of selection did not arise. Comments were also submitted by Sri Majumdar, the counsel on behalf of R 5 against the various decisions/articles relied on by the Appellant on selection patent. In the 'Dupont' case, he submitted, that even a selection invention essentially required an unpredictable property so as to constitute inventive step which was missing in the Appellant's case. In F.H. & B Corporation, v. Unichem - referring the portion in para 16 "an invention may be held to possess subject matter provided the substances produced are not only new but useful, though this is subject to the qualification that substances produced must be truly new, as opposed to being merely additional members of a known series and that then useful qualities must be the inventor's own discovery as opposed to make verification by him or previous prediction", he said in the present case the crystal form of imatinib mesylate was merely a verification of previous prediction. Against I.G. Farbenindustrie case reference (supra) he said in the present case the comparison was made with the base and not with various other similar polymorphs other than polymorph alpha admittedly being metastable and unsuitable. Even the beta crystal form of imatinib mesylate was not compared with imatinib mesylate; Refering to the decision in Technograph v. Mills & Rockey (supra) where the finding of the Hon'ble Court was that none of the prior art suggested the method in the patent in suit. In the present case the entire basis of selection was the combination of higher stability and enhanced bio-availability and such attributes of polymorphs were clearly taught in the prior Article Furthermore, as stated earlier, no comparison was made between beta crystal form of imatinib mesylate and imatinib mesylate. Comparing the Bayer AG's application (supra) where the Court lays down "if the cited prior art shows that this problem is the selection of a novel agent from a known class (polyureas) than it can generally also subsequently be argued that the problems consists in selecting the surprisingly improved agent", he said in the present case, the higher stability and bio-availability of polymorph was wholly predicted in the prior art and therefore it was only a question of degree to which such attributes were enhanced. But the basic fact of such improved properties was never surprising. In the European IP Review article on selection patent in para 2 at page 1 it was clearly stated that a selection had to be an inventive selection and the essential requirement of selection patent would be no different from any other patents. Paragraph 2 at page 2 thereof stated that in absence of an inventive step a selection did not stand. He said in the present case there was no such inventive selection or any inventive step to claim for a selection patent. He also referred to the "Manual of Patent examining Procedure" in USA which gave a guideline to determine a selection or obviousness.

Shri A. Ramesh Kumar, learned Counsel also appearing on behalf of R 5 argued on Section 3(d). He submitted that the submissions of R 5 under inventive step/obviousness squarely applied to Section 3(d) as well which was an extended subset of the doctrine of obviousness. In avoiding "obviousness" there had to be an element of unexpected benefit of any alleged invention and same was the case under Section 3(d) which required significant efficacy. If an enhanced efficacy was obvious or expected, the degree of the enhancement was not material or significant. Referring to the judgment of the Hon'ble Madras High Court in the case of Novartis AG. v. Union of India and Ors. (supra) he submitted that the Hon'ble Court while dealing with the legality of Section 3(d) made several observations which clarified the true purport and the scope of Section 3(d). In that connection, he relied on the following passages in particular from the said decision:

> *'12. ...But, however, we are clear in our mind that the portions of the amended section and the Explanation under attack is definitely referable only to the pharmacology field namely, drugs ...*
>
> *13. ...As we understand the amended section, it only declares that the very discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance, will not be treated as an invention. The position therefore, is, if the discovery of a new form of a known substance must be treated as an invention then the, Patent application should show that the substance so discovered has a better therapeutic effect. Darland's Medical Dictionary defines the expression "efficacy" in the field of Pharmacology as " the ability of a drug to produce the desired therapeutic effect" and "efficacy" is independent of potency of the drug Dictionary meaning of "Therapeutic'" is healing of disease-having a good effect on the body." Going by the meaning for the word "efficacy" and "therapeutic" extracted above, what the patent applicant is expected to show is, how effective the new discovery made would be in healing a disease / having a good effect on the body? In other words, the patent applicant is definitely aware as to what is the "therapeutic effect" of the drug for which he had already got a patent and what is the difference between the therapeutic effect of the patented drug and the drug in respect of which patent is asked for. Therefore, it is a simple exercise of, though preceded by research, - we state- for any Patent applicant to place on record what is the therapeutic effect / efficacy of a known substance and what is the enhancement in that known efficacy. The amended section not only covers the field of pharmacology but also the other fields. As we could see from the amended section, it is made applicable to even machine, apparatus or known process with a rider that mere use of a known process is not an invention unless such a known process results in a new product or employs atleast one new reactant. Therefore, the amended Section is*

comprehensive provision covering all fields of technology, including the field of pharmacology. In our opinion, the explanation would come in aid only to understand what is meant by the expression "resulting in the enhancement of a known efficacy" in the amended section and therefore, we have no doubt at all that the Explanation would operate only when discovery is made in the pharmacology field.

19. ...We have borne in mind the object which the Amending Act wanted to achieve namely, to prevent evergreening; to provide easy access to the citizens of this country to life saving drugs and to discharge their Constitutional obligation of providing good health care to it's citizens...'

Citing the above passages he submitted that from the definition of "efficacy" made by the said Court the 30% enhanced bio-availability could not be considered as enhancement of known efficacy and the Appellant had failed in establishing the enhanced efficacy of the beta crystal form of imatinib mesylate over the known substance imatinib mesylate and thus failed in satisfying Section 3(d) and the decision of R 8 was justified.

He finally prayed for the dismissal of the appeal in question with costs.

(6) Counter-arguments on behalf of R 1, R 2 and R 8:

Shri M. Ravindran, Learned Additional Solicitor General appearing on behalf of Union of India, i.e. R 1, R 2 and R 8 brought our attention to the TRIPS Agreement and its different provisions particularly relating to Patents. In this connection, he read out Articles 27.1, 27.2, 27.3 (a) & (b), 29.1, 30, 31, 33, 34 thereof. He also stated that the TRIPS Agreement left some room to deal with various issues at national level such as the definition of an invention, exception to exclusive rights, compulsory licenses and others. India, to a large extent complied with its obligations under the TRIPS through a series of amendments to its existing laws. The Patents Act, 1970 was first amended by the Ordinance in December 1994 which was replaced by the Patents (Amendment) Act, 1999 (Act 17 of 1999), which was deemed to have come into the force on 1.1.1995. The first amendment was mainly for allowing filing of product patent applications in the field of drugs which was familiarly called as 'mail box' applications, and also for providing Exclusive Marketing Rights (EMR). The Indian Parliament made further amendments in the Patents Act, 1970 through the Patents (Amendment) Act, 2002 (Act 38 of 2002) which came into force from 20.05.2003 along with the Patents Rules, 2003 with a view to fulfilling India's further obligations under the TRIPS Agreement. The third amendment to the Patents Act, 1970 was introduced through the Patents (Amendment) Ordinance, 2004, w.e.f. 01.01.2005. The Ordinance was later replaced by the Patents (Amendment) Act, 2005 (Act 15 of 2005) with retrospective effect from 01.01.2005 thus meeting the deadline of the transitional period of 10 years upto December 31, 2004 extending product patents to food, pharmaceutical products, agrochemicals and microorganisms.

The amended patent law of 2005 adopted a specific policy with regard to claims regarding salts, esters and other form of known substances by amending Section 3(d). This unique section which had been specifically introduced in the Indian Patents Act provided a part that the mere discovery of a new form of a known substance which did not result in the enhancement of the known efficacy of that substance was not patentable. While this clause had no precedent in any other patent laws in the world it was specifically drafted so as not to misuse the rediscovery of an already known item and patent it. The objective of the said provision was clearly to limit the proliferation of patents around existing pharmaceutical products. He read out and described the said Section 3(d) as an unique provision.

He also explained that in order to be patentable, any salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance must differ significantly in the properties with regard to efficacy. Further, in case the new form was further converted into another new form, the comparison was to be made between the already existing form and another form but not between the base compound and another new form. This section prohibited patenting of new forms of existing pharmaceutical substances that did not demonstrate significantly enhanced efficacy. This was intended to prevent companies from attempting to obtain follow on patents for minor improvements to an existing patent before it expired. He also read out the relevant different passages of the decision passed by the Hon'ble Madras High Court in Novartis AG v. Union of India and Ors. (supra) which inter-alia held that the amended Section 3(d) was not in violation of Article 14 of the constitution of India and also gave the meaning of "efficacy" as the "ability of a drug to produce the desired therapeutic effect".

He further submitted that the impugned orders rejecting the Appellant's application were made in accordance with the requirements of Section 3(d) brought into force by the Act. Because, the said Section 3(d) was unexceptionable in law, the Appellant had chosen to challenge the constitutional validity of Section 3(d) itself. He also read out the following passages from the common counter affidavit of Mr. S. Chandrasekaran, Ex. Controller General on behalf of the Union of India. in the W.Ps challenging the vires of Section 3(d).

1 I respectfully submit that the impugned order has been made strictly in accordance with the requirements of Section 3(d) and the contentions to the contrary made in caption A under Section 3(d) cannot be sustained in law. I respectfully submit that the contention that Section 3(d) does not apply is hard to be countenanced. To dispose of the application the provision to be applied in disposing the application is only Section 3(d). I respectfully submit that the question whether the subject comes within the purview of the invention as per Section 2(1)(j) of the Act has to be determined not in isolation but in conjunction with Section 3(d) and the authority had done exactly what is required of him to do in law.

2. I respectfully submit that the contention of the petitioner that the subject compound is at two steps removed from the prior art is not tenable. The known prior art compound is imatinib mesylate and not imatinib free base as contended by the petitioner. The US Patent No. 5521184 hereinafter called 'the 1993 patent' claim imatinib base and its pharmaceutically acceptable salts. The methanesulfonic acid is mentioned as one of the salt forming groups in the specification. Further the specification states that the salts can be obtained in a customary manner. Hence, the present invention claims only a polymorphic form of the known substance viz., imatinib mesylate..

3. I respectfully submit that whether 30% enhancement of bio-availability over known substance is found or out of 30% what would be the utilization in the human system are all matters for the experts to decide. Further the enhancement of bio-availability in a product will not mean that the entire enhancement of said invention would be absorbed in the human system so that the efficacy on such bio-availability would be higher. On this, no evidence was produced before the Authority. Further it is not axiomatic that more the enhancement of bio-availability the more will be the actual absorption in the system.

On anticipation he submitted that the compound Imatinib mesylate was anticipated by the US Patent 5521184 (1993 patent), Claims of 1993 patent claim the free base imatinib and pharmaceutically acceptable salts thereof.

Moreover, the applicant specifically mentioned in the said patent specification, methanesulfonic acid as one of the possible acids with which the free base could react to form a salt. In addition, FDA orange book data showed that the New Drug Application numbers 021335, 021558 were for imatinib mesylate under the trade name Gleevec based on the 1993 patent indicating that the said drug was anticipated by the 1993 patent. He also added that the 1993 patent claimed pharmaceutically acceptable salts of imatinib. The said specification also stated that the acid addition salts could be obtained in a customary manner. The disclosure was sufficient for those skilled in the art to make the required salt of imatinib. Further, the patent term extension certificate issued by the US Patent office for the 1993 patent specifically mentioned imatinib mesylate as the product. He submitted that if there had been any difficulty in obtaining the salt, the same had not been brought out by the Appellant in the impugned application for patent.

On the issue of disallowing the date of priority he submitted that the same was not insisted upon and given up. He concluded that the provisions of the Indian Patents Act was enacted and amended considering Indian conditions, completely in line with the TRIPS Agreement. The Controller rightly applied the law while examining and considering the impugned application. The appeals had no merit The Appellant's efforts to bring in new evidence and new concepts of selection patent law before the Appellant authority was nothing but abuse of process of law and prayed that the R 8's orders be upheld and the appeals dismissed with costs.

(7) Appellant's replies to the counter-arguments of R 4:

Shri Shanti Bhushan, learned senior counsel forcefully contradicted the various arguments placed before the Appellate Board by R 4. On the R 4's preliminary objections on new affidavits he submitted that the procedure for an appeal before the Appellate Board was laid down by Section 117B of the Act which made the Section 92 of the Trade Marks Act, 1999 applicable to the patents Appellant Board also. Under the said Section 92, specific rules governing the procedure had been formulated by the Appellate Board as Intellectual Property Appellate Board (Procedure) Rules, 2003. Rule 8(2) of these Rules stated:

> 8 (2) Every appeal shall be in triplicate in paper book form and shall be accompanied by the copies of the order, at least one copy of which shall be a certified copy against which appeal is filed along with evidence in the form of affidavit." In fact, Section 92(2) of the Trade Marks Act expressly provided that the Appellate Board for the discharge of its functioning under the Act would have the power of receiving evidence. These provisions made it clear that the Appellate Board in deciding the matter was not confined to the material before the Controller, but was entitled to receive further evidence and the Rule 8(2) prescribed that this evidence shall be tendered along with the appeal in the

form of affidavits. On the objection of new introduction of a chart in page 305, Vol. B, he submitted that the very chart was contained in Annexure A to the affidavit of Dr. Massimini except the footnote mentioning that beta crystalline form of imatinib mesylate had 30% increased efficacy. On page 5 of that Annexure A, it was clearly mentioned that beta crystalline form had 30% higher effectiveness compared to the free base of imatinib which was very significant. It was also stated on that page that this higher bio-availability was a result of higher solubility of the salt. In that connection, he also referred to the book "The science and Practice of Pharmacy", 19th Edition filed by R 4 which showed that solubility directly affected bio-availability of a drug. On the R 4's objection that the affidavits of experts relied upon by the Appellant, were contradictory of Section 45 of the Evidence Act, he submitted that when evidence in the form of affidavits could be filed under Rule 8(2) of the Intellectual Property Appellate Board (Procedure) Rules, 2003, the provisions of the Evidence Act did not apply to such evidence at all, which was clear from Section 1 of the Evidence Act. Even Section 45 of the Evidence Act permitted an expert to give evidence of his opinion on any matter of science and there was no limitation under Section 45 which would make the evidence of the four experts inadmissible. It could not be disputed that they were experts of very high order and the mere fact that some of them might have been working for the Appellant did not al all detract from the value of their opinions in the affidavits.

He expressed R 4's total lack of comprehension of what was the disclosure of the 1993 patent and why beta crystalline form of imatinib mesylate was a new invention on the principles applicable to selection patent. The specification in the 1993 patent merely showed that it suggested a large number of salts containing imatinib free base and those salts would have an effect on cancer diseases, since each one of those salts contained imatinib as the active ingredient. However, it was only on the basis of a large number of painstaking, expensive and time consuming research carried on by the Appellant on many of these compounds in different manner that it found a particular compound out of all these, i.e. imatinib mesylate and that also in a particular form namely beta crystalline form which had enhanced efficacy and therefore, it was suitable for the development of a cancer drug. This research had always been recognized as an invention by the Indian courts as well as by the other courts and in fact, had now been made a part of the Indian enactment in Section 3(d). There was nothing in the specification contained in the 1993 patent which could at all give any hint to any person skilled in the art that one of the salts in a particular form namely beta crystalline form of imatinib mesylate was likely to have enhanced efficacy on account of higher bio-availability of 30% and higher stability in room temperature, less hygroscopicity and higher solubility, which considerably added to the efficacy of this compound. He also submitted that the 1993 patent, which was obtained in a large number of other countries was not obtained in India at all since pharmaceutical composition of matter patents were not available in India at that time and therefore, there was nothing to prevent any of the Respondents from utilizing the information contained in the specification of the 1993 patent to develop a drug but evidently they did not do so because it required extensive research, investment of huge amount of money and time consuming work by several scientists. He stated further that in the event that the Appellant's application for patent being granted, the exclusive rights of the Appellant would be confined only to the beta crystalline form of imatinib mesylate and it would still be open to any of the Respondents to use the information contained in 1993 patent specification because that patent was not obtained in India which alone otherwise would have resulted in any drug containing imatinib to be within the exclusivity of the Appellant and therefore, even today, it was open to any of the Respondents to develop a drug containing imatinib as an active ingredient so long as they develop some salt even imatinib mesylate in some other crystal form other than the beta form. He also referred to R 7 who claimed to have already developed another crystal form of imatinib mesylate, namely, the H1 form for which it had already applied for a patent (Vol. B, page 479, Appellant's compilation) and R 4 obtained a license for the alpha form of the drug from the Drug Controller in India (Vol. B, Page 496, Appellant's compilation). He also referred to the R 4's representation under Section 25(1) (Vol. B, page 405) wherein it was stated that : "Various companies have applied for alpha form of methanesulfonic acid addition salt of imatinib. The drug Controller has recognized the fact that whatever the name given to the molecule it is the same methanesulfonic acid addition salt of imatinib for which clinical trials have been conducted and for which permission has already been granted. Accordingly, R 5, R 4 and some other companies have been granted licenses for manufacturing and marketing of the said drug which falsified the argument of R 4 that the salt could not exist in alpha form and the salt inherently existed only in beta form. Moreover, the impugned specification of the Appellant itself contained a chart comparing the various qualities of alpha crystalline form with beta crystalline form of that salt, which established that the said salt could exist in both forms. The beta form having better flow properties, less hygroscopicity and higher stability was developed by the Appellant and launched in 2001.

On the R 4's contention of selection patent being alien to the Indian law he submitted that the doctrine of selection patent had always been applied as a basis for an invention even in Indian cases particularly in AIR 1969 Bom 255. Moreover, the Indian Parliament had made it a part of the statutory law by enacting Section

3(d) of the Act, which said that unless a different form of a salt of a known substance could be shown to have enhanced efficacy, it could not be regarded as an invention and such different form would not be patentable. This being incorporated in the statute, established the doctrine of selection patent in India. Even this plea was taken in the Appellant's reply to the representation under Section 25(1) by R 4. It was also pointed out that imatinib mesylate in its beta crystalline form had enhanced efficacy [Vol B, Page 415, Appellant's compilation]. In fact, in the written submissions filed before R 8, a specific reference was made to the various case laws relating to selection patent and particularly to the case of Synthon B.V. v. Smithkline Beecham (Supreme court of Judicature, UK). It was, therefore, preposterous for R 4 to suggest that the principle of selection patent was not relied upon by Novartis before R 8. On the R 4's contention that enhanced efficacy should also have been demonstrated in the specification itself he submitted that what should be contained in the specification in an application for patent was stated in Section 10(4) (a to d) of the Act and these requirements included the description of the invention, its operation or use and the method by which the invention would be performed and a claim or claims defining the scope of the invention for which a particular product protection was claimed. The Appellant's impugned specification fully complied with the requirements of the said section. If a controversy was raised that a particular form of the particular salt namely beta crystalline form of imatinib mesylate salt for which a patent was claimed did not have enhanced efficacy over imatinib free base, this would be an issue which would require evidence to be led to establish that there was enhanced efficacy. The invention described how a new crystal form was found under certain conditions which was described as beta crystalline form and which had very advantageous properties. He also pointed out that the enhanced efficacy was actually meant for of a drug or advantageous properties in a drug stood for the same thing. He also referred to the impugned specification where enhanced efficacy was actually meant for the advantageous properties of beta form of imatinib mesylate with its more thermodynamic stability at room temperature, lesser hygroscopicity, better storability and easier processability. A detailed comparison between alpha and beta crystalline form of imatinib mesylate with the utility of beta crystalline form for different diseases particularly as an anti-cancer drug, methods of preparation of the same were also described in detail. He also mentioned that at the time of making the application, Section 3(d) in the present amended form did not exist and therefore, the question of stating in the specification in the same language as contained in Section 3(d) did not arise. He also stated that the Indian law required establishment of novelty, non obviousness, non-anticipation and enhanced efficacy as mentioned in Section 3(d). In fact all these had always been a part of the law of selection patent and when this very patent was granted by the Appellate Authority in USA after reversing the decision of the Examiner, all these aspects had been taken into consideration. Referring to the decision of the said Appellate Authority (Vol. A, pages 172-181) wherein it was held that the 1993 patent did not contain sufficient disclosure to support a finding on anticipation. It was also found that the assertion that beta crystalline form of imatinib mesylate was inherently produced was also not correct. The question of novelty and non-obviousness were decided in favour of the Appellant at Vol. A, pages 178-179 where very advantageous properties of beta crystalline form of imatinib mesylate were also referred. On the R 4's contention of non-applicability of any persuasive value of patents granted in other countries because of differences in laws he submitted that there was no difference between the Indian law and the law in other countries in respect of novelty/anticipation, nor in respect of obviousness, nor in respect of enhanced efficacy or corresponding advantageous properties and therefore, the fact that so many countries rejected all these arguments and granted the patent showed that there was good reason for India also to grant a patent for the same drug. In fact, the TRIPs agreement to which India was a signatory along with all other member countries required that w.e.f. 01.01.2005 the condition under which the patents would be granted in India would be identical with the patent systems recognized in different countries. The language of the law might be different, but underlying principles were identical. There was no violation of the TRIPs agreement. On the R 4's contention that the Appellant's reference of 'Gleevec' in the US patent term extension of US 5521184, (1993 patent) was only imatinib mesylate in beta crystalline form, he submitted that in spite of the fact that the discovery by extensive research on beta crystalline form of imatinib mesylate was a new invention but it also continued to be covered by the 1993 patent being a salt of imatinib. Therefore, in those countries, where the 1993 patent had been obtained even for imatinib free base, a salt or any other form thereof, would be covered by that patent also. Since, 'Gleevec' was a salt of imatinib in a particular form - beta crystalline form, it would be covered both by the 1993 patent as well as patents subsequently granted on the basis of the 1998 application. Further, when R 4 claimed that it had obtained licence from the Drug Controller for alpha crystalline form of imatinib mesylate it would be idle for them to contend that imatinib mesylate existed only in the form of beta crystal. He also pointed out that R 4 did not produce any witness in support of the reports of the experiments in IIT, Delhi and IICT, Hyderabad who would have thrown light on the question as to how these experiments were carried out. He also brought to our notice to the said two reports which was shown to be almost verbatim copies of each other. Vol. B, page 322 of the Appellant's compilation stated that imatinib base was supplied to IICT by R 4 and preparation of imatinib mesylate salt using different solvents was studied in the laboratory of IICT. With the help of a comparative table annexed to the written submission, he submitted that significantly, not only the preparation of imatinib mesylate followed identical solvent in the same order by IICT and IIT but the language describing the process was also identical using the same parameters, same timings, same temperature and so on. He further submitted that the procedure which these two institutions had followed was also not the exact procedure described in the specification of the Appellant in its patent application for the preparation of alpha crystalline form. Under the Appellant's specification for producing alpha form of imatinib mesylate crystals, the methanesulphonic acid was to be added drop wise over a period of twenty minutes and then only the solution was to be heated in reflux for another 20 minutes. Neither IIT nor IICT seemed to have followed this important direction as above. He also questioned the source

from which R4 obtained the imatinib free base as the same was not freely available in the market. Was that from "Gleevec" itself that by reverse engineering R4 had prepared imatinib free base?. In that event, as deposed to, by the expert Dr. Frarnpton in his affidavit (Vol B, page 364, Appellant's compilation) in paragraphs 13-19 thereof stating that the series of experiments that the IICT started by employing conditions which were known from the disclosure of the subject application were to result in the formation of beta crystalline form of imatinib. It was also pointed out therein that even if a procedure for the preparation of alpha crystalline form was followed after beta form was prepared, since beta form was better stable and also it was scientifically known that if in that laboratory and in that equipment, there was a trace of more stable crystal form of that salt then the comparatively less stable form would never get formed. It was also pointed out in the report that in the material supplied to the institutions by R 4, there must have been traces of beta crystalline form which would prevent formation of less stable crystalline form like alpha (seeding phenomenon). The affidavits of Dr. Frampton and that of Dr. Sutter completely destroyed any utility of the IICT and IIT reports. It would be necessary to read these affidavits as R 4 was relying on the reports of IIT and IICT without filing any affidavits in support thereof. He also brought to our notice the fact that when R 4 was selling VEENAT in UK, it was imatinib free base in beta crystalline form covered by both the patents of the Appellant namely 1993 patent as well as the subsequent one for beta crystalline form and a settlement was entered into by the Appellant and R 4 in which R 4 gave an undertaking that it would not sell VEENAT within the territory of UK during the period of the life of either of those patents. The copy of the settlement was in Vol C pages 190-210 of the Appellant's compilation. On the question of R 4 as to why bio-availability data required under Section 3(d) was not included in the specification and such study was conducted only in the year 2005 he submitted that the "known substance" imatinib free base had no "known Efficacy" when the present application was filed as it was never employed as an active ingredient in a drug product. The drug product "Glivec" marketed by the Appellant containing Imatinib mesylate in the beta crystal form was not an improved version of an earlier drug, but a break-through medicine. The Appellant had to generate "Efficacy" data for the "known substance" imatinib during the prosecution of the patent application.

(8) Appellant's reply to the counter-arguments on behalf of R6 and R7:

> Shri Shanti Bhushan, learned senior counsel on behalf of the Appellant referring to Shri Lakshmi Kumaran's example of carbon in different allotropic forms particularly diamond in the present case stated that It was known that diamond was only carbon in a different form, but if one applied the process of converting ordinary carbon into diamond and was able to produce diamond whose chemical composition was the same, could anybody contend that a person would not be entitled to a patent for diamond and the process of its production? On Shri Lakshmi Kumaran's argument on anticipation by referring to prior published articles namely, Cancer Research (1996), Blood (both of 1997) [see paragraph 7(3) above] he submitted that the substance disclosed in these three articles was a salt of imatinib, namely, imatinib mesylate and not its any crystalline form namely the beta crystalline form which according to the Appellant had enhanced efficacy on account of several factors including 30% higher bio-availability, in addition to its less hygroscopicity and its stability at room temperature that this form of imatinib mesylate was chosen by the Appellant to produce a drug for the market.

In the first article, "Cancer Research" (1996) one of the joint authors, Jurg Zimmerman, was the inventor of imatinib free base for the 1993 patent. In the said article imatinib free base was referred to as CGP57148 and imatinib mesylate as CGP57148B. However, he emphasized that there was no disclosure of beta crystalline form of imatinib mesylate nor the significant advantages of beta crystalline form, its stability at room temperature, its non-hygroscopicity nor its enhanced bio-availability in the prior Article At this juncture, we posed a question to the learned senior counsel Shri Shanti Bhushan that when the mesylate salt of imatinib was known in the art vide the published "Cancer Research" article as back in 1996 why the same was not acknowledged in the impugned specification as the prior art?. To this question, he replied that the disclosure of prior art was not essential in the Indian law. What was required to be described in the specification is given in Section 10(4) of the Act, and the Appellant has fully complied with the requirements. Moreover, though the said salt was disclosed in 1996 there was no disclosure of any process as to how the same could be prepared. Accordingly, the same was not available to the public and therefore, could not be regarded as a "prior art'. He also submitted that the Appellant was not claiming a patent for imatinib mesylate in all its forms in the present appeals. It was only asking for a patent for beta crystalline form of imatinib mesylate alone and in the event of the patent being granted to the Appellant, none of the respondents would be prevented from producing and distributing imatinib mesylate in any form other than its beta crystalline form or any of the other hundreds of salts of imatinib in any of their forms. The same was the position for the other two articles published in 1997 referred to by Shri Lakshmi Kumaran. These articles also merely disclosed imatinib free base and imatinib mesylate. Neither of them made any reference to the beta crystalline form of imatinib mesylate nor any of these articles described the method for the preparation of beta crystalline form of imatinib mesylate and thus the arguments of Shri Lakshmi Kumaran on anticipation based on these articles was totally misconceived. He also submitted that for the first time beta crystalline form of imatinib mesylate as well as the method of its preparation was described in the Appellant's present patent application on 17.07.1998. Before the said date, neither the substance in question nor the method of its preparation was disclosed. Its

stability and its being less hygroscopic compared to the alpha form and the better storage and processing ability and the fact that in its crystal form, it was particularly well suited for pharmaceutical formulation, were also disclosed for the first time in this application in 1998.

On the contention of Shri Lakshmi Kumaran that no evidence had been produced before this Bench of the Appellate Board that beta crystalline form of imatinib mesylate had enhanced efficacy over imatinib mesylate in other forms, he submitted with reference to the aforesaid article "Cancer Research" of 1996 where "no significant difference in results could be seen between the two forms of CGP 57148" and "all in vivo experiments were performed using CGP 57148 B" that this clearly showed that there was no significant difference between the efficacy of imatinib free base and the efficacy of imatinib mesylate. That made the affidavit of Dr. Massimini (paragraphs 6 - 11, Vol B pages 429-432 Appellant's compilation) very important. While the article of 1996 showed that there was no significant difference between the imatinib free base and imatinib mesylate salt, the imatinib mesylate in its beta crystalline form had 30% improvement in bio-availability compared to the free base and therefore, the beta crystalline form of imatinib mesylate differed significantly in properties with regard to the efficacy when compared to the free base. Without prejudice to the above, he submitted that this objection lacked any factual basis as no other form of imatinib mesylate was in the public domain when the Appellant's patent application was filed. All studies that were reported in scientific papers published before the filing date of the present application were conducted using material provided by the Appellant. The person skilled in the art could not conclude from the publications what crystal form was used as correctly pointed out by the Counsel arguing for R 5 in his counter-arguments. He further added that it was well known that in a cancer drug, bio-availability was a very important feature of the drug because if in a particular form the bio-availability of the drug could be enhanced, it was possible to give lower doses of the drug which could not be equally effective so far as the disease to which the present patent application was concerned and yet the lower doses would reduce the adverse effects of that drug to a very significant extent. This therefore, enhance the efficacy of the drug in its present beta crystalline form and therefore, met the requirements of Section 3(d) fully. On the contention of Shri Lakshmi Kumaran that in the experiments on rats that crystalline form of imatinib mesylate had to be dissolved in water before it was administered to the rats and in that process the salt ceased to retain its crystal form he submitted that in the Annexure A to the affidavit of Dr. Massimini it was clearly showed that the drug was administered to the rats in the form of capsules. Since it was only in the crystalline form, particularly the beta crystalline form that the drug was most effective, the rats were not administered the drug by first dissolving in water and that was why the crystals were administered to the rats as crystals in a capsule. It was well known that when a drug was to be administered without first dissolving it in water, the same had to be administered in most cases by putting it in a capsule and directly given the capsule to a patient whether a human being or a rat. On the contention that bio-availability and efficacy were defined separately and therefore bio-availability was totally irrelevant in arriving at a conclusion as to whether or not a new form of a known substance had enhanced efficacy within the meaning of Section 3(d) of the Act, he submitted that sometimes, particularly in the case of anti-cancer drug where there was a dose limitation on account of very strong adverse reaction of the administration of a drug, higher bio-availability led to enhanced efficacy and this was the case with the drug in question. If it was not possible to increase the dose of a drug because the increased dose would have very serious adverse reaction and yet it was necessary that the required amount of the drug reached the affected cells, such enhanced efficacy of the drug could only be achieved by changing the form of the drug if the changed form could achieve higher bio-availability and thus could enhance the pharmacological efficacy of that drug.

On the contention of Shri Lakshmi Kumaran that whenever the salt imatinib mesylate was produced, it could be produced only in its beta crystal form as that was the most stable form of that salt as supported by paragraph 14 of the affidavit of Prof. Frampton filed by the Appellant as that statement in said paragraph was not properly followed. Prof Frampton did not state that alpha crystal could not be produced even if beta crystal form was present in the laboratory on account of the phenomenon known "as seeding". What he had said was "in that case, the process of manufacturing alpha crystalline form would have to be conducted under stringent purity conditions, under exclusion of beta seed crystals." It was, therefore, clear that IIT, Delhi and IICT, Hyderabad had not taken any steps to remove the contamination of beta crystal seeds from their laboratory and had not conducted the process of preparation of imatinib mesylate under stringent purity conditions as required. Further, if the salt could inherently exist only in beta crystalline form and it was not possible to make the alpha crystalline form the comparative experiments conducted on the two forms of crystals of the same salt as indicated in the Appellant's specification would not have been possible. He further, stated that R 4 had also applied for a patent claiming alpha -2 crystal form of imatinib mesylate. Moreover, as stated before, even R 4 had obtained a drug licence from the Drug Controller for marketing the alpha crystal form of imatinib mesylate and even R 7 had also applied for a patent for imatinib mesylate in its crystalline form H1 (Vol. B, page 479, Appellant's compilation). It was therefore, idle for the respondents to contend that imatinib mesylate could not exist in its different crystalline form other than beta. On the argument of Shri Lakshmi Kumaran on selection patent he submitted that the law of selection patent was strongly relied upon by the Appellant before the Controller also and quoted its written argument (page 486) stating "However, there is a difference between disclosure and claim. A subject matter which is merely embraced by patent claims, but which is not being specifically disclosed in the prior art can still be validly claimed in a patent as a selection patent/invention". He also quoted in that connection, paragraph 51 from the case of **Synthon B.V. v. Smithkline Beecham** (2006) 1 Reports 685 (House of Lords) which was stated to be extracted on that page in the said written argument. Even cases on selection patent were also referred to in paragraph 3 thereof at page 488, namely, E.I. Dupont and IG. Farbenindustrie A.G's cases which were the leading cases on the law

of selection patent. On the contention of Shri Lakshmi Kumaran that the requirements of establishing the right to a selection patent had not been shown in the present case Shri Shanti Bhushan submitted that the settled law of selection patent showed that if there was a possibility by the earlier art to produce a number of salts and different forms of those salts, then a selection patent for one of those salts in a particular form would be available only if it could be shown, that a particular form of that particular salt had improved advantages over the other salts or other forms. These requirements on selection patent had been clearly established in the various affidavits of experts which were relied upon by the Appellant before this Bench of the Appellate Board. In fact, even in the Appellant's specification the selection of beta crystalline form of imatinib mesylate was given in the following manner:

> It has now been surprisingly found that a crystal form may under certain conditions be found in the methanesulfonate salt of this compound, which is described hereinafter as ß-crystal form and which has very advantageous properties.

In the said specification different advantageous properties of the beta crystalline form of imatinib mesylate as compared with alpha crystalline form were also described. The discovery of these properties in the beta crystalline form of imatinib mesylate had been referred to therein as an innovation.

On the arguments of Shri Lakshmi Kumaran on Section 3(d) Shri Shanti Bhushan submitted that the discovery of beta crystalline form of imatinib mesylate could not be regarded as mere discovery under Section 3(d). A discovery which required huge amount of research work and testing various alternatives in different conditions and then finding a particular salt in a particular form which could be used for the preparation of a drug could not be called a mere discovery and this would have to be regarded as an invention for the purposes of the Act. The known substance for the purposes of Section 3(d) would have to be treated as imatinib free base which had in fact been prepared and tested as preclinical studies including tests demonstrating the inhibitions of the growth of human bladder carcinoma cells in isolation and in mice as described in the 1993 patent (Col 5, 1,66 to Col 6, 1.53). That patent merely suggested the possibility of its being converted into various kinds of salts which had neither been prepared nor tested for their qualities. If imatinib must be considered to be the known substance for the purpose of Section 3(d), then the beta crystalline form of imatinib mesylate could not at all be treated as mere discovery of a new form of a known substance. Further, beta crystalline form of imatinib mesylate could not possibly be described as a new form of imatinib free base. Further, even if the explanation to Section 3(d) was applied and the salts of a known substance, imatinib mesylate and their beta crystalline form were treated as the same known substance, namely, imatinib free base, even then, if the new form differs significantly in properties with regard to the efficacy, it could become patentable, and it had already been shown that beta crystalline form had enhanced efficacy from several aspects. On the argument of Shri Lakshmi Kumaran relying on a decision of the US Court of Appeals in Schering Corporation, v. Geneva Pharmaceutical Ltd., particularly at paragraph 6 at page 72 of Ranbaxy -2 "compilation Shri Shanti Bhushan submitted that it was difficult to see how this paragraph could help his clients, namely, R 6 and R 7. The Appellant was not preventing any one from making use of the prior art contained in the 1993 patent or in various articles published in 1996 and 1997 or from preparing any salt of imatinib, even imatinib mesylate in any other form, except beta crystalline form.

(9) Appellant's replies to the counter -arguments on behalf of R 3:

> Shri Shanti Bhushan, while replying to the arguments advanced by Shri Grover submitted that Shri Grover primarily reiterated and adopted the arguments which had been advanced by the other Counsels on anticipation, novelty and obviousness. Since appropriate replies were given by the Appellant to all those arguments it was not necessary to deal with the same any further. In response to Shri Grover's contention that the grant of patents in 35 or more countries should not have any persuasive value as the laws in those countries were different and his reference to the different Articles, particularly Articles 1, 7, 8 and 27 of the TRIPS Agreement, Shri Shanti Bhushan said that the reference to these Articles by Shri Grover was in an endeavour to persuade the Court not to interpret Section 3(d) of the Act consistently with the TRIPs Agreement. However, this approach to the interpretation of Section 3(d) would be hopelessly unjustified and nothing in the Articles of the TRIPS Agreement supported this contention. A reference to the Article 1 showed that the protection to Intellectual Property was guaranteed by the TRIPs Agreement and the same could not be reduced and permitted the members in their laws to give more extensive protection than was required by the TRIPs provided such more extensive protection did not contravene the provisions of the Agreement. In fact, he said, it was settled law as per the decision of the Supreme Court of India that an Act of Parliament as far as possible, ought to be construed in a manner so as to conform to international agreements to which India was a party. He referred in that connection to a decision of the Supreme Court in MANU/SC/0039/2005 where it is stated:
>
> > 41. Thus international treaties have influenced interpretation of Indian law in several ways. This Court has relied upon them for a statutory interpretation, where the terms of any legislation are not clear or are reasonably capable of more than one meaning. In such cases, the Courts have relied upon the

meaning which is in consonance with the treaties, for there is a prima facie presumption that Parliament did not intend to act in breach of international law, including State treaty obligations. It is also well accepted that in construing any provision in domestic legislation which is ambiguous, in the sense that it is capable of more than one meaning, the meaning which conforms most closely to the provisions of any international instrument is to be preferred, in the absence of any domestic law to the contrary. In this view, Section 3(2)(d) is to be read keeping in view the Paris principles.

Even Article 8 of the TRIPs agreement clearly provided that a member country formulating or amending rules or regulations adopted measures necessary to protect public health and nutrition and to promote public interest in sectors of vital importance to their socio-economic and technological developments, provided that such measures were consistent with the provisions of this agreement. In fact, the Act took care to make the availability of drugs at a reasonably affordable price by providing for compulsory licenses in Section 84. Further, Section 92 also gave a power to the Central Government, in case of an extreme urgency, to grant a compulsory licence at any time after the grant of patent of a drug on such terms and conditions as the Controller deemed fit. It was, therefore, not possible to accept an argument that the interest of patients had to be ensured by giving a distorted interpretation to Section 3(d) of the Act in a manner which would be totally violative of the TRIPS agreement.

Quoting & reading out the Article 27 of the TRIPS agreement he stated that the said Article 27, sub-paragraph guaranteed the availability of a patent for any invention whether the product or process in all fields of technology, provided the invention was new, involved an inventive step and was capable of industrial application. This guarantee was only subject to the provisions of sub-paragraphs 2&3 of Article 27. Sub-paragraph 2 of Article 27 only provided for exclusion from patentability of an invention if such exclusion was necessary to protect public order or morality or to protect human, plant life or health or to avoid serious prejudice to the environment which had already been ensured by the Act by Section 3(b). Sub-paragraph 3 of Article 27 also permitted exclusion from patentability of technological, therapeutic and surgical methods for the treatment of humans or animals. Those exclusions only covered methods of treatment and did not include a patent for a product. This had also been achieved by Clause (i) of Section 3 of the Act. He further submitted that Section 3(d) had to be construed in a manner consistent with the TRIPS agreement and therefore, if the Appellant used the information contained in the 1993 patent and did an extensive research to select a particular salt in a particular form, which had additional advantageous properties, the drug would be patentable under the TRIPs agreement and Section 3(d) should be so construed so that the same drug also remain patentable under the Indian Act. This meant that if a particular form of a drug made it more effective drug for the treatment of a particular disease such as the development of a new drug i.e. beta crystalline form of imatinib mesylate being more effective for the treatment of cancer would meet the requirements of Section 3(d) and would have to be treated as patentable under the Patents Act 1970 also. In response to Shri Grover's reference to a declaration in the Ministerial Conference of World Health Organisation on 14.11.2001 (Vol. 3, page 645 of CPAA) particularly to paragraphs 5(b) and (c) and 7 Shri Bhushan said that paragraph 5(b) & (c) reiterated the right of member countries to grant compulsory licenses and to determine the grounds on which such compulsory licenses would be granted as well as the right to determine what constituted a national emergency or other circumstances of extreme urgency and that health crisis including those relating to HIV/Aids, Tuberculosis and other epidemics could represent a national emergency or other circumstances of extreme urgency. Paragraph 7 of that declaration also provided that the least developed countries would not be obliged with respect to pharmaceutical products, but implement said section of the TRIPS Agreement until 01.01.2016 and accordingly, these applied only to the least developed countries but not India. So far as countries like India were concerned they had been permitted a period of 10 years from 01.01.1995 not to enforce the provisions relating to product patents till 01.01.2005. Therefore, after 01.01.2005, the product patents became applicable to India and the same law became applicable to India as well as to other countries who were parties to the TRIPs agreement in regard to the patentability of a product. In response to Shri Grover's reference to Article 4 bis of the Paris Convention, he submitted that the said Article only meant that if a patent was granted by the authorities in one country, it could not create any right in other countries and a person wanting a patent would have to apply in each country to obtain the exclusive rights relating to that invention for each country as well. Appellant was not claiming that it was entitled to any exclusive rights in India by virtue of the fact that it had got patents in 35 or more countries rather it had filed for a separate application for patent in India for the instant invention. On the contention of Shri Grover that money spent in developing the drug in question was although huge, was not spent entirely by the Appellant and it received grants from Government or others and only 10% expenditure was incurred Shri Shanti Bhushan submitted that this argument was totally irrelevant in so far as the question of patentability of the drug was concerned. If a drug was developed by a company after incurring huge expenditure in the research, which resulted in the discovery of a particular form of a particular salt having enhanced efficacy, it was wholly immaterial under the patent law whether the entire amount was spent by the company, which was entitled to the patent or it was assisted in that effort by other organizations by contributing for that research. It was, therefore, not necessary to enter into those facts. On Shri Grover's contention of Appellant's claim of wrong priority Shri Bhushan stated that nothing turned upon the priority date since all the documents on which the Respondents were relying on the question of anticipation and the prior art documents were prior to 18.07.1997. If there was any public disclosure between 18.07.1997 and 17.07.1998, the Indian filing date, something could turn on this

question and the point would have been argued as to whether the Appellant was entitled to claim priority from the Swiss application. However, he submitted that there was no doubt that Switzerland was a convention country under Section 133 of the Act as it stood today and since the Appellant's application for the grant of product patent in question could not have been considered till the product patent was introduced in India w.e.f. 01.01.2005 its application had to be considered according to the law as it stood subsequent to the date of introduction of product patents in India. Since under the Act of 2005, by which product patent was introduced w.e.f. 01.01.2005, it was by that very Act that the definition of convention country was also changed by replacing old Section 133 with a new Section 133 and therefore, it was the new concept of convention country which could be applicable for a consideration of an application for a product patent like the Appellant's application. This would mean that Switzerland had to be treated as a convention country for the purpose of a product patent and no notification was required to declare Switzerland as a convention country. Accordingly, it was necessary to take cognizance of the change in law which the Parliament had made and could not take into consideration those provisions that had already been repealed. Therefore, Switzerland had to be treated as a convention country for the consideration of all applications for product patents and the Appellant would be entitled to get 18.07.1997 as the priority date under Section 135 of the Act.

On Shri Grover's contention on the non-disclosure of the required protocol on the experiment conducted on rats by the Appellant to determine bio-availability of the beta crystalline form of imatinib mesylate with respect to imatinib free base Shri Bhushan submitted that the document contained in Annexure A to the affidavit of Dr. Massimini clearly disclosed the study design as to how the experiment was conducted and also disclosed in tabular form the results in several pages and also the conclusion of the study. Protocol was nothing else but a study design and since all parameters of the study were indicated, a complete protocol was disclosed in the document which was signed by five experts.

Shri Shanti Bhushan in reply to Shri Grover's two publications namely "An integrated approach to the selection of optimal salt form for a new drug candidate" by Morris et al and "Salt selection for basic drugs" by Gould et al at pages 458 and 467 of Vol. 2 of R 3's paper book had drawn our attention to the "introduction" in page 467 and submitted that this article gave a very detailed account of how this painstaking and extensive research had to be carried out. He added that merely because a chemist knew how this painstaking research had to go on and how various salts in various forms had to be tested for various properties and then those properties had to be compared and then seen whether the required compromise could be reached to make it a safe drug did not mean that any chemist could reach the conclusion. The law of selection patent had been developed by the Indian Courts and other courts on this basis that since a large number of salts and possibly their various forms including possible amorphous or different crystal forms were possible and the alteration of salts of the formation of these salts might affect their chemical properties also, it was a very difficult research endeavour to find out whether a pharmaceutically acceptable form originating from a particular chemical would be discovered which could thereafter be developed into a crystal form. The invention consisted of going through all these complicated procedures and discovering a particular form of a particular salt which would have all the required chemical and physical properties to enable it to be a proper candidate for a drug for a particular disease. Going through all these steps were inventive steps which resulted in an advance of scientific knowledge and therefore the result became patentable. It was through very extensive research that a particular form of a particular chemical compound would be found which would have all the optimal qualities necessary for a drug for a particular disease so that it could be formulated as a drug. The reward of a patent was, therefore, a reward for this painstaking research. Of course, how chemical and pharmaceutical research was to be carried out had been studied by various scientists and the roads to that research were indicated in various scientific articles, but that did not mean that by going through that extensive research one could not make an invention which would result in a drug. It was important to keep in mind that the invention as claimed could not be predicted to exist. In the instant case, the advantages of better physical properties such as higher stability and lower hygroscopicity of the beta crystalline form of imatinib mesylate was totally unexpected and therefore, unobvious. The acceptance of the argument of Shri Grover would be that hereafter no drug at all would qualify for a patent because it was known as to how drug research had to be carried out and therefore, if anybody who went through all these steps of research and ultimately reached a particular drug, there would be no invention involved in developing a drug and this would, therefore, be totally destructive of the law of patent in so far as it related to patent for drugs.

In response to Shri Grover's reference to the House of Lords decision in the case of Synthon BV v. Smithkline Beecham, Plc (2005) UKHL 59 he analysed and explained different paragraphs of that decision and stated that the matter in that decision was merely concerned with the method of crystallization of a known compound which according to the house of Lords, was a simple process, known to every chemists. In the Appellant's present case, the Appellant was not claiming the crystallisation process as part of its invention. It was claiming that out of the various salts of imatinib and the various forms in which various salts could exist, it was its discovery by extensive research of the special qualities of beta crystalline form of imatinib mesylate which constituted the invention, which entitled it to a patent. The decision of the House of Lords in Synthon case, accordingly, had no application to the present case.

On the contention of Shri Grover that even though the affidavits of Dr. Frampton and Dr. Sutter had been filed along with the appeal, they could not be relied upon as the Appellant had not made any application under Order I, Rule 27 of CPC which provided for the Appellate Court receiving additional evidence which was not available to the Trial Court Shri Bhushan submitted that this Appellate Board was not governed by the

procedure laid down in the CPC. This was made clear in Section 92(1) of the Trade Marks Act, 1999. On the other hand Rule 8(2) of the Intellectual Property Appellate Board (Procedure) Rules, 2003 framed for this Appellate Board under Section 92 of the Trade Marks Act, expressly provided that an appeal would be accompanied by copies of the order against which the appeal was filed and the evidence in the form of affidavits. Since the rules themselves not only permitted but required the evidence which was not before the Controller to be filed along with the appeal, it was clear that no application was required to be filed to take the new evidence in the form of affidavits which was not before the Controller under the law. The reference made by Shri Grover to the decision of the Supreme Court in 1951 SCR 288, which was a case of the Appellate Court governed by the CPC, had, therefore, no application to the present appeals.

On the contention of Shri Grover that on the rat study to determine the higher bio-availability of beta crystalline form of imatinib mesylate, a comparison made only between beta crystalline form of imatinib mesylate and imatinib free base rather than with imatinib mesylate as a salt he submitted that the 1996 Article in which Mr. Jurg Zimmerman was a co-author which had been referred to by all the Respondents expressly stated that no significant difference was found between imatinib free base and imatinib mesylate after the experiments which were made with those substances. Since the effectiveness of imatinib and the compound imatinib mesylate did not show significant difference between the properties of the two compounds it was only necessary to compare the properties between imatinib and beta crystalline form of imatinib mesylate which disclosed that in the beta crystalline form of the salt there was 30% enhanced bioavailability leading to enhanced efficacy. Without prejudice to the above, he submitted that the objection lacked any factual basis as no other form of imatinib mesylate was in the public domain when the patent application was filed. Also the alpha crystal form of imatinib mesylate was found by the Appellant and described for the first time in the same patent filing. All studies that were reported in scientific papers published before the filing date of the present application were conducted using material provided by the Appellant. The person skilled in the art could not conclude from the publication what crystal form was used as correctly pointed out by the Counsel arguing for R 5.

On Shri Grover's objection to the absence of any reference to C max in the conclusion of study on rats to make that statistically significant Shri Bhushan submitted that a reference to the study which was contained in Annexure A to the affidavit of Dr. Massimini would show that the study also contained reference to C max. However, for a selection patent, it was not necessary that a particular form of a particular compound must be found to be statistically significant in respect of all features, so long as it was statistically significant in respect of an important feature like AUC, which would be enough for that particular form chosen for a particular drug for a particular disease. Since AUC value corresponded to the total amount of drug substance absorbed by the individual hence, it was a key aspect for the bio-availability of a drug substance.

(10) Appellant's replies to the counter-arguments on behalf of R 5:

Shri Shanti Bhushan submitted that R 5 had made some very important concessions in favour of the Appellant:

i) that the prior art, namely, the 1993 patent, 1996 Article (Cancer) and 1997 Articles (Blood) did not disclose a crystalline form of imatinib mesylate or in fact any crystalline form of that substance Therefore, it was not possible for the Respondents to raise a contention on the ground of disclosure of beta crystalline form of imatinib mesylate being a part of the prior art;

ii) that beta crystalline form of imatinib mesylate was a new form and therefore, it could also not be challenged on the ground of lack of novelty;

iii) that so far India was concerned, no patent having been obtained by the Appellant on imatinib or any compound containing imatinib there could be no question of evergreening and it was not possible for the Respondents to rely upon the principle of ever greening in the present case;

iv) that what was contained in Section 3(d) brought in by amendment in 2005 was nothing new and was already a part of the law of patents. This was claimed on the basis of a decision of U.S. Supreme Court in 107 US 192(1883) Atlantic Works v. Brady. Quoting the passage from the said decision as relied upon by Shri S. Majumdar, the learned Counsel for R 5, "The design of the patent laws ---------- ordinary progress of manufactures" (vide paragraph 7(5) above, Shri Bhushan submitted that it was always the law that there had to be a substantial discovery and a step in advance in the useful arts and this grant of monopoly was not applicable to every trifling device. This was the principle which was articulated in Section 3(d) of the Act. He further submitted that the main argument of R 5 was that even though beta crystalline form of imatinib mesylate was not disclosed by the prior art before 1998 either in 1993 patent or in the articles published in 1996 and 1997, these did disclose the compound imatinib mesylate although not any of its crystalline forms. Therefore, the Appellant could not claim a patent on the basis of its discovery of its salt imatinib mesylate and its claim had to be confined to the conversion of that salt

to the beta crystalline form of imatinib mesylate. On this argument of R 5, the Appellant's submission was as had been stated before, that its invention consisted in finding a particular salt from a group of salts, that also in a particular form which had enhanced efficacy, which had to be regarded as an invention comprising of an inventive step according to the established law of selection patent.

He then referred to the affidavit filed on behalf of Union of India which also stated the same law about selection patent in para 14 thereof which is given herein below:

> *'The claimed crystal modification of N-Phenylpyrimidineamine derivative is a patent application filed in India is nothing but a "selection patent application", is a patent under which a single element of a small segment which a large known group i.e., "93 patent is "selected" and independently claimed, based on a particular feature not mentioned in the large group. If the large group of elements is already patented, the patent owner may use the selection patent to extend the term of protection beyond the expiration of the original patent at least for the selected subset. While accepted in some jurisdictions when the selected elements possess a surprising advantage, selection patent have been denied when the supposed advantage, is a property shared by all or nearly all of the large group.'*

He added that as the 1993 patent would show, it had been found that imatinib had certain anti-cancer properties and the claim was that any salt which contained imatinib would have anti-cancer properties. Various salt forming acids were suggested to make various salts. It was at that time not known, that any of these possible salts from hundreds or thousands of possibilities would have special advantageous or enhanced efficacy to make such selection of one of these salts in a particular form patentable. It was only the result of very extensive and expensive research work undertaken by the Appellant that led to the selection, first of imatinib mesylate and then its conversion into a particular crystalline form - namely beta crystalline form, it was found that this ultimate compound had significant pharmaceutical advantages leading to enhanced efficacy and therefore, it was patentable. The "invention" of the Appellant had, therefore, been correctly claimed as a two step invention and the Appellant was legally entitled to the reward of patentability for having carried out such extensive and expensive research.

On the contention of R 5 that alpha form of imatinib mesylate was metastable and the beta crystal form, was used for the drug being stable to impart stability only which had nothing to do with its pharmacological efficacy, he submitted that this contention was totally fallacious. If a drug company was able to discover a substance which was metastable i.e, not stable in ordinary condition, it was clear that it could not be developed into drugs. Therefore, its pharmaceutical efficacy would be very low since that drug would require to be manufactured in very difficult condition, stored in special conditions and even a patient would require special condition to keep the same. Thus, the pharmaceutical efficacy of a drug required it to be in a form which was stable at the room temperature.

On the reference of R 5 to the publications on polymorphism showing the purpose and objects of polymorphism which might be required to solve stability problems and to improve the process of manufacture and bio-availability and the argument of R 5 that polymorphism had no connection to therapeutic effectiveness Shri Bhushan submitted that the said argument was not supported by the own literature referred to by R 5 particularly on "polymorphic transitions of cimetidine during manufacture of solid dosage forms," in International Journal of Pharmaceutics 140 (1996) 195 - 206 [see paragraph 7(5) above)]in which it was stated at page 196 being extracted below:

> Furthermore, the crystal structure is crucial for the dissolution behaviour and therapeutic effectiveness of drugs and dosage forms.

He also referred in that connection to the extracts submitted along with his written submission from the various pharmaceutical text books and reputed journals which were stated to be demonstrating conclusively that by increasing bio-availability of drug enhanced its efficacy.

On the reference of R 5 to the decision in the case of Takeda Chemical Industries Ltd. and Anr. v. Alphapharm Pty. Ltd. and anr. dated June, 28, 2007 [see paragraph 7(5)] he submitted that so far as the principles were concerned, this decision fully supported the case of the Appellant.

On the reference of R5 to the decision of the US Court of Appeal in Pfizer Inc. v. Apotex, Inc, at page 28 where the Court observed - "*As we have said before, [e] very case, particularly those raising the issue of obviousness under Section 103, must necessarily be decided upon its own facts*," he said that it was a well settled proposition of law that every case had to be decided on its own facts. Further, referring to the observation of the Court at page 37 of the judgment - "However, there is precious little (if any) evidence to support any implicit finding by the district court that amlodipine maleate is actually the closest prior art compound to amlodipine besylate. Indeed, the prior art of Schmidt, spiegal, Carabateas, and Barth,

discussed above, evidences that one skilled in the art would expect an acid addition salt made from bezene sulphonate to have good physicochemical properties.", he said that it was clear that this decision was rendered on the ground of paucity of evidence in that case. He added that even more importantly it was the unrebutted testimony from Apotex that had convinced the Court for its conclusion as observed on page 38 of the judgment - "Unrebutted testimony from Apotex's expert evidence that, given the range of 53 anions disclosed by Berge, one skilled in the art would expect those anions to provide salts having a range of properties, some of which would be superior, and some of which would be inferior, to amlodipine maleate. Pfizer has simply failed to prove that the results are unexpected Boesch, 617 F. 2d at 278."

On the argument of R 5 that bio-availability was not mentioned in the application for patent he submitted that what factors were required to be mentioned in the specification for a patent application under Section 10 of the Act were already been dealt with. It would be clear that it was not necessary to refer to bio-availability in the patent specification. However, he pointed out that the specification contained the advantages of the beta crystalline form relating to flow properties, its thermodynamic stability, being less hygroscopic, better storage and better processibility. He also submitted that the contention of R 5 relating to reports of NT, Delhi and IICT, Hyderabad had already been dealt with earlier. On the argument of R 5 referring to para 13 of the judgment of Hon'ble Madras High Court observing "enhanced efficacy" in Section 3(d) referred to better therapeutic efficacy he said that it was already shown from various text books/reputed journals cited earlier that increased bio-availability led to enhanced therapeutic efficacy. The principle laid down by Madras High Court supported the case of the Appellant and it stood by the same.

(11) Appellant's replies to the counter-arguments on behalf of R 1, R 2 and R 8:

> Shri Shanti Bhushan in response to the arguments on behalf of R 1, R 2 and R 8 stated that the Ld. Addl. Solicitor General (ASG) had not advanced any new argument, but only read the orders of R 8, some portions of Madras High Court judgment dealing with the validity of Section 3(d) and some paragraphs of the counter affidavit filed on behalf of the Union of India. Ld. ASG also referred to different Articles particularly Article 27 of the TRIPs agreement which had already been dealt with earlier. In that connection Shri Bhushan brought a reference to the Article 64 of the TRIPs relating to dispute settlement and Articles 65 and 66 relating to transitional arrangements. He stated that by said Article 64, it was always open for a member country to take a dispute to the dispute resolution body against any violation of the TRIPs agreement by another member country and it was this reason that all member countries must construe their own law in a manner which was in conformity to TRIPs as otherwise the member country violating the TRIPs would be exposed to the risk of being dragged to the Dispute Settlement Board and made answerable for not conforming to the TRIPs Agreement.

Shri Shanti Bhushan alleged that the Ld. ASG had contended in his counter-arguments that it was only if the Controller failed to take into consideration relevant factors jurisdiction of the Appellate Board would come in. To this, Shri Bhushan replied that the appeal to the Appellate Board was not a restricted appeal but a full fledged appeal including facts and laws under Section 117A of the Act. The Appellate Board was fully competent to take its own view on the facts and laws and rules. Evidence in form of affidavit could also be taken cognizance of. In that context, he referred to following passages from three Supreme Court decisions:

(i) 1962 supp. 1 SCR 933 at page 939 where the following proposition has been laid down:

> *The Distinction between an appeal and a revision is a real one. A right of appeal carries with it a right of rehearing on a laws as well as fact, unless the statute conferring the right of appeal limits the rehearing in some way as, we find, has been done is second appeals arising under the Code of Civil Procedure.*

(ii) (2003) 6 SCC 669 para 17

> *An appeal is continuation of the proceedings; in effect the entire proceedings are before the Appellate Authority and it has the power to reviewthe evidence subject to statutory limitations prescribed. But in the case of revision, whatever powers the revisional authority may or may not have, it has no power to reviewthe evidence, unless the statute expressly confers on it that power. It was noted by the four judge Bench in Hari Shankar v. Rao Girdhari Lal Chowdhury that distinction between an appeal and a revision is a real one.*

(iii) MANU/SC/0532/1994

The Act provides for a regular first appeal to the High Court under Section 8A, from the order passed by the Forest Tribunal. On a mere look of Section 8A of the Act, we are of the viewthat in deciding the appeal under Section 8-A of the Act, the High Court has got very wide powers. It is not hedged in by any limitation. When the matter comes up before the High Court, it is the correctness and propriety of the order under appeal which arises for consideration. The High Court can independently consider the evidence and satisfy itself whether the findings and conclusions arrived at by the Forest tribunal are proper. The High Court is competent to adjudicate all questions of fact and lawand record its findings. It can reappraise and re-evaluate the evidence an arrive at its own findings and conclusions.

12) Supplementary arguments on behalf of R 4:

A) Section 10(4): Contents of Specification:

The Appellant relied upon Section 10(4) to contend that the Appellant was not supposed to incorporate the prior art and the significant characteristics of the invention/product in its specification because there was no such mandate under the Act. On this contention R 4 submitted that such an argument was totally erroneous and absurd. Clause (a) of Section 10(4) mandated that "every complete specification shall fully and particularly describe the invention". In order to fully describe the invention one had to demonstrate in the specification as to how the claimed invention involved feature of technical advance as compared to existing knowledge as per the requirement of Section 2(1)(ja), of the Act. For such comparison, existing knowledge i.e. prior art and more importantly closest prior art had to be disclosed in the specification. Unless and until the existing knowledge was disclosed and the same was compared with the claimed invention, the feature of technical advance could not be shown or claimed. Similarly, to establish novelty and patentability against the objection of Section 3(d) (as applicable here) disclosure of the closest prior art was absolutely necessary. Even for establishing a case of selection patent as the Appellant was contemplating, disclosure of prior art from which identification or selection of advantageous compounds or properties was made was specifically needed. Thus, the Appellant's plea in this regard was totally unsustainable.

(B) Rule 8(2) of the IPAB (Procedure) Rules, 2003:

The Appellant relied upon Rule 8(2) of the IPAB (procedure) Rule, 2003 to advance the argument that an Appellant while preferring the appeal before this Board might file any additional/further evidence without any leave. On this contention, R 4 submitted that the Appellant had completely misread and misconstrued the provision of said Rule 8(2). The said rule merely suggested that evidence might be filed along with the appeal. The 'evidence' occurring in the said Rule 8(2) should not be stretched to mean "additional evidence." The order of the Ld. Controller could not be impugned on the basis of evidence which the Ld. Controller had no occasion to advert to. For any additional evidence/material to be taken on record, a clear case had to be made out by a party and such party must make an interlocutory application/petition setting out grounds for not filing such evidence before the Ld. Controller. There was precedence that this Hon'ble Appellate Board had dealt with the matter relating to additional evidence. Without the prejudice to the above and in any case, the affidavits of Dr. Sutter and Prof. Frampton had been submitted for the first time, before this Appellate Board. Evidence of Dr. Sutter was filed as an evidence in a separate suit before the Hon'ble High Court of Mumbai. The said suit had already been withdrawn without any leave and liberty. Said Affidavit was filed and taken as evidence for the purpose of the said suit and Dr. Sutter never deposed before this Board. Similarly, affidavit of Prof. Frampton, the US Court decision as well as IPER had not been filed before this Appellate Board as evidence. Therefore, even though the contentions of the Appellant was taken as correct, these materials could not be considered as "evidence" within the meaning of said Rule 8(2).

(C) Clear proof of admission of anticipation over 1993 patent:

The Appellant had categorically admitted on page 29 of its written submission that the beta crystal form of imatinib mesylate although a new invention continued to be covered by the 1993 patent. It further stated that in countries where 1993 patent had been obtained, the salt and other forms were covered by both the 1993 patent as well as the impugned application. These averment and arguments made it amply clear that the Appellant admitted that the salt of imatinib mesylate was inherently existed in the beta form and as such the claim to the beta form in the impugned invention was hit by anticipation. No higher proof was required.

(D) Document relating to the study conducted on rats for determining relative bio-availability not acceptable being only a draft:

R 4 also objected to the document relating to the study conducted on rats for determination of relative bio-availability as being only a "draft' as mentioned therein. No importance, therefore, could be given to the said study and document. Consequently, the affidavit of Dr. Massimini also could not be legally valid and acceptable.

13) Supplementary arguments on behalf of R 6 and R 7:

Shri Lakshmi Kumaran, learned Counsel for R 6 and R 7 also made some additional objections as supplementary arguments which are given below:

(A) Appellant did not disclose prior art within its knowledge that was relevant for making a judgment regarding patentability of invention:

He submitted that the senior counsel appearing on behalf of the Appellant had categorically admitted during the course of the hearing from a query from the Appellate Bench that imatinib mesylate was known prior to 1998, the said compound was disclosed in "Cancer Research" article of Jan.1 1996 and that in order to ensure full and fair patent examination complete disclosure from the patent applicant was expected and was a customary practice. Since granting a patent was a tremendous concession on the part of the society to forego competition with respect to a granted invention, the Applicant (Appellant) being with intimate knowledge of the field of its invention was expected to give the full disclosure of the invention including the prior Article While the Appellant had argued that it was under no duty to disclose prior art, it did cite another 1996 "Nature Medicine" Article. Unlike the 1996 Cancer Research article, this article did not contain any reference to the salt of imatinib. The Appellant cited this article to reiterate its position that no salt of imatinib was disclosed prior to the impugned application. Thus, the Appellant's action clearly increased the scope of the invention, that was possible before the Patent Office. The implications of such a failure were also far reaching. Clearly beta crystal form was not two steps removed as imatinib mesylate was already known. The examination of novelty, non-obviousness and Section 3(d) also would change when the prior substance being compared to was imatinib mesylate as opposed to imatinib. Thus, disclosure of prior art within the knowledge of the Appellant became important. He added that the bounds of an invention could not be determined unless the prior art surrounding the invention was known. For determination of novelty and inventive step (non-obviousness) prior art was extremely important as a patent was not to be granted for products or processes that already existed in the prior Article International Search Report for the PCT application found that the 1993 patent disclosed the acid addition salt of imatinib such as imatinib mesylate, applying the test as provided in

the EPO guidelines relied on by the Appellant. Further, the Guidelines itself alluded to the fact that disclosure along with the generally available knowledge about preparation of the product, enabled it to be made and therefore, it became prior Article Since the 1993 patent had indicated the means for preparing imatinib mesylate the 1996 Cancer Research article must be considered as the prior Article Thus, the failure to disclose the prior art was an important consideation in this case.

(B) No comparison provided between properties of imatinib mesylate and beta crystalline form of imatinib mesylate:

Shri Lakshmi Kumaran further submitted that in order to satisfy Section 3(d), new form of a known substance must exhibit enhancement of known efficacy. In the present case, it was established that the known substance was imatinib mesylate and not imatinib free base. However, the Appellant only provided data comparing bio-availability of free base with that of beta form of imatinib mesylate. Without prejudice to the argument provided that bio-availability could not be equated to efficacy, the Appellant was required to provide data comparing efficacy of imatinib mesylate and the beta form of imatinib mesylate. Though the Appellant forwarded an argument raised (for the first time) before this Appellate Board during rejoinder that imatinib and imatinib mesylate had the same properties and therefore, the data for one could be adopted for the other. The basis of this contention was a single sentence from the 1996 Cancer Research article which stated as "No significant difference in results could be seen between the two forms of CGP 57148." To this Shri Lakshmi Kumaran submitted that this single sentence cited by the Appellant did not support the view that the properties of the two forms were same. The article clearly provided that the results and not properties of the two forms had no difference. The difference in results and properties was significant. Result referred to the desired therapeutic activity that a compound could have, while property encompassed the physicochemical characteristics displayed by a compound. Shri Lakshmi Kumaran explained the matter with an illustration of two drugs, namely, Saridon and Amruthanjan, used to cure headache. He said the result of using these drugs was the same that of reduction/curing of headache. But that did not mean that properties of solubility, hygroscopicity and stability were same. For example, Saridon was sold in solid tablet form while Amruthanjan was available in semi-liquid state. Therefore, while the results of the two drugs could be same, the properties need not be the same. In certain cases, the salt forming groups could also have therapeutic effect and hence it became necessary to test the different forms of the compounds to ensure that the same desired therapeutic effect was observed. In the present case, imatinib free base had cancer inhibiting effect on Chronic Myeloid Leukemia (or "CML"). Imatinib mesylate, which was a salt of imatinib formed from a reaction with methanesulphonic acid, could be used for inhibiting cancer only if it displayed the same effect or results as imatinib i.e. the salt forming group must not modify the therapeutic effect. In this paper in question, the authors undertook the tests to verify that imatinib and imatinib mesylate had the same effect on cancer (much like the above Saridon and Amruthanjan example). The authors found that the two forms of the compound indeed displayed the same result. However, he submitted that this determination could not be extended to suggest that the properties and characteristics of imatinib free base and imatinib mesylate were the same, such as solubility, hygroscopicity and stability. He added that the contention that the authors were concerned with the final effect of the two forms

on cancer and not their properties, was supported by the overall reading of the paper. For example, the physicochemical properties of the two forms of their comparison were nowhere discussed in that article. Further, the findings were focussed on the effect of imatinib on different forms of cancer. Thus, the "results" that the article contemplated was only with regard to whether the different forms of imatinib were suitable for curing cancer and not whether imatinib free base and imatinib mesylate exhibited the same properties. He also invited to the Berge article titled "pharmaceutical salts" [see paragraph 7(3) above] specifically Table III where methanesulphonic acid was used to increase solubility. It was, therefore, inconceivable how a reputed company like the Appellant could make a statement that imatinib free base and imatinib mesylate salt (other than beta form) would have same bio-availability. He submitted that the properties of imatinib and imatinib mesylate could not be equated. Consequently, it could not be contended that experimental evidence shown for imatinib vis- à -vis beta form of imatinib mesylate could be adopted for the comparison between the data for imatinib mesylate and the beta form of imatinib mesylate. Since such adoption of data was not possible, the Appellant had failed to demonstrate enhanced efficacy of the beta form with reference to imatinib mesylate (known substance) and hence failed to satisfy Section 3(d). The Appellant also did not reply to this argument of R 6 and R 7 in its written submission.

(C) 1993 patent covered Gleevec, the beta Form of Imatinib mesylate:

The Appellant in its reply in writing to R 4's argument stated that the 1993 patent covered Gleevec, which was the beta form of imatinib mesylate, the 1993 patent must, therefore, anticipate the drug. The Appellant did not explain their position on this submission. Hence 1993 patent anticipated the impugned application. The impugned application must, therefore, be rejected.

(D) Higher solubility and bio-availability of salt not unexpected properties:

The Appellant again contended that the conversion of the free base imatinib into imatinib mesylate showed unexpected properties. On this Shri Lakshmi Kumaran submitted that methanesulphonic acid was specifically used to improve the solubility (and automatically the bio-availability) of the salt compared to the base. He again brought our attention to the article titled "pharmaceutical Salts" where Table III (supra) clearly showed that the expected property of using methanesulphonic acid was to increase solubility of the free base compounds. Therefore converting imatinib to its mesylate salt was expected to have improved solubility and therefore did not show any unexpected property.

(E) The impugned application silent regarding efficacy:

Shri V. Lakshmi Kumaran submitted referring to the Appellant's contention that extensive research and different tests were conducted to arrive at the beta form of imatinib mesylate. The impugned application also described many advantageous properties such as improved stability, improved flow properties and lower hygroscopicity. However, while such properties of the product were discussed, no mention of enhanced efficacy or safety was discussed. He further submitted that these properties were not discussed because these improvements were not in contemplation when arriving at the beta form of imatinib mesylate. He added that the properties such as thermodynamic stability, flow properties and hygroscopicity were important to formulate the active ingredients in

capsule or the desired product form. However, these properties did not affect the actual therapeutic effectiveness of the compound, which the Appellant could not be imputed in duty to discuss enhanced efficacy in the impugned application as the concerned provision was only conceived and legislated after the application was made, it was nevertheless important to note that while other properties were extensively discussed, the application remained silent on properties relating to efficacy. Therefore, it was safe to conclude that the Appellant's efforts were not directed to improving the efficacy of the ingredients but merely to improve its delivery and formulation. Under the Section 3(d) the efforts directed to the improvement of efficacy were recognized as patentable but not those encompassing improvement to other properties and thus the impugned application failed in satisfying Section 3(d).

F) Affidavit of Massimini inadequate:

Dr. Massimini's affidavit on the method of administration of the drug in solid compound or in solution form in the tests on the rats was unclear. In his original argument Shri Lakshmi Kumaran had submitted that in vivo testing in rats typically the drug was to be administered in solution form rather than solid capsule form considering the small size of the rats and in line with ethical consideration as stated by Dr. Massimini. The sole basis for the Appellant's contention was the phrase "Formulation: Three capsules per rat" to support its view. He submitted that formulation was not the same as administration. Formulation merely referred to the dose equivalent that was to be provided to the rat for testing. In the present affidavit, the test report had not provided any protocol for administering the capsules to the rat. In the absence of such a protocol, this affidavit was inadeqauate in explaining whether a solution form or solid beta form of imatinib mesylate was administrated to the rats. Further, the affidavit of Dr. Massimini stated that tests were conducted in line with ethical considerations. Therefore, It was more probable than not, that the drug was administered in solution form. Since, crystalline form would be lost upon dissolution in the stomach, it was unlikely that this method of administration also would be showing efficacy of the beta form. The Appellant replied to the above submission by introducing a 1983 article that described how capsules could be administered to rats. It was submitted by R 6 & R 7 that this 1983 article did not prove that rats must have been administered as capsules and second it could not make up for the deficiency in the affidavit. Referring to that article, it was further submitted by R 6 and R 7 that while the article did provide a means of administering capsule, it did state that it was not always desirable, because the process was not ideal to stress the animals particularly if the administration had to be repeated on regular basis. The other problem was the difficulty in making minicapsules required for such use. Thus it was unlikely that such tortuous method was used for the administration. Even if such method was used, according to the said article the capsules were dissolved immediately in the stomach. Since crystalline form would be lost upon dissolution, it was unlikely that this method of administration also showed efficacy of the beta form. Rather, it was safe to conclude that the relevant data was only applicable for imatinib mesylate and not the beta form.

14) Appellant's supplementary replies to the further arguments on behalf of R 6 and R 7.

Shri Shanti Bhushan in response to a reference to the further arguments of Shri Lakshmi Kumaran on behalf of R6 and R7 at the hearing to the rat study for the determination of comparative bio-availability contending that it was not possible to feed rats with capsules as the mouth and gullet of a rat was so small that it was impossible to put capsules through the gullet in the stomach of the rats, submitted that it was indeed possible

to feed the rats with mini capsules orally in solid form.

In that connection, Shri Bhushan referred to an article "A simple Method for Oral Administration of Drugs in solid Form to Fully Conscious Rats" published in 1983 by the Appellant. A copy of the same was also annexed to the supplementary written submission as Annexure G. Referring to a passage therefrom he submitted that often pharmacological investigation required the drugs to be administered only in solid form orally. That was achieved by packing the drug in a gelatin capsule and placing this in oesophagus or stomach of the animal with a stomach tube etc. and miniature capsules of the drug being recently commercially available helped in administering the drug on solid forms. Thus, the rats were fed with the drug in solid form only and not in solution form as per the "study design" in the experiment which was actually the protocol of the experiments. On the non-inclusion of a reference of imatinib mesylate as prior art in the specification available in the article of "Cancer Research" dated Jan 01, 1996 relied upon by R 6 & R 7 in their argument, Shri Bhushan submitted that the said article did not constitute a prior art nor any reference to it was required to be given in the specification under Section 10(4) of the Act. He added that since the Appellant's invention was related to a selection patent, this was fully described in the specification which further required that the selection must show special advantages and since the imatinib mesylate by itself had not shown any advantage whatsoever over imatinib free-base, it was only later when its beta crystalline form was discovered which was found to have various advantageous properties that this discovery became an invention under the law of selection patent. In fact, apart from imatinib mesylate, other salts even hundreds of them containing imatinib might have also been prepared and experimented upon by the Appellant. It would be ridiculous to expect a reference being made to all those failed salts in the application for patent. That was why it was important that the Patents Act only required the invention alone to be specified in the application and not all the possible experiments, which the patent applicant might have conducted on various substances before he was able to make the invention, for which alone he was asking for a patent. Further, the method of preparation of the product for which patent was being claimed, another requirement under said Section 10(4), was also clearly described in the application. The another further requirement was furnishing of the claim or claims defining the scope of the invention, which the Appellant had also duly complied with. He further added that the said article of 1996 did not disclose anywhere as to how imatinib mesylate could be prepared. This fact would demonstrate that the 1996 article could not be regarded as part of the prior art in this context. In this connection, the Appellant made a reference to the Guidelines for Examination in the European Patent Office - Chapter IV under the heading "Enabling disclosure of a prior document" a copy of which was also annexed with the written submission, containing the following extract therefrom:

> *Subject-matter described in a document can only be regarded as having been made available to the public, and therefore as comprised in the state of the art pursuant to Article 54(1), if the information given therein to the skilled person is sufficient to enable him, at the relevant date of the document (see IV, 7.3) to practice the technical teaching which is the subject of the document, taking into account also the general knowledge at that time in the field to be expected of him (see T 26/85, OJ 1-2/1990, 22, T 206/83, OJ 1/1987, 5 and T 491/99, not published in OJ).*
>
> *Similarly, it should be noted that a chemical compound, the name or formula of which is mentioned in a prior-art document, is not thereby considered as known, unless the information in the document, together, where appropriate, with knowledge generally available on the relevant date of the document, enables it to be prepared and separated or, for instance in the case of a product of nature, only to be separated.*

He submitted that the patent law, therefore, made it clear that if a chemical compound whose name or formula was mentioned in a document, but which did not disclose as to how that compound could be prepared would not be regarded as a known compound. In fact this very proposition had also been laid down by the House of Lords in the matter of Asahi Kogyo KK's Application [1991 RPC 485]. The House of Lords at page 517 observed as thus: "The mere disclosure of a product without any directions as to how to make it, where such is not inevitable made plain from the mere disclosure of the product, does not make the product "available to the public". If the public do not know and are not told how to make something, then it is not available to them. Only an "enabling disclosure" suffices to anticipate." He also added that the Appellant could not be held guilty of suppression of facts by not making reference to imatinib mesylate in its application for patent as alleged by the Respondents because it would be pointless to make a reference to imatinib mesylate particularly when in vitro it did not show any improvement in its properties against imatinib free base. Further, no significant difference in results between the two forms namely imatinib mesylate and imatinib free base could be seen as evident from the said article dated Jan 01, 1996 itself.

(15) Appellant's supplementary replies to the further argument on behalf of R 4:

> On the contention of R4 that the reference of 1996 Cancer Research Article (supra) should have been included in the Appellant's patent specification as it fell under the requirements of Section 10(4) of the Act, Shri Shanti Bhushan submitted that the matter was already dealt with earlier. The Appellant had fully complied with the requirements of said Section 10(4)(a) to (d) by fully disclosing the invention contained in the specification. Accordingly, there was no such requirement to include therein the reference of the said article of 1996.

On the objection of R 4 that Dr. Sutter's affidavit could not be taken on record as the original suit, namely, the Exclusive Marketing Rights, which was filed in the Bombay High Court had been withdrawn, Shri Bhushan submitted that there was no such law that same affidavit could not be used in two different proceedings. If the affidavit had been filed in the Bombay High Court for the purpose of the EMR suit, there was no restriction in law that same affidavit could not be used as a part of the evidence of the Appellant for the purposes of the patent appeal before this Appellate Board. A photocopy of a document was normally regarded as reliable unless its contents were challenged. What was important was that Dr. Sutter had made this statement in an affidavit. So long as by producing a photocopy which would show to this Appellate Board that Dr. Sutter had made this statement in an affidavit, it would be prima facie very reliable and could be relied upon by the Appellate Board. This objection should, therefore be disregarded as being frivolous as also no reason whatsoever had been given. He added that this transferred appeal was originally an appeal pending in the Madras High Court which earlier had been filed in the form of a writ petition and that very writ petition had been converted into an appeal under an order of the said High Court. Along with the said writ petition, the affidavit of Dr Sutter had been filed in support thereof which ultimately became an appeal, which now stood transferred to this Appellate Board. A Counter-affidavit had been filed by the Respondent in the High Court also, which was also on the record of this Appellate Board. No objection against Dr. Sutter's affidavit on the ground that instead of filing the original in the High Court, a photocopy of the affidavit had been filed, had been taken in the reply filed in the High Court and therefore, on this ground also, this objection deserved to be rejected. An affidavit which had been sworn for the purposes of one legal proceeding did not lose its veracity merely by the fact that, that legal proceeding stood withdrawn. It continued to be a statement by a person on oath and therefore, ought to be relied upon until it was shown that it did not contain a true statement.

On the further argument of R 4 that the document relating to the study conducted on rats concerning determination of relative bio-availability (supra) furnished by the Appellant was described as a "draft" only, Shri Bhushan pointed out that the authors of the document were Wiegand H. and Picard F. and the document status was shown to be "draft" and the release date was shown to be September 16, 2005. However, this was signed by the five experts on the next page on September, 21, 2005. These facts would demonstrate that when this study report was submitted, its draft had been prepared by Weigand H. and Picard F. But it became a final document only after the same was approved by the Group Leader Camenisch G. and Section head of Absorption Distribution Metabolism and Excretion, Gross G., and, Section Head of Bio-analytics Kretz O. It was after these three experts who approved the document and signed the same on 21, September, 2005, that its status ceased to be that of a 'draft' and it became a final document making the results of the study authentic. In fact, Dr. Massimini filed his affidavit one day subsequent to the date when the study was approved by all the experts and signed and the entire document relating to the study was annexed to his affidavit.

8. Disposal of the Misc. Petition No. 33 of 2008 made by R 3:

R 3 in its Misc. Petition dated 13th Nov. 2008 [Paragraph 7(4) above] had sought to introduce fresh evidences as Exhibits A, B, C and D enclosed therewith by way of prior art documents pertaining to this case which were some articles published during 1996 and 1997. It states in its petition that these documents could not be produced earlier despite the exercise of due diligence. It also states that these documents are necessary to enable the Appellate Board to pronounce a proper judgment on the issue of patentability of the alleged invention after taking judicial notice of these documents. After hearing the learned Counsel and perusing the petition, we are of the opinion that the admission of these additional documents would be justified as the documents were not available to the R3 notwithstanding the exercise of due diligence and the same would be required so as to enable this Bench of the Appellate Board to pronounce order. More importantly, there is no objection raised by any of the parties including the Appellant against the taking on record of the said additional evidences. We, accordingly allow the miscellaneous petition and take the additional documents on record.

9. Preliminary issues in dispute and findings thereon:

We are confronted with a few preliminary issues which needs to be resolved before analyzing and evaluating the main issues in the appeals (paragraph 6 above). The said issues and our findings are given below:

i) Admissibility of new affidavits/documents/arguments relied on by the Appellant.

R 3 and particularly R 4 objected to the introduction of new evidences at the appellate stage by way of affidavits of Dr. Sutter and Dr. Frampton, footnote to the bar chart at page 305 and chart/graph at pages 306 and 307 of Vol. B of Appellant's compilation, new documents, namely, IPER, appeal filed before the Appellate Authority in USPTO and the decision thereon with related papers on behalf of the Appellant without any miscellaneous petition/leave of this Appellate Board as

required under the CPC, 1908. We have considered the response by the Appellant thereto [paragraph 7(7) and 7(9) above]. We observe that these evidences/documents are a part of the instant appeals from the High Court of Madras which were originally filed along with Writ Petitions under Article 226 of the Constitution, converted into appeals by the High Court and transferred to this Board for adjudication (see paragraph 2 above). In a writ there is no limitation imposed to the petitioner on the introduction of any new evidence/document/argument in support of its case. In the instant case, the Appellant appears to have adduced these matters in the said writ petitions to strengthen its case which is permitted by law. We don't find any fresh document filed by the Appellant subsequent to the said writ petitions (later converted into appeals) and were transferred to this Appellate Board. As such this Appellate Board did not take on record any fresh evidence/document for which any miscellaneous/interlocutory petition or any leave of the Appellate Board is required. The Procedure laid down by the Code of Civil Procedure, 1908 does not apply to the Appellate Board. However, after filing an appeal if the Appellant desires to add any new evidence/document it needs to take leave of the Board by filing miscellaneous petition as prescribed in the IPAB (Procedure) Rules, 2003. In any case, Sub-rule 55(4) of the Rules, does not apply here as the instant proceeding is not before the Controller. On the R 4's further objection that affidavits of Dr. Sutter and Dr. Frampton were not deliberately submitted before R 8 and only submitted at the appellate stage we find that the Appellant has not responded to the same.

Regarding the admissibility or otherwise of the new affidavits / documents in a transferred appeal, under the provisions of Section 117G of the Act, any pending proceedings before the High Court and transferred to the Appellate Board pursuant to that section provides that the Appellate Board may proceed with the matter either de novo or from the stage it was so transferred. Thus the Appellate Board has the discretion to proceed in such transferred proceedings de novo or from the stage it was transferred. In the present appeals this Appellate Board felt that it may not be feasible to start the proceedings afresh because that would definitely take a longer time and it will not be in the interest of litigating parties. Therefore, the Appellate Board has proceeded from the stage it was so transferred this Appellate Board. In view of this, the Appellate Board is not required to go into the issues whether the new affidavits / documents in question ware validly filed or not. The Appellate Board, having decided to proceed from the stage the proceedings / appeals so transferred by the High Court of Madras, we do not consider it necessary to traverse through the decisions cited by the parties.

Respondents also generally objected that a new argument of selection patent has been raised only at the hearing at the Appellate stage. [see paragraph 7(7) to 7(11) above] We have noticed that the Appellant had indeed presented its case before R 8 in the pre-grant oppositions also as a selection patent. The Appellant's written arguments (dated Dec. 21, 2005) submitted to the R 8 defending opposition by R 3 had also made a reference of "selection patent". Same was the case in its written arguments dated Oct.. 21, 2005 in the opposition by R 4 and dated Nov. 11, 2005 in the opposition by R 7. We also observe that R 4 in its written arguments dated Oct. 21, 2005 in the opposition before R 8 in p 7-8 had also responded to the applicability of "selection patent" in respect of this case (see also page 440, Vol. B, of Appellants compilation). The R2 has also in his common affidavit stated at paragraph 14 that the Appellant's patent application filed in India is nothing but a "selection patent application." Respondents also got sufficient opportunity to counter the same. We see R 8 has not made any reference of selection patent in the impugned orders. Therefore, the Appellant is in its right to raise the issue again in these appeals. In the present case, the Appellant's line of argument of its invention as a selection patent, cannot be said to be a new argument. The objection that the argument of selection patent is raised at the appellate stage, therefore, cannot be accepted.

ii) Admissibility of affidavits as a part of withdrawn suit

R 4 objected to the affidavit of Dr. Sutter (and also Dr. Frampton) not to be considered in this appeal on the ground that the same were a part of withdrawn suit filed by the Appellant before the High Court of Mumbai and consequently the contents of the same deemed withdrawn and also had no legal value. We have duly considered the Appellant's response thereto [paragraph 7(7) supra] and also agree to the same including that there is no restriction in law that same affidavit can not be used as a part of the evidence for the purposes of the patent appeal before this Board. We observe that R 4 is not disputing the existence of the original affidavits, legality or authenticity of the contents thereof. In our

opinion, if an affidavit is duly sworn in, its contents therein are his own statement made by the deponent on the sworn date and is true to his knowledge and belief. In the instant case, the Appellant has relied upon the same being relevant and appropriate in its consideration by filing the copies thereof in the present transferred appeals (originally Writ Petitions). The contents of these copies of the affidavits have not been disputed by any of the Respondents as being tampered with or falsified. We have already stated that the affidavits in question having been transferred by the High Court as a part and parcel of the records of appeal, we do not consider it necessary to go into the legality or otherwise of their filing with the Writ Petitions. Accordingly we are of the opinion that the copies of the affidavits of Dr. Sutter and Dr. Frampton can not be rejected on the ground that these are a part of a withdrawn suit.

iii) Reliability of affidavits where the experts have not conducted experiments themselves

R 3 & R 4 objected to the affidavits of Dr. Manley & Dr. Massimini who had not done any independent study/experiment themselves to give their expert opinion and have not disclosed the protocol followed in the experiments. We have found that the Appellant has not made any specific response to this. However, we have observed that the deponents here are the Project Team Head and Group Leader, respectively, in the company. In our opinion, it is not necessary for a Group Leader or Project Head of any organization to carry out an experiment himself for getting a result of any particular experiment. He usually supervises the experiments through a technical team of experts who are supposed to carry out the experiments under his supervision and guidance and report to the Head or Group Leader and on the basis of the report, the leader comes to the conclusion. In the instant case also we have no reason to disbelieve that these deponents have made their conclusions based on the experiments carried out by their trusted and reliable team of experts. In the case of Dr. Massimini's affidavit the study on rats referred to in para 9 thereof was carried out by different specialists approved by different Group Leader / Section Heads in the Appellant's laboratory. The deponents have also declared on oath that their statements are true and correct to their knowledge. Accordingly, we have no reason to reject these affidavits on the ground that their statements or conclusions are based on experiments not done by themselves.

iv) The report of the rat study is just a draft

To this objection of R 4 we have analysed the response thereto by the Appellant [see paragraph 7(15) above]. We agree with the plea of the Appellant that initial draft report dated September 16, 2005 has been approved by the Group Leader and other Heads on September 21, 2005 and this full document is required to be taken into consideration. After the approval by the Project Team Head or Group Leader, as the case may be, the report becomes complete and therefore, we are inclined to take cognizance thereof.

v) Admissibility of affidavits avering false/misleading statements

R 4 objected to the affidavits of Dr. Manley and Dr. Massimini which contain false and misleading averments, namely "only base disclosed not salt" in the 1993 patent, whereas salt is in fact disclosed. However, the Appellant has stated in its response that the salt is disclosed but not enabled. We observe that in para 6 of Dr. Manley's affidavit it is stated that "said compound was exemplified in its free form, ("Free Base") and not as a salt" in the 1993 patent is correct. In fact, in the 1993 patent no acid addition salt of the active compound (of formula 1) was exemplified. Same observation applies to Dr. Massimini's affidavit also. As such, we do not find any false statement given by these deponents. Other objection, namely, Dr. Massimini's affidavit states that salt exhibits higher bio-availability whereas the Appellant's specification categorically states that all the inhibitory and pharmacological effects of the free base can be found in the salt and thus misleading, we find that the Appellant

has also not made any specific response thereto. However, we observe that there can not be any confusion as both the statements are correct. The matter is expected to be clearer when we proceed further and deal with the main issues of the appeals. Similarly R 4 objected to the statement given by Dr. Manley & Dr. Massimini and other deponents in their affidavits that "base" was never tested before, whereas the 1993 patent discloses otherwise. We have also seen that the Appellant has not made any specific response thereto. However, what we understood is that the base was never tested for evaluating relative bio-availability. We, therefore, don't find any falseness or ambiguity in these affidavits and therefore there is no valid reason in rejecting the aforesaid affidavits.

vi) Admissibility of affidavits if biased/partisan:

R 4 objected to the admissibility of the four affidavits relied upon by the Appellant being sworn in by its employees on the ground of bias and hence unreliable. We have also examined carefully this matter by going through each of these affidavits in question and also the Appellant's response thereto [see paragraph 7(7) above]. We agree with the Appellant that the deponents are indeed experts of high order in their respective fields of specialization, also particularly related to the technology involved in the impugned invention. Except Dr. Frampton, rest of the deponents are either the employees of the Appellant or its group company. Dr. Sutter also is one of the inventors in the present invention in question. Each deponent has given his own expert opinion on the matter. It is not unlikely that their opinions match with that of the Appellant or vice-versa. However, we have also found that these deponents have put forward their averments which strongly favour or back the Appellant's case. For instance, Dr. Massimini, an employee of the Appellant in his affidavit in paragaraphs 8 and 11 has acted as an agent or representative of the Appellant to meet the requirement of the Patent Office objection under Section 3(d) on patentability of the impugned patent application inferring that increased bio-availability means increased efficacy by a rat study and thus meeting Section 3(d). He has clearly worked for the Applicant (Appellant) and his averments in paras 8 & 11 can not be called his unbiased opinion. Similarly, Dr. Manley, also an employee of the Appellant, in paragraph 9 of his affidavit also argues or speaks on behalf of the Appellant as a spokesperson or an agent inter-alia to establish that imatinib mesylate has improved efficacy with respect to the free base, which is a disputed matter thus increasing the Appellant's prospect in the case. Similarly, Dr. Sutter also an employee of the Appellant, in its affidavit in paragraph 9 argues in favour of the Appellant and speculates that the samples of imatinib free base provided to the Indian Institute of Chemical Technology (IICT) would invariably contain seed of imatinib mesylate beta crystalline form (Thermodynamically more stable) as a contamination and thus any crystalline imatinib mesylate produced therein must also inevitably contain the beta crystalline form of imatinib mesylate. We don't find that his above statement is supported by any actual experiment on the subject compound but based on a presumption from a number of cases published in scientific literature referred therein. The said literature does not give any indication that the observation made therein is actually or invariably applicable also to the imatinib mesylate of the instant case. Thus, the averments of Dr. Sutter cast doubt about the correctness thereof. In the case of affidavit of Dr. Frampton, who of course is not an employee of the Appellant, in paragraphs 12-19 of the affidavit argues even with decided case laws as a technolegal counsel on behalf of the Appellant in its favour on the disputed matters in the present appeal. From the analysis of these affidavits we are of the opinion that the deponents have lost their impartiality in making the averments, thus reducing much of their evidentiary value. However, it is an established fact that the decision on patentability is to be determined by the Judge and not by any expert or other witness [see under "Expert evidence" in page 588, the book "Patent Law" by P. Narayanan (4th Ed.) where it is reported that "*In an action for infringement it is necessary to examine each patent separately and to ascertain first what the*

patented invention really is; and, secondly, whether the defendants have used that invention. The nature of the invention must be ascertained from the specification, the interpretation of which is for the Judge, and not for any expert. The Judge may, and indeed generally must, be assisted by expert evidence to explain technical terms, to showthe practical working of machinery described or drawn, and to point out what is old and what is newin the specification. Expert evidence is also admissible, and is often required to showthe particulars in which an alleged invention has been used by an alleged infringer, and the real importance of whatever differences there may be between the plaintiff's invention and whatever is done by the defendant. But the nature of the invention for which a patent is granted must be ascertained from the specification, and has to be determined by the Judge and not by any expert or other witness". [Lindley, L.J. in Brooks v. Steel & Currie (1897) 14 RPC 46 at 73] also relied upon by R 4]. The same applies to the present case also.

vii) Rats were fed with solutions, not in solid form, thus the object of the study lost:

R 6 and R 7 contended that in the rat study conducted by the Appellant and as reported in the Dr. Massimini's affidavit to determine the relative bio-availability, the rats were fed with only solution of imatinib mesylate and not in the solid capsule form, we have gone through the response thereto by the Appellant [see paragraph 7(14) supra]. We observe that it is possible that the rats could be fed with the drug in solid form in minicapsules in conducting the study. Since the object of the study was to determine the relative bioavailability of the beta crystal form of imatinib mesylate as a solid formulation, it is expected that the rats were fed with minicapsules as given in the Annexure A under 'Study design' to the affidavit of Dr. Massimini. In the circumstances, we don't see any valid reason to doubt the Appellant's said study.

viii) Almost immediate dissolution of crystal form of the mesylate salt in the stomach loses its beta value.

To the issue raised by R 6 and R 7 that in the rat study, the mesylate salt in beta form in minicapsules, apparently administered to the rats (Annexure A; Dr. Massimini's affidavit) dissolutes almost immediately thereby losing its crystalline character and therefore losing its efficacy, we have not found any answer from the Appellant in its oral or written submission. However, we have analysed this issue. If the crystalline form of the salt disappears fast in the stomach it should at least be converted into a solution of imatinib mesylate (without any crystal form). Being also a salt, it should be very easily bio-available and show its efficacy. Therefore, we may not be wrong to infer that the relative bio-availability of beta crystal form of imatinib mesylate and simple imatinib mesylate (say amorphous) are same or at least comparable [see also sub-paragraph (xxiv) hereunder].

ix) Test data on increased bio-availability conducted on rats not statistically significant

R 3 has objected to the data on increased bio-availability of the mesylate salt (beta) being not reliable on the ground that the same is not statistically significant. We have seen the response of the Appellant thereto. We have noticed that the Appellant has contradicted this objection. [paragraph 7(9) supra]. We have also noticed that AUC (o-48) difference is shown as statistically significant ($p < 0.05$) as stated in the concluding portion of the report of the test on the rats (Annexure A of the affidavit of Dr. Massimini). It is known that the salt form improves bio-availability and other properties of a lead drug substantially. The rat study has shown that imatinib mesylate in its beta form improves bioavailability by 30% over imatinib free base. We don't find any unusualness in the result. In the circumstances, we can not reject the data derived on the rat study on the determination of relative bio-availability on the doubt that the test data is not statistically significant. Moreover, the patentability does not depend on whether the test data on the rat study is statistically

significant.

x) Appellant has sought to introduce its own conclusion to the data on the bio-availability study

R 3 and R 4 have objected to the data on the bio-availability study given in addition to Annexure A to the affidavit of Dr. Massimini by introducing footnotes to the table at page 305 and chart/graph at page 306-307 of Vol. B of the Appellant's compilation and seeking to introduce its own conclusion without support of any affidavit. We have noted the response thereto of the Appellant [paragraph 7(7) supra]. The Appellant has accepted the fact that Annexure A to the affidavit of Dr. Massimini did not contain the said footnotes mentioning that beta crystalline form of imatinib mesylate had 30% increased efficacy. But it still refers to page 5 of that Annexure A wherein he states that beta crystalline form after p.o. administration had 30% higher effectiveness compared to the free base imatinib which was very significant. We have carefully analysed the objection and the reply thereto. We observe that in Dr. Massimini's affidavit in page 5 of Annexure A, there is no specific reference of "30% higher effectiveness" for the beta crystal form over imatinib as claimed by the Appellant. Cancer curing active moiety of the drug is imatinib (CGP57148) as per the "Nature Medicine" Vol. 2. No. 5, May 1996. Its effective dose has been determined by clinical studies. As per Dr. Massiini's affidavit (Annexure B), "The recommended dosage of Glivec is 400 mg/ day for patients in chronic phase CML. Chronic phase CML is defined when all of the following criteria are met: blasts < 15% in blood and bone marrow peripheral blood basophils < 20%, platelets > 100 x 10^9/l. The recommended dose of Glivec is 600 mg/day for patients in accelerated phase. Accelerated phase is defined by the presence of any of the following: blasts = 15% but < 30% in blood or bone marrow promyclocytes = 30% in blood or bone marrow blasts plus (providing <30% blasts), peripheral blood basophils = 20%, platelets < 100 x 10^9/l unrelated to therapy." The said affidavit (Annexure B) also recommends to a maximum dose of 800 mg. That shows that even further increased dose also is not efficacious. If reduced dose is administered as being suggested by the Appellant, we understand there would be no cure for cancer though side effect may possibly be proportionately reduced. Thus the bio-availability study does not lead us to conclude that lower dose of imatinib in beta mesylate form would have same cancer curing effect as its use in the base form with a normal dose. Dr. Massinini also in his affidavit had not made such conclusion. According to the Oncology Clinical Trial Glossary of Novartis under the definition of "Efficacy" a drug passes efficacy trials if it is effective at the dose tested against the illness for which it is prescribed. In absence of any expert evidence by way of affidavit in support of this conclusion of the Appellant, we reject the same.

xi) IICT and NT experiments and the reports thereon not supported by any witness or affidavit - what is the conclusion?

The Appellant questioned that R 4 relied upon the reports on the experiments conducted at IIT(Delhi) and IICT (Hyderabad) to prove that imatinib mesylate exists only in the form of beta crystal without production of any affidavit or witness in support of those reports which or who would have thrown light on the question as to how these experiments were carried out. Appellant also questioned that although the reports were independently carried out on different dates not only the preparation of imatinib mesylate follows identical solvent in the same order by the said two agencies but the language used in describing the process is also identical using the same parameters, same timings, same temperatures and so on. We have noticed that R 4 has avoided the exact reply thereto, however, it has contradicted the Appellant's objection by stating that no one could doubt the veracity of experiments conducted by these very reputed institutes. We have carefully examined this issue. We also don't find any valid reason and answer to these questions. However, Dr. Frampton in his affidavit relied upon by the Appellant has thrown some light. His finding allows the conclusion that the study design was established by R 4 which sponsored both

the studies. We also have verified the same from the reports that the project was sponsored by R 4. Coincidence of the similarity in language of the experiments could be due to that. However, another thing comes out of Dr. Frampton's affidavit is that he has not doubted or contradicted the results of the experiments by these two institutes and that imatinib mesylate was produced in the beta crystal form only in these experiments. Appellant has also made no endeavour to disprove the results of these institutes. Thus, we can at best conclude that whether through contamination or not, imatinib mesylate in the beta form could be produced also by methods other than the ones described by the Appellant as the processes carried out in these institutes differ from the ones claimed by the Appellant. But the said experiments do not conclusively prove that imatinib mesylate exists only in beta crystal form as we know there are possibilities of number of other forms in which it can exist.

xii) 1993 patent covers GLEEVEC, the beta form of imatinib mesylate, thus anticipated

R 4, R 6 and R 7 raised the issue from the Appellant's written submission in page 29 wherein it states that "the discovery by extensive research of beta crystalline form of imatinib mesylate was a new invention but it also continued to be covered by the 1993 Patent being a salt of imatinib free base, a salt or any other form thereof would be covered by the patent also. Since Gleevec is a salt of imatinib in a particular form - beta crystalline form, it would be covered both by the 1993 patent as well as the patents subsequently granted on the basis of the 1998 application." We have carefully analysed this issue. The Appellant appears to be correct in its above statement. The said statement does not mean that the crystal form was known or anticipated before the priority date of the impugned application. A subsequent information or knowledge can not be regarded as a basis for determining anticipation of a patent application.

xiii) Disclosure of prior art is not mandatory, only invention should be disclosed

The Appellant in its argument on a query posed by this Appellate Board submitted that under the law [Section 10(4) of the Act], prior art is not mandatorily required to be disclosed in the specification. R 4, R 5, R 6 and R 7 contradicted this view in their counter-arguments [see paragraphs 7(5), 7(12)(A), 7(13)(A) supra]. We have carefully examined this issue with respect to the response made by the Appellant in its written submission in supplementary replies to R 4, R 6 and R 7 [see paragraphs 7(14) and 7(15) supra]. We agree with the Appellant that the furnishing of prior art is not mandatorily required under the Act unlike in the EPO- Rule 26 requires "... indicate the background art which, as far as known to the applicant, can be regarded as useful for understanding the invention, for drawing up the European search report and for the examination, and, preferably, cite the documents reflecting such art". But to establish novelty, anticipation, inventive step and to overcome objection under Section 3 particularly 3(d) and even to avoid opposition and future litigations it becomes absolutely necessary for an applicant for patent to disclose the relevant prior art where applicable including the closest one, to his knowledge and distinguish its alleged invention over the same. However, still, Indian law requires (Section 8 of the Act and Rule 12 of the Rules) information relating to objection, if any, in respect of novelty and patentability of the invention and any other particulars as the Controller may require. To our view, unless the relevant prior art including the closest one is disclosed the patent applicant can not be said to have discharged its duty or obligation of disclosing the invention under Section 10(4) of the Act. In the present age almost every invention is made by way of some improvements of existing technology as a further solution of some existing technical problem in a given field. Thus, it is almost certain that an applicant for patent to establish an invention for patenting he has to distinguish sufficiently his invention over the existing art so that it is not held to be trifling and/or attempt to make evergreening. Therefore, disclosure of relevant closest prior art is unavoidable by the applicant for securing a patent. Even, in the instant case also, the Appellant had to disclose the reference of the prior art of 1993 patent etc. to establish the further technological advancement it had

claimed to have made in its impugned application. Thus, it is not true to say that an applicant has only to disclose the invention in question for patent. We are of the view that the closest relevant prior art is also necessary to be disclosed in the patent specification.

xiv) Appellant did not disclose prior art within its knowledge that was relevant for making judgment regarding patentability of invention:

R 6 and R 7 objected that the Appellant intentionally did not disclose the prior art of "Cancer Research" article of January 1, 1996 which disclosed the compound imatinib mesylate but disclosed another article of 1996, the "Nature Medicine" where there has been no reference to the salt of imatinib which has clearly increased the scope of patentability of the invention before the Patent Office [see paragraph 7(13) supra] to which the Appellant contradicted [see paragraph 7(14) supra]. We have carefully analysed this issue. We have already observed that the disclosure of relevant closest prior art is necessary to establish novelty, anticipation, non-obviousness, etc. The said "Cancer Research" article of January 1, 1996, we notice, has disclosed the existence of imatinib mesylate as CGP 57148B and is in use in inhibiting Abl and platelet-derived growth factor (PDGF) receptor protein tyrosine kinase in-vitro and in-vivo. The impugned application also has used imatinib mesylate as the starting material for preparing the subject compound of the alleged invention and used in the same field (see text of the impugned specification). If this salt is in existence, the beta crystal form is not two steps removed from imatinib. We agree with R 6 and R 7 that examination of novelty, non-obviousness and determination of patentability under Section 3(d) would change when the prior substance being compared to is imatinib mesylate as opposed to imatinib.

Since the disclosure of the imatinib mesylate salt and its cancer curing effect also is disclosed prior to the date of priority of the impugned application the reference of this prior art has to be a guiding factor in determining patentability of beta crystalline form of the salt claimed in the impugned application. Thus, we find that the disclosure as reference of this prior art was an important obligation on the part of the Appellant which the appellant has failed to meet.

xv) No comparison provided between properties of imatinib mesylate and its beta crystalline form

In response to the arguments by the Respondents, particularly R 3, R 6 and R 7 that in the bio-availability study comparison was made between imatinib free base and its beta crystalline form rather than a comparison between imatinib mesylate as a salt and its beta crystalline form, the Appellant submitted that 1996 Cancer Research article, referred to by all the Respondents, had expressly stated that no significant difference was found between imatinib free base and imatinib mesylate after all the experiments which were made with those substances. Since the effectiveness of imatinib and imatinib mesylate did not show significant difference between the properties of the two compounds it was only necessary to compare the properties between imatinib and beta crystalline form of imatinib mesylate which was found that in the beta crystalline form of the salt there was 30% enhanced bio-availability leading to enhanced efficacy. R 6 and R 7 have responded that equating properties of imatinib and imatinib mesylate done by the Appellant is not correct. The information which the cancer article provided was that the "results" and not "properties" of the two forms had no difference. In the said article the authors undertook the tests to verify that imatinib and imatinib mesylate had the same effect on cancer. The authors found that the two forms of the compound displayed the same result [see paragraph 7(13) supra]. We have analysed the issue carefully and find that the Appellant has tried to mislead the Appellate Board by its aforesaid statement. In the written reply to the arguments of R6 and R7 the Appellant has acknowledged that the 'Cancer Research' article of 1996 has shown that there was no significant difference between the "efficacy" of imatinib free base and the efficacy of imatinib mesylate [see para 7(8) supra], but in its supplementary written replies to the counter-arguments on behalf of R 3 it has referred to "properties". We find that the reference of the "results" in the "Cancer Research" article is comparison between the substances was in respect of the effect on cancer and not with respect to other properties. We agree with the

Respondents that the properties of imatinib and imatinib mesylate could not be equated and the experimental evidence shown for imatinib vis-a vis its beta form of the salt could not be adopted for the comparison between the data for imatinib mesylate and the beta form of imatinib mesylate. Appellant has not replied to the Respondents' argument also. We, are therefore of the opinion that in the circumstances, the study on bio-availability of the beta form is not complete without corresponding comparison with imatinib mesylate salt.

xvi) Whether imatinib mesylate is a known substance before the priority date of the impugned application:

Appellant has contended that imatinib mesylate is not a known substance whereas the Respondents have argued otherwise. We have examined this issue carefully. It is a fact that we don't have any prior record/citation which has actually described experimental isolation of imatinib mesylate before the impugned application. USP 5521184 (Zimmerman patent) claims one of the salts of imatinib as the mesylate also. According to US patent law a claim is allowable if it is enabled. In the said patent the description mentioned is that the salt can be prepared in a manner known per se. Thus, a person skilled in the art can make the same without any further experiment. We have also 'Cancer Research' article of Jan. 01, 1996 (56, 100-104) relied upon by the Respondents which actually used the substance imatinib mesylate for tests. The Appellant's specification also refers to the use of this salt stated to be reported in "Nature Med." 2, 561 -6 (1996). Thus, there is no doubt that such a substance was in existence or in use in 1996 before the priority date of the impugned application. Appellant has contended that no where in the said articles the actual method of preparation of imatinib mesylate was disclosed and cited Guidelines for Examination in the European Patent Office in Chapter IV under the heading "Enabling disclosure of a prior document". Further, the Appellant also referred to the House of Lords decision in the matter of **Asahi Kasei Kogyo KK's Application** 1991 RPC 485 at page 517, (see para 7 (14) supra). From the above references what we understood is that for deciding whether imatinib mesylate is a known substance or available to the public, it is not necessary that it has to be actually known or available to the public. It is sufficient if the information given in a prior art document enables a skilled person in the art to prepare the same substance. Further Section 2(1)(l) of the Act which gives the definition of "new invention" means "any invention or technology which has not been anticipated by publication in any document or used in the country or elsewhere in the world before the date of filing of patent application with complete specification, i.e. the subject matter has not fallen in public domain or that it does not form part of the state of the Article" As stated above, imatinib mesylate as a product has been used and published before the impugned application. Therefore, it is a known substance according to the above definition of "new invention." Even the Appellant's own impugned specification accepts that imatinib mesylate is a known substance. For example, the Appellant in specification gives the following as a basis of its invention:

> It has now been surprisingly found that a crystal form may under certain conditions be found in the methanesulfonate salt of this compound, which is described hereinafter as ß-crystal form, and which has very advantageous properties.

A careful reading of this statement would reveal that the Appellant has only found a new crystalline form, the ß form, having very advantageous properties in methanesulfonate salt. The inference naturally comes that a skilled person knows "methanesulfonate salt" but not beyond. By that statement in the disclosure, the Appellant accepts the existing technology upto imatinib mesylate. What the Appellant has surprisingly found is its alleged invention. This is further proved from the Claim 13 (see also paragraph 3 supra) and the corresponding description and example. It claims processes for preparing the ß-crystal form taking one of the starting materials as "an amorphous starting material of the methanesulfonic acid addition salt of a compound of formula 1" i.e. imatinib mesylate. Unless the starting substance is available to a skilled person he can not carry out the allegedly invented process of the Appellant to get the desired product. The 1993 patent gives a disclosure of the salt as well as how to make it, that is known per se, which means, there is nothing to be inventive to prepare the imatinib salt from imatinib. Therefore, a skilled person having general knowledge in the field will be able to prepare imatinib mesylate from imatinib. Even, the doubt that while preparing imatinib monomesylate, di-or-tri mesylate could be prepared because of the existence of plurality of basic groups is

ruled out because before the priority date of the impugned application imatinib monomesylate was in fact prepared and used. There is no report that there has been any difficulty in making imatinib mesylate in accordance with the information available in the prior art [as argued by R1, R2 and R8 (supra)]. From the above discussion one can safely infer that imatinib mesylate is a known substance. Still we can put a question of anticipation for imatinib monomesylate if a patent application would have been filed for imatinib monomesylate only as a subject compound instead of the present impugned application whether the claim for this compound would pass the test of anticipation in view of the prior cited documents? We believe, it won't. In view of the above, we are convinced that imatinib mesylate is a known substance and also is available to the public.

xvii) The specification silent about bio-availability/efficacy. Can it make out a case of patent by providing data at a later date on efficacy?

Respondents argued in general that the impugned application described many advantageous properties such as improved thermodynamic stability, improved flow properties and lower hygroscopicity but no mention of enhanced efficacy or safety is discussed. The Appellant avoided exact reply thereto. Instead it referred to Section 10(4)(a) to (d) of the Act which provide the requirements in relation to the contents of a patent specification which the Appellant claims to have met fully. We have also carefully considered this issue. We have noticed that the Respondents are right in saying that the impugned specification mentions many advantageous properties of the beta crystal form of imatinib mesylate but there has been no reference of bio-availability in the specification. Appellant's argument based on Dr. Sutter's affidavit by importing a new property of improved bio-availability was stated to be to meet a patent office objection on amended Section 3(d) which required significant enhancement of efficacy of a new form of a substance as a criterion for patentability. Thus, the Appellant accepts that the original object of its alleged invention was not to demonstrate enhancement of efficacy of its subject compound- beta crystal form of imatinib mesylate. It carried out further detailed experiments/study for the purpose and submitted new data which was not originally disclosed as a part of the specification. A patent is granted on the basis of its full disclosure of the invention in the specification furnished on the priority date of the application. Even an amendment is also not allowed in the specification which in substance is not disclosed therein (see Section 59). The patent law debars an applicant a grant of patent for belated discovery of a new thing which is not disclosed which may or may not be pivotal in determining patentability. Thus, the Appellant is not entitled to make out a case for patent in its favour by importing a new matter in the specification which was later on discovered/established. The patentability, therefore, if any, will have to be established on the basis of original disclosure contained in the specification.

xviii) Whether bio-availability is same as therapeutic efficacy?

There exists no reference of the term "bio-availability" in the Act. However, "efficacy" has been referred to in Section 3(d) but not defined. Appellant has argued that bio-availability and efficacy are one and the same. It has also furnished several literature references which demonstrate that enhanced bio-availability leads to enhanced efficacy. Respondents have contradicted stating that bio-availability does not automatically lead to therapeutic efficacy (supra). R 6 and R 7 have submitted a clear picture on the subject. They have given following dictionary meanings of these terms:

According to Dorland's Illustrated Medical Dictionary

Efficacy : 2. in pharmacology, the ability of a drug to produce the desired therapeutic effect; it is independent of potency, which expresses the amount of the drug necessary to achieve the desired effect. According to the Oncology Clinical Trials Glossary of Novartis:

Efficacy (of a drug or treatment). The maximum ability of drug or treatment to produce a result regardless of dosage. A drug passes efficacy trials if it is effective at the dose tested against the illness for which it is prescribed. The Hon'ble Madras High Court in its decision on the issue of constitutional validity of Section 3(d) in the

W.P. filed by the Appellant (supra) also accepted the meaning of efficacy according to the said Dorland's Medical Dictionary and adding meaning of "therapeutic" it gives a meaning of "efficacy" as healing of disease - having a good effect on the body.

The Dorland's Illustrated Medical Dictionary defines bio-availability as "the degree to which a drug or other substance becomes available to the target tissue after administration." The Respondents also have cited the reference of the book "The pharmacological Basis of Therapeutics" (8^{th} Ed.) which explains the difference between efficacy and dose, and argued that bio-availability is independent of efficacy. R 6 and R 7 in their written submission have also explained the same with the help of drug action process which is stated as absorption, binding and response. Absorption relates to the amount of active ingredient that has been absorbed by the body. After the active ingredient is absorbed by the body for it to act, it must bind with the relevant reception of the target cell. This binding is the crucial step that determines effect. Where there are less number of receptor sites, increased availability of the active ingredient does not produce any therapeutic response. Therefore, binding and not absorption, is the key to healing the disease. Subsequently, after the receptor-drug binding occurs, the subsequent response can be measured. This response is typically in the form of increase or decrease of some parameters (in this case white blood cell count). Bioavailability relates to the absorption and not the binding stage of drug action and therefore is not a measure of efficacy of a drug. [see paragraph 7(3) supra]. Appellant has neither responded to this argument nor contradicted. The cited text book references relied upon by the Appellant also establish that bio-availability and efficacy are not the same. For example, the book "Martin's Physical Pharmacy and Pharmaceutical Sciences".

(Fifth Ed.) cited by the Appellant at page 357 states as under:

> Thus, bio-availability is concerned with how quickly and how much of a drug appears in the blood after a specific dose is administered. The bio-availability of a drug product often determines the therapeutic efficacy of that product because it affects the onset, intensity, duration of therapeutic response of the drug.

From the above passage in that book, we can form the opinion that bi- availability and therapeutic efficacy are not the same. This is also proved from the definition of efficacy, which states that therapeutic effect is independent of potency (i.e bio-availability). An example in this connection seems appropriate. If a dose of a drug is increased to double with respect to the recommended dose would the healing process be enhanced to double. We don't believe so. Thus, we are convinced that bio-availability and efficacy are generally not one and the same.

xix) Whether or not grants of patents in 35 or more countries have any persuasive value:

Respondents in general contradicted the Appellant's claim that because of uniform product patent regime available under the TRIPS Agreement to which India also is a member, with changed law in place following the same underlying principles as given in the TRIPS, Indian law is no different than that of the other countries of the world and when 35 or more countries including US, where even the patent was granted on appeal, reversing the examiner's rejection, Appellant is also entitled to a patent in India as well. The arguments and counter-arguments can be seen (paragraph 7 supra). We have also examined this issue carefully. What we understand is that TRIPS gives a broad guidelines of minimum standards of IPR protection for adoption by the member states/countries. Each member state has made its patent law according to its socio-economic needs while maintaining the standards mandated with flexibility available under the TRIPS. We find that mostly law of one country differs from one another. One keeps liberal standard while another does not do so. India's law is vastly different from those of other countries while remaining within the minimum standards given by the TRIPS. It appears India has adopted stricter standard of protection with respect to novelty and inventive step taking consideration of its public welfare particularly health concerns permitted by Doha declaration as pointed out by R 3, R 1, R 2 and R 8. Several exclusions have been included in the law which are not called inventions. A patent granted by a country is in accordance with its own law. Relatively, stricter standards of

patentability adopted by India thus give sufficient possibility that a patent may not be grantable for all the inventions in India. According to Paris Convention/TRIPs each country's decision of grant/refusal is independent of others. Accordingly, we can not accept the argument that patent grant in other countries would have any persuasive value on the grant/refusal of patents in India.

xx) Whether establishment of inventive selection as a case of selection patent would enable one to get a patent in India:

Respondents argue that even if a case of selection patent is established the Appellant has to satisfy Sections 2 and 3 of the Act for the grant of a patent. We have also examined this issue. We find that establishment of inventive selection as a case of selection patent is equivalent to establishment of an inventive step including the novelty. But that is not enough. An application for patent for satisfying patentability of an invention has to be screened through the test of patentability under Sections 3 and 4 of the Act which list out several inventions which are not patentable. Thus, even if the Appellant succeeds the case as a selection patent we don't agree that it is automatically entitled to grant of a patent.

xxi) Whether enhanced efficacy and advantageous properties in a drug stand for the same:

Appellant has presented its application in its specification by way of surprising discovery of advantageous properties, viz., thermodynamic stability (thus better storable), lower hygroscopicity (thus longer shelf life) better flow properties (thus better processible) in a crystal form in the methanesulfonic acid addition salt of imatinib. Because of better shelf life, better storability and improved flow properties, the Appellant claims its newly invented subject compound the beta form of imatinib mesylate is more efficacious in curing cancer. The Respondents disagree (see paragraph 7(2) to 7(6) supra). We have also carefully examined this issue and considered the arguments of all the parties. Common sense tells that efficacy is a property which is related to curing effect of a drug, whereas better shelf life, better storability and better flow properties are something which is related to formulation or presentability of a drug/pharmaceutical substance which has no relationship with the curing effect. Hon'ble Madras High Court with the help of a dictionary on pharmacology has given a meaning of efficacy as therapeutic effect in healing a disease or having a good effect on the body."(supra). We also are respectfully in full agreement with this meaning. We also can not imagine a situation that improved stability, storability and flow properties can directly lead or contribute to any curing effect of a disease. In our view, these properties in a medicine or drug helps in only maintaining its presentability as a drug in solid formulations but has nothing to do with its effectivity or disease curing effect.

xxii) Whether CGP57148B is the beta form of imatinib mesylate, the active ingredient of GLEEVEC:

Appellant in its written replies to the counter-arguments of R 4 has given the following statement: "It may also be mentioned that it was only after the beta crystalline form of imatinib mesylate was put in the market in the form of "Gleevec" by Novartis that the other companies like the respondents came forward to try to make a generic version of this drug". Appellant's own document to US Drug Authority and the patent term extension certificate by the USPTO mention GLEEVEC (imatinib mesylate) as CGP57148B. Thus, we are sure that CGP57148B is nothing but the code name of beta crystalline form of imatinib mesylate.

xxiii) Is imatinib mesylate most effective in its beta form as an active ingredient of Glivec?

Appellant has argued that imatinib mesylate is most effective in its beta crystal

form (vide paragraph 7 supra). We have endeavoured to investigate the truth in it. We find that the Appellant has not provided any evidence in support of its said claim. However, on a careful study of Dr. Massimini's affidavit it would reveal that the Appellant's said claim is not true for which a reference is invited to the Annexure B [page 53 & 54 of the Summary of Product Characteristics as approved in the European Union for 400mg film-coated tablets of Imatinib mesylate (Glivec (tm)] of the said Affidavit. The said document inter alia describes the "posology and method of administration" of the drug Glivec under paragraph 4.2 wherefrom we find that "the prescribed dose should be administered orally with a meal and a large glass of water to minimise the risk of gastrointestinal irritations" and "For patients unable to swallow the film-coated tablets, the tablets may be dispersed in a glass of mineral water or apple juice. The required number of tablets should be placed in the appropriate volume of beverage (approximately 50 ml for a 100 mg tablet and 200 ml for a 400mg tablet) and stirred with a spoon. The suspension should be administered immediately after complete disintegaration of the tablet(s)." From the above information what we have understood is that Glivec need not be administered in solid form at all to manifest its efficacy, otherwise it would have been recommended for only direct swallowing or chewing. There is also no statement in the affidavit that the drug efficacy is at its maximum in its solid beta crystalline form. Rather, it is stated that the drug should be taken along with water to minimise the risk of gastrointestinal irritations. Thus, this information leads us to conclude that the activity of the drug does not depend upon its crystal form/shape at all or in other words, beta form in particular has no role to play in curing the cancer for which it is meant.

xxiv) Is imatinib mesylate and its beta form same substance with respect to efficacy?

From the Annexure B of the affidavit of Dr. Massimini as referred to in sub-para (xxiii) supra it is known that Glivec tablet containing imatinib mesylate in beta form should be administered orally with a meal and with adequate water to minimize the risk of gastrointestinal irritations. Moreover, those who are unable to swallow the tablets, the same should be taken orally in the form of a suspension after complete disintegration of the solid tablets. Thus, it is more of a necessity that the drug be administered preferably not in solid form. We don't believe that such a procedure as stated above has been adopted at the cost of efficacy of the drug. This would mean that the efficacy of the beta form of mesylate is same when it is in solution form, which is nothing but imatinib mesylate without any crystalline form. Thus, we conclude that imatinib mesylate and its beta form are the same substance with respect to efficacy.

xxv) Why should imatinib and beta form of imatinib mesylate be considered same substances when there is a difference in relative bio-availability of 30% between them?

This argument of the Appellant has been contradicted by the Respondents. We have carefully considered the issue. There is no dispute that imatinib and beta form of imatinib mesylate are different substances. While the former is a free base, the latter is a salt of it in specific crystal form. The former is very slightly soluble in water (0.001g/100 ml.) whereas the latter is very highly soluble (130g/100ml). There are also several physical characteristics of the beta salt which are not shared by the base (see Dr. Manley's affidavit). Molecular formula of imatinib is $C_{29}H_{31}N_7O$, Mol. wt.493.60, m.p.is 211-213°C whereas the same for the mesylate salt are $C_{29}H_{31}N_7O$, CH_3SO_3H, 589.71 and 226°C respectively(see Merck Index). By the rat study it has also been known that beta salt has 30% increasead bio-availability as compared to the base (Dr. Massimini's affidavit). But we have already observed in paragraph 9(xviii) above that bio-availability is not the same as therapeutic efficacy. Bio-availability is a property of a therapeutic substance which demonstrates the degree to which the substance becomes available to the target tissue after administration. Whereas efficacy is the ability of a drug to produce the desired therapeutic effect. The therapeutic effect (cancer curing effect) of imatinib is known from the Zimmerman patent (or 1993 patent). It is also seen that the

active moiety of the drug imatinib showing its cancer curing effect is because of its chemical structure which is given a name of CGP 57148 as per "Nature Medicine" Vol. 2, No. 5. May 1996 (supra). Accordingly, any substance containing imatinib moiety (CGP57148) will have cancer curing property. This is also an argument of the Appellant (supra). Thus, any of the derivatives of imatinib with various substituents including any of its salts will have the cancer curing property because of the basic imatinib moiety present in it. This has been established as per Zimmerman patent. As per the said patent (column 4) the compounds of formula I are different N-phenyl -2- primidineamine derivatives including salts thereof which include imatinib and its salts. In that patent "the reference to the free compounds should be understood as including the corresponding salts, where appropriate and expedient". From the said patent, it becomes clear that though a salt is a different substance as compared to its free base compound their effectivity with respect to cancer curing is same or equivalent. According to Berge article "Pharmaceutical Salts" in Journal of Pharmaceutical Sciences (1977) (supra) referred to by the Respondents. "The salt form is known to influence a number of physicochemical properties of the parent compound including dissolution rate, solubility, stability and hygroscopicity. These properties, in turn, affect the availability and formulation characteristics of the drug." Thus, it becomes clear that salt formation of a drug is for imparting bio-availability, stability and determining formulation characteristics etc. but has no contribution to the curing or healing effect of a drug. Thus, we are convinced that though the free base and its salt form are different substances they have same general therapeutic effectiveness. In the instant case also therefore, imatinib and imatinib mesylate or its beta crystal form should be same substances with regard to therapeutic efficacy. This is of course actually experimentally proved also as reported in the "Cancer Research" article of Jan 1, 1996 relied upon by the Respondents where "No significant difference in results could be seen between the two forms of CGP 57148" This implies (as analysed supra) that there is no significant difference in efficacy between CGP57148 (imatinib) and CGP 57148B (imatinib mesylate) in its beta form (as now known) (supra). The Appellant has also admitted in its impugned specification that "However, it is also mentioned that inhibitory and pharmacological effects of imatinib mesylate preferably in the beta crystal form are also found with the free base imatinib." (see also paragraph 3 supra). Thus, we have no doubt in concluding that imatinib and its mesylate salt in beta crystal form though have a difference of 30% bio-availability they are same substances with respect to therapeutic efficacy.

10. Evaluation of the main issues in dispute and findings thereon:

In the following sub-paragraphs, we shall analyse and evaluate the arguments/counter-arguments of the parties to reach to our findings in deciding the main issues raised in the appeals against the impugned orders of R 8.

The main issues raised in the appeals are:

i) Priority date

ii) Novelty/Anticipation

iii) Inventive step/non-obviousness

iv) Selection Patent

v) Section 3(d) of the Act

(I) Priority date:

The Applicant (Appellant) claims swiss priority date 18.07.1997 for its impugned patent application filed in India on 17.7.1998. The Appellant has argued in its written argument that the issue of priority could not be taken as a ground for rejection of its application in pre-grant opposition since it was not covered by Section 25(1) of the Act. This argument of the Appellant is not

correct. Issue of convention priority is one of the grounds of that opposition and could, therefore, be a ground for rejection of a patent also. However, in its oral arguments it says that when the application is examined and patentability is considered under the patent law as amended to provide the provision of product patents in the amended patent law, the provision of priority date would also have to be considered on the same law as amended which is in force from 01.01.2005. Respondents in general have objected to the grant of protection of priority date as Switzerland, where the basic application was made, was not a convention country on the date of filing of the present impugned application i.e. 17.07.1998. However, R 1, R 2 and R 8 have finally given up their objection on this issue. R 3 additionally has stressed that the Appellant is not entitled to get the protection of priority date because the amended relevant provision of Section 133 of the Act does not automatically apply retrospectively to the present application as that section has not been specifically enacted to apply retrospectively and also R 3 has relied upon the provisions of Section 6 of the General Clauses Act, 1897 for the purpose. In its reply argument [in paragraph 7(9) supra], the Appellant inter-alia has submitted that by the amended patent law of 2005 the definition of convention country has been changed to the new Section 133 of the Act. He has added that it is necessary to take cognizance of the change in law which the Parliament has made repealing the earlier one. Accordingly, Switzerland has to be treated as a convention country under the changed law and is entitled to get the priority date of 18.07.1997. We have already considered the arguments of all the parties to this effect. We observe that the law debarred the examination of all 'mail box' applications including the one of the impugned application of the Appellant filed before 01.01.2005. When the examination report on patentability is based on the amended patent law effective from 01.01.2005, then why the convention priority date would have to be decided according to the old or unamended law? In the decision dated 07.09.2005, in the case of **Agouron Pharmaceuticals Inc. v. Controller of Patents in the High Court at Calcutta (special Jurisdiction, Original side) (AID No. 2 of 2001)** Hon'ble S.K. Mukherjee, J. has observed "it is well settled that the appellate Court is entitled to take into consideration any change in law and give proper relief on that basis." Accordingly, we do not agree with the arguments of the Respondents and find that the Appellant is fully justified and entitled to get the convention priority date 18.07.1997 under the amended Section 133 of the Act. Provision Section 6 of General Clauses Act, 1897 does not apply here as the original Act has not been repealed. We thus reverse the R 8's finding on this issue.

(II) Novelty/Anticipation:

R 8 observed in its impugned orders that the Appellant's alleged invention was anticipated (paragraph 5 supra).

The Appellant has submitted in the appeals (originally writ petitions) that the subject compound imatinib mesylate (should have been beta crystalline form of imatinib mesylate) ought to have considered to be novel and not anticipated as long as there was no specific and enabling disclosure in the prior Article In the present appeals it adds and relies upon new documents such as IPER, decision of the Board of Patent Appeals and interferences of USPTO and related documents in its favour which we have allowed also to be considered in these appeals [see paragraph 9(i) supra]. The arguments/counter-arguments of parties on the subject are given in the paragraph 7 supra. R 5 has admitted that the subject compound is novel and not anticipated by any of the prior Article But other respondents have seriously disputed the issue. Here, they, what we understood, have meant by novelty and anticipation is that if the invention is anticipated it shall be held not to be novel. The term "anticipation" has not been defined in the Act. According to the Chambers Dictionary, the word anticipation means "an act of anticipating", "expectation", "imagining beforehand". However, Section 2(1)(l) of the Act gives a definition of "new invention" which means "any invention or technology which has not been anticipated by publication in any document or used in the country or elsewhere in the world before the date of filing of patent application with complete specification, i.e, the subject matter has not fallen in public domain or that it does not form part of the state of the art". Further Sections 29 to 34 of the Act provide some exceptions to that which say no anticipation by reason

only of prior publication, prior communication to government, public display etc. Fortunately, we have identified guidelines culled out from different decided cases on anticipation as reported in the book, Patent Law by P. Narayanan, (4th Ed.), pp 380-381 which read as, "For a document to anticipate a claim it must contain clear and unmistakable directions to the claimed invention or there must be evidence that carrying out what was suggested in the document inevitably resulted in the claimed invention. The clear and unmistakable direction must amount to an enabling disclosure. To consider whether carrying out such instructions as might be found in the prior document would inevitably result in the claimed invention, the Court must have regard specially in the field of high technology, to expert evidence as to the effect of carrying out the instructions [Quantel v. Spaceward 1990 RPC 83]." Further, "the information given in the prior document must be sufficient to enable the instructed reader at once to perceive and understand and be able practically to apply the discovery without the necessity of making further experiments. "Experiment" in this context means experiments with a view to discovering something not disclosed and does not mean ordinary methods of trial and error **[Van der Lely N.V. v. Bamfords** [1963] RPC 61 at 71 and **Bugges Insecticide v. Herbon** [1972] RPC 197 at 209, 210]." In Goodyear Tire and Rubber Company (Rineharts' Appln.) Graham, J. observed that a later process claim is anticipated in the strict sense if the result of carrying out a process described in a prior document in fact inevitably results in something fairly falling within that claim even if the description itself may not be sufficient to act an anticipation alone." [1970] RPC 127 at 133. See also Amchem Products' Inc's Patent [1978] RPC 271. Further, to establish anticipation based on what was known before the priority date of the claim it must be shown "that in some prior publication there is to be found information about the alleged invention equal to the purposes of practical utility to that given in suit". Different decisions are referred to in that connection in p 380 of the book. Also, we refer to another case in page 371 from the same book "For a claim to be anticipated, the prior disclosure must contain a clear description of something or clear and unambiguous direction to do or make something that would infringe the claim if carried out after the grant of the patent. Where something within the claim had been disclosed it did not matter that the disclosure was less preferred. General Tire Rubber Co. v. Fire Stone Tyre and Rubber Co. Ltd. [1972] RPC 457 at 485 - 486 (CA) Applied." Still further, "It is not enough to make a mosaic of prior publications and to say that the whole invention has been disclosed." **[Martin & Biro Swan v. H. Millwood** [1956] RPC 125 at 133]

From the submissions of R 4 on the ground of anticipation following arguments precipitate:

> (i) Impugned application is fully anticipated by the prior 1993 Zimmerman patent read with Appellant's own documents filed with US Drug Authority (of 2001) and US term extension certificate (of 2004). Appellant has disputed the same which can be seen in paragraph 7(7) above.
>
> (ii) Beta crystal already exists in the prior art as the Appellant has argued it as a case of selection patent
>
> (iii) Imatinib mesylate of Zimmerman patent always spontaneously exists in the beta crystal form as established by the expert evidence of IICT and IIT.

We have carefully studied the Zimmerman Patent equivalent to 1993 patent specification which inter-alia claims different N-phenyl-2-pyrimidineamine derivatives (of foumula I) including imatinib, and pharmaceutically acceptable salts thereof with at least one salt forming group. The said compounds have been found to have valuable pharmacological properties and can be used, for example, as antitumoral drugs etc. The said pyrimidine derivatives can be converted into various salts including pharmaceutically acceptable ones. The said specification also mentions methanesulfonic acid as one of the salt forming acids. The said compounds of formula I and salts thereof are stated to be prepared in accordance with processes known per se. However, 1993 patent has not given any working example as to how a salt of imatinib could be made including of imatinib mesylate.

Following the principles laid down in the above cited case laws, we don't find any of the cited documents by R 4 either individually or collectively disclose or give any idea of any specific crystalline form of imatinib mesylate as a substance, leave apart the beta crystalline form, any pharmaceutical composition containing the same or any process for making the said beta form. The disclosure given in the 1993 patent, in our view, can at best lead to the preparation of imatinib mesylate as the exact

preparation of any salt has not been disclosed therein. A person skilled in the art just can not predict the polymorphism and prepare the subject compound from the available disclosure therein. The documents related to the application to US drug Authority and U.S term Extn., certificate and the test reports of IIT and IICT were not known/available before the priority date i.e. 18.07.1997 of the instant application. We, therefore, cannot accept these as prior publications for consideration and cannot agree with the R 4 that these documents anticipate the Appellant's subject compound. We have already observed that IICT and IIT experiments do not lead one to conclude that imatinib mesylate exists only in the beta form [see para 9(xi) supra]. We are, therefore convinced that R 4 has failed to establish a case of anticipation against the Appellant's impugned application.

R 6 and R 7's arguments on anticipation in brief lead to following documents for consideration

(i) Zimmerman patent or 1993 patent of 1993 claiming imatinib mesylate

(ii) Application for patent term extension of the Appellant to USPTO (of 2001).

(iii) Appellant's Reply Affidavit to the common counter affidavit by the patent authority where the Appellant admitted the enablement of preparation of imatinib mesylate from the 1993 patent.

(iv) Appellant's Reply affidavit admitting CGP 57148B stood for imatinib mesylate.

(v) "Cancer Research" article dated Jan., 1 1996 wherein imatinib mesylate (CGP57148B) was stated to be synthesized.

(vi) "Blood" article, Nov. 1, 1997 and Dec 15, 1997 referring imatinib mesylate as CGP 57148 B

(vii) International Preliminary Examination Report which considered that monomethane sulfonic acid salt of imatinib has been disclosed in the 1993 patent.

(viii) Affidavit of Dr. Sutter admitting only the beta form of imatinib mesylate was commercialized (of 2005) and their claim for anticipation is based on the above disclosures.

We have carefully considered these arguments of R 6 and R 7 vis-à-vis the Appellant's replies thereto(supra). The contents of the documents listed in sl No. (ii) to (iv) and (vi) to (viii) are known or available subsequent to the priority date of the instant impugned application and therefore cannot be considered for anticipation. The 1993 patent now added with information of imatinib mesylate as CGP57148B does not give any indication of polymorphism or any crystalline form either individually or together. In our opinion there is no anticipation by prior publication.

R 6 and R 7 also argued for inherent anticipation. They argued that Dr. Sutter's affidavit confirms imatinib mesylate in beta form as the most thermodynamically stable. Accordingly, no form other than beta can be obtained. Thus, anybody practising prior art would lead only to the beta form of imatinib mesylate and no other form. Alfa form will also be converted into beta because of global contamination. R 6 and R 7 have given reference of the decision in Schering Corporation v. Geneva Pharmaceutical, 339 F 3d 1373 for the purpose (supra).

We have carefully examined the issue. We observe that no concrete method has been disclosed in the prior art to prepare even imatinib mesylate. Since, it can exist in several other polymorphic forms also as has been argued by the Appellant and not disputed by the Respondents that no one can say with certainty that one would reach directly to beta by a generally conventionally known prior art procedure. IICT and IIT experiments getting only beta do not prove that any process for converting imatinib to imatinib mesylate will inevitably lead to the beta form [see paragraph 9 (xi) supra]. If that be the case then how several other forms of it could be prepared from imatinib which are still in existence? It would be an inventive effort to find out the exact process conditions to get to a particular form including that of the beta form. It is not always correct that only the stable form would only result out of a chemical reaction or a stable form can not be converted into a relatively unstable one. We also do not have any evidence on record which suggests that a given from of imatinib

mesylate automatically converts itself to only the beta form on storage. Thus, Reference of R 6 and R 7 to the decision of Schering v. Geneva (supra) has no application in establishing inherent anticipation. In view of our above findings we reject the arguments of R 6 and R 7 on inherent anticipation.

The ground of anticipation by R 3 in brief is that from the prior art common general knowledge imatinib mesylate was known and one stalled in the art could produce imatinib mesylate. Since practising conventional method as done by IICT and IIT imatinib mesylate was formed only in the beta form, this form is inherently anticipated. In support, it gives reference of decision in US Court of Appeals for the Federal Circuit, in Smithkline Beecham Corporation v. Apotex, 403 F.3d 1331(2005) [See para 7(4) supra]. We have already observed (supra) that inherent anticipation fails when there are possibilities of formation of multiple forms, and the same applies here also. We give here further elaboration. There is no prior document cited by R 3 which describes any method for inevitably and inherently producing the beta form of imatinib mesylate even in trace amounts. Moreover, the Appellant claims a substance which is pure or essentially pure beta form of imatinib mesylate but not a mixture of its polymorphs where beta is present in trace amount. Further, existence of multiple polymorphs was not known before the priority date of the impugned application. Thus, inherent anticipation is ruled out. Therefore, the reference of Smithkline Beecham Corporation v. Apotex, 403 F. 3d 1331(2005) has no application here. On the R 3's argument that beta crystalline form of imatinib mesylate is inherently formed at least in certain conditions from practising conventional methods of producing the mesylate salt we have to say that this argument is also not tenable for inherent anticipation as there has been no prior exact conditions known in the art which could lead a skilled person in the art to prepare inevitably the beta form of imatinib mesylate. To find the appropriate conditions to reach to beta is a subject of research that the present Appellant has done. No uninventive man, in our view, could find out those conditions before the priority date of the impugned application to reach to the beta form. We reiterate here that IICT & IIT experiments do not prove without any doubt that practising conventional methods lead to preparing imatinib mesylate only in the beta form. When there are existence of multiple polymorphic forms of imatinib mesylate, question of the burden of disproving the inherency by the Appellate does not arise. R 3 has also raised another argument quoting the decision of House of Lords in Synthon B V v. Smithkline Beecham plc, (2005) UKHL 59(see para 7(4) supra). The replies thereto by the Appellant can be seen in paragraph 7(9) supra. We have carefully analysed the decision of the House of Lords in the above case. We do not agree with this argument of R 3 that the aforesaid decision has any application in the present case. We have already observed (supra) that by using common general knowledge in the art and by ordinary methods of trial and error which involves no inventive step no one can reach to the beta form of imatinib mesylate before the priority date of the impugned application. The same observation applies in the above case also.

R 1, R 2, & R 8 have not put forth any additional argument on anticipation except the reference of FDA orange book data which shows that New Drug Application numbers 021335, 021588 for imatinib mesylate under the trade name Gleevec are based on the 1993 patent. We have examined the said data. We have not found any reference of crystal form of imatinib mesylate which is the subject matter of the impugned application. Moreover, these are documents of 2005, much after the priority date of the instant application. Thus, anticipation is not established based on the above documents. Board of Appeals and Interferences of USPTO also upheld that the impugned alleged invention is not anticipated including of inherent anticipation. IPER by the EPO also have acknowledged the novelty of the subject compound. We thus, observe that none of the Respondents could establish "anticipation" of the instant impugned invention as a product, the beta form of imatinib mesylate, a pharmaceutical composition comprising he same and a claim for the process for preparing the said beta form of imatinib mesylate as given in the statement of claims. Use claims being not patentable are excluded for consideration. We thus reverse the impugned orders of R 8 on the ground of "anticipation".

However, It is important to note that in the case of pharmaceutically active substances, in particular in different forms, compositions as products etc. as the case herein, the concept of novelty/ anticipation would finally be re-evaluated as to whether or not the said substances, compositions fall within the category of "not an invention" under Section 3(d) of the Act which says a new form/derivative of a known substance will be considered same (known) substance unless it displays significant enhancement of property with regard to efficacy. Thus, patentability of the claims relating to the said products herein would depend on the outcome of the test of

patentability under Section 3(d) which is dealt with under subparagraph (V).

(iii) Inventive step/non-obviousness

R 8 has held in his impugned orders that the Appellant's alleged invention is obvious for the reason of prior publication (paragraph 5 supra). The Appellant has contradicted the same and advanced two-fold inventive steps formula as well as selection patent argument for the purpose. It has also relied on new documents such as IPER and the decision of the Board of Patent Appeals and Interferences of USPTO in its favour which also upheld inventive step of the impugned invention. These new documents have been allowed by us as part of these appeals [see paragraph 9(i) supra]. The arguments and counter-arguments of parties on the subject are given in paragraph 7 above.

The meaning of inventive step is found in Section 2(1)(ja) of the Act which means "a feature of an invention that involves technical advance as compared to the existing knowledge or having economic significance or both and that makes the invention not obvious to a person skilled in the art". R 4's arguments in brief are two-fold inventive steps are totally missing in the specification/claim. Even plea of selection patent fails as the beta crystal salt must form part of 1993 Zimmerman patent which is not the case. Further, imatinib mesylate always exists in crystal form only which now has been named as beta. A skilled person having regard to the state of the art, including "Nature Medicine" document of 1996 and 1993 Zimmerman patent can easily prepare the beta crystal from the base and no innovative skill is necessary to prepare the same. We have considered the broad reply thereto by the Appellant. [see paragraph 7(7) (supra)]

Appellant's claims in the impugned application relate to the beta crystal form of imatinib mesylate, pharmaceutical composition containing the same and process for preparing the said beta crystal form of imatinib mesylate. We discard the use claims as these are not patentable and there is no dispute on that. As stated in the preceding sub-paragraph(II), Zimmerman Patent or the 1993 patent names different N-phenyl -2- pyrimidineamine derivatives including imatinib and various acid addition salts thereof which include mesylate also though this is not separately named and identified. There are multiple choices of free base including imatinib and their salts as cancer curing drug. No one is specially identified as important. Thus, an uninventive man has no magic formula to choose mesylate from the big list of salts given in the 1993 patent. However, mention of imatinib mesylate in "Nature Medicine" or other documents in the art would generate motivation to prepare imatinib mesylate. Though no working example for preparing a salt has been given in the said 1993 patent we are of the opinion that it is not impossible for a person skilled in the art to prepare imatinib mesylate from imatinib by a conventional process as suggested in the said 1993 patent. But as no possibility of polymorphism, which is not a general phenomenon of a salt, can be predicted from that salt from any prior document, it is not possible for an uninventive man to discover the same and reach to the beta crystal form of imatinib mesylate, or to find its advantageous properties or to find a suitable process for its preparation or make a solid pharmaceutical composition containing the said crystal form. Though, we do not agree with the Appellant of two fold inventive step but agree with atleast one which leads it to reach to the present discovery. We also believe that without a thorough research such a discovery could not have been possible. The Appellant has surely made a technical advance as compared to the existing knowledge by way of demonstration of polymorphism, isolation, characterization of beta (and alpha) crystal forms of imatinib mesylate, identifying suitable properties in the beta crystal form usuable in the making of oral solid drug formulation for curing cancer. We shall see a little later whether the Appellant has any case of selection patent or not. However, we don't agree with R 4 that imatinib mesylate always exists in crystal form now named as beta form. R 4 has not submitted any evidence that prior to this impugned application any person other than the Appellant has prepared imatinib mesylate and found it to be present only in beta crystal form. Thus, we can not agree with R 4 that the impugned invention lacks inventive step.

R 6 and R 7's arguments on "inventive step" in brief are that with reference to the Journal of Pharmaceutical Sciences titled "Pharmaceutical Salts" of 1988 by Berge et al (Berge article) would motivate a person skilled in the art to try at least to prepare the mesylate salt from imatinib. According to that article salt forms are chosen to influence a number of physico-chemical properties of the parent compound including dissolution rate, solubility, stability and hygroscopicity responsible for formulation characteristics of a drug. It is a routine job for a person skilled in the art to verify the

physico-chemical characteristics of each salt and find out the most suitable salt as observed in the Pfizer Inc. v. Apotex, Inc 480 F, 3d 1348 (Fed. Cir. 2007) (supra). Accordingly, increased bioavailability of new form of mesylate salt, reduced hygroscopity, a requirement for preparing pharmaceutical tablets etc. are obvious. Thus, the beta crystalline form of imatinib mesylate is obvious over the Zimmerman patent in view of the Berge article. The Appellant has denied the same [paragraph 7 (8) supra]. We have carefully examined the issue and observed that R 6 and R 7 have not added any new argument than what R 4 has done. We therefore, reiterate our observation as stated above on the issue of inventive step. However, we add that reference of Pfizer Inc v. Apotex Inc (supra) has no application here as in the cited case there was a new choice of besylate salt of the lead drug molecule over maleate which was held to be obvious over Berge article. In the instant case, it is totally different. The Appellant discovers a new form within imatinib mesylate for which there was no prior hint or motivation for trial to a person skilled in the Article We, therefore, don't agree with R 6 and R 7 also that the Appellant's alleged invention is obvious or lack inventive step.

R 3's argument in brief is that pharmaceutical salt selection to mesylate from imatinib by the prior art methods is obvious. Further, it is expected that different polymorphic forms will have different physical properties such as flow properties, hygroscopicity etc. It is therefore, obvious for a person skilled in the art to evaluate the crystal structure and look for different forms with different physical properties. Thus beta form of imatinib mesylate is obvious [see paragraph 7(4) supra]. Appellant's reply in rebuttal in brief is that merely because a chemist knows how various salt in various forms are tested for various properties and then properties compared and seen whether required compromise can be reached to make it a safe drug, does not mean that any chemist can reach to the conclusion [see paragraph 7(9) supra]. We have carefully examined this issue. We observe that this Respondent also has not submitted any new argument. Therefore, our observation on inventive step as given above is reiterated. We agree with the argument of the Appellant and add that R 3 and other Respondents have presumed polymorphism in imatinib mesylate and had advanced their arguments accordingly. We don't have any evidence or document on record which can give any hint of possibility of polymorphism in imatinib mesylate. 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 instant case also there is no exception. Thus, we don't agree with R 3 also on this issue.

R 5's argument in brief on inventive step [see paragraph 7(5) supra] is based on some articles on polymorphism published in 1995 and 1996 which say that polymorphs affect the chemical stability of drug substance as well as physical stability of the dosage forms. Further, as a rule the metastable, i.e. thermodynamically instable modifications show best solubilities, fastest dissolution rates and highest bio-availabilities. Both stable and metastable polymorphs demonstrate bio-availability with metatable showing higher bio-availability but the metastable has problems with regard to stability. When both alpha and beta form of imatinib mesylate were made together and comparative studies of these two forms showed that beta was suitable and alpha was unsuitable. Therefore, the Appellant admittedly knew that with the thermodynamic stability of the beta crystal form of imatinib mesylate there is reasonable expectation of success to solve the problem of stability which was the 'surprising finding' of the Appellant. Considerations of the alleged invention were better processing and storing attributes but not to solve problem relating to bio-availability. R 5 also relied on the judgment in the US Courts of Appeals for the Fed.Circuit in Case No. 2006-1261 (Pfizer v. Apotex) [also relied upon by R 6 and R 7 on the issue of determining inventive step (supra)]. With this knowledge, the Appellant had to only verify as to what were the characteristics of alpha and the beta crystal form with respect to stability and it was bound to try various crystal forms of imatinib mesylate and see which one has higher stability. The Appellant in its reply [paragraph 7(10) supra] says that it has already dealt with the issue and said no new matter to add. We have analysed the issue. We find that R 5 has also not added any new matter to what the other Respondents particularly R 6 & R 7 have done to which we already have attended. We add here again that this Respondent presumes the property of polymorphism in imatinib mesylate for establishing obviousness on the priority date of the impugned application. 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. Thus, we can not agree with any of the Respondents that the Appellant's alleged invention

lacks inventive step. IPER and the decision of the Board of Appeals and Interferences of USPTO also upheld existence of inventive step. We, thus reverse the R 8's decision on inventive step in his impugned orders.

However, as observed in the case of novelty/anticipation under sub-paragraph (II) above, the inventive step thus evaluated for a pharmaceutically active substance in particular, as the case herein, would finally have to be re-evaluated as to whether or not the claimed products viz. substances, compositions fall within the category of "not an invention under Section 3(d) of the Act which says a new form/derivative of a known substance will be considered same substance unless it displays significant enhancement in properties with regard to efficacy. The said re-evaluation will follow hereafter in sub-paragraph (V).

(IV) Selection Patent:

We have already observed (paragraph 9(i) supra) that the Appellant is in its rights to take up this issue in these appeals.

From its arguments [paragraph 7(1) supra], the Appellant has projected that it is entitled to a patent protection as a selection patent by way of an inventive selection as a surprising discovery of a crystal form named as beta crytal form under certain conditions in the mesylate salt of imatinib. Different possible salt forms of imatinib apparently has been disclosed in the prior USP 5521184 (Zimmerman Patent) etc. In support of its argument, it refers to Section 3(d) of the Act which according to the Appellant, allows patentability if an enhanced efficacy could be established. It relies upon an article titles "Selection patent" by Julien Jeffs [E.I.P.R. 1988, 10(10), 291-296] and other different related judgments including of one from the Bombay High Court F.H. & B Corporation v. Unichem Laboratories reported in AIR 1969 BOM 225. [See paragraph 7(1) supra].

The Respondents have in general objected to the Appellant's arguments on the applicability of selection patent including of cited judgments giving their individual counter-arguments [paragraph 7(2) to 7(6) supra]. We have carefully analysed the arguments and counter-arguments made by all the parties and cited documents and the court decisions vis-à-vis Indian law. What we observe is that there is no reference of "selection patent" as such in the Indian patent law i.e. the Act. The patentability of an alleged invention is basically determined by establishment of novelty (anticipation), inventive step and industrial applicability of a product or a process [Section 2(1)(j), and 2(1)(l) of the Act] to the exclusion of inventions which are not patentable listed in Section 3 and 4 of the Act. However, in our mind we can not totally deny that there can not be any possibility under the Indian law, where the required conditions as above can not be fulfilled, for the grant of a patent in India where the inventive step is demonstrated by way of an inventive selection.

From the said cited article and the cases decided, we understand that the applicant for patent asking for a selection patent has to demonstrate the inventive step by way of "inventive selection" from a field that is in general terms, already known. Further, "In the context of a selection patent the inventive step will generally lie in making the discovery that what has been selected provides a genuine advantage over the generality from which it was selected. The advantage being one that could not be predicted". We further quote the portion of the judgment of Maugham J (as he then was) in the I G Farbenindustrie A.G's Patents (supra) also referred to by the Appellant.

> This case seems to be the first which has arisen in these Courts in which the question of the validity of a chemical selection patent has been directly considered. It may be observed that chemical patents in recent years have consisted of two sharply divided classes. The first class is that of patents based on what may be described as a originating invention, that is, the discovery of a new reaction or a new compound. Such patents may be called for brevity "originating patents". The second class comprises patents (the so-called selection patent) based on a selection of related compounds such as the homologues and substitution derivatives of the original compounds which presumably have been described in general terms and claimed in the originating patent. The number of combinations possible is really surprising. The mono-azo dyes with which the patents in suit are concerned are, as we have seen, the

result of combining with a diazo component a coupling component of a certain kind. Any arylamine containing the amine (NH_2) group can be diazotised and can be coupled with any phenol (the compound produced by the introduction of a hydroxyl, OH, group into the benzene ring of an aromatic compound). In 1897 it was estimated by Burlow in his "azofarbstoffe" that from the amines and phenols then known some 23,000 simple azo dyes of this type were possible, and, if dyes containing two azo groups were included, the number rose to over three million. It is said that over ten million are now known to be capable of manufacture. It is evident that the inventive step involved in the originating patent, for example, such a step as the Griess reaction to which I have above referred, differs in kind from the systematic investigation or research required to ascertain that some of the combinations possible under the originating patent, for example selected arylides and diazo compounds made according to the prior specifications, possess distinctive and it may be unexpected properties. The question has been raised in the present case whether it is possible to show subject-matter in respect of a selection patent in the sense in which I use the word. I have come to the conclusion that such a patent may well be valid and that properly considered. There is no more difficulty in such a case in establishing subject matter than there is, say, in a mechanical or a combination patent. It must be remembered, of course, that the selected compounds have not been made before, or the patent would fail for want of novelty. If the selected compounds, being novel, possess a special property of an unexpected character, for example if a mono-azo dye were to be made by selecting components not hitherto employed which resulted for the first time in a green dye, I cannot see that the inventive step essentially differs from the step involved in producing a new result by a new combination of well known parts or indeed from using the common and well-known factors (cranks, rods, toothed wheels and so forth) employed in mechanics in the construction of a new machine.

The article referred to by the Appellant also make three general propositions. First, a selection patent to be valid must be based on substantial advantage (which includes avoiding substantial disadvantages) to be secured by the use of the selected members; second, the whole of the selected members must possess the advantage in question; Third, the selection must be in respect of a quality of a special character which can fairly be said to be peculiar to the selected group. The said article also adds how to draft a specification in case of a selection patent. In case of selection patent, the essence of the inventive step, that is necessary for the patentee to define in clear terms the nature of the characteristics which he alleges to be possessed by the selection for which he claims a monopoly. He has in truth disclosed no invention whatever if he merely says that the selected group possesses advantages. That apart altogether from the question of what is called sufficiency, he must disclose an invention; he fails to do this in the case of a selection for special characteristics, if he does not adequately define them. We also refer to a paragraph in page 437 of the book by P. Narayanan on "Patent Law" (4th Ed.) wherein a reference is made to the Ld. Judge's observation in Beecham Group Ltd.'s (Amoxycillin) Appln.[1980] RPC 261 at 292 (Buckley, LJ) that the principle of selection must equally apply where the alleged invention relates to only a single member of a known series of family. The said passage is given as follows:

Although these propositions were enunciated in relation to a patent for a selected group of members of a known series or family of substances, the principle must apply equally where the alleged invention relates to only a single member of a known series of family. The alleged invention must be based on some substantial advantage to be gained from the use of that selected member and must be peculiar to it. The substance must however be truly new and the advantage to be gained from its selection must be the

inventor's own discovery, as opposed to mere verification by him of previous predictions or of what was previously predictable; in other words, it must be unexpected. The selected member must be novel and must possess a special property of an unexpected character which must be useful.

From the aforesaid referred article and the case decisions we notice that particularly in chemical patents the concept of "selection patent" where the inventive step (also novelty) is demonstrated by way of an inventive selection of even a new, unexpected or unpredictable single member having surprisingly advantageous properties previously not known from a known series of a family disclosed in the art can be accepted in the Indian law also. For its applicability in the instant case we shortlist the following minimum requirements as per the guidelines by different authorities aforesaid:

(1) Whether there is any statement in the specification where the nature of the invention concerns with some kind of selection.

(2) Whether the selection is from a class of substances which is already generally known.

(3) Whether the selected substance is new.

(4) Whether the selection is a result of any research by human intervention and ingenuity opposed to mere verifications.

(5) Whether the selection is unexpected or unpredictable.

(6) Whether the selected substance possesses any unexpected and advantageous property.

To test whether the said requirements are fulfilled in the present case, we find that there is a statement in the specification that "It has now been surprisingly found that a crystal form may under certain conditions be found in the methanesulfonate salt of this compound which is described hereinafter as ß-crystal form, and which has very advantageous properties". This statement in the specification is a primary ground for selection which we find has been met. This selection is made from already generally known big number of salts of imatinib from the Zimmerman patent (or 1993 patent) the originating patent. The Zimmerman Patent in general terms disclosed different pyrimidineamine derivatives of formula 1 disclosed therein which include imatinib and different possibilities of salts, one of which generally inter-alia mentioned as obtainable from methanesulfonic acid as the salt forming acid. The Appellant as per its argument, after a painstaking research has identified this particular salt imatinib mesylate and within it, it has surprisingly found a crystalline form named as beta form which is also surprisingly discovered to possess, very advantageous properties as disclosed in the specification which we don't disagree. We further observe that the said crystalline form (the beta form) is not known or disclosed or published anywhere though the use of salt imatinib mesylate was known before. The isolation of this new form, its characterization by physico-chemical methods and particular utility as a cancer curing solid dosage formulation with good storage capacities and advantageous properties are all surprising, unexpected or unpredictable and can not be termed as mere verification. The beta crystalline form is a new form of imatinib mesylate only as a substance, so covered by the originating patent, the 1993 patent. Thus, we observe that the Appellant's impugned application satisfies all the minimum requirements or conditions as identified by us from the guidelines made by the authorities for determining a case of selection patent in the instant case.

Arguments of the Respondents in general are not acceptable as they have not followed the stated guidelines. It is not necessary that originating patent has to disclose generally the different crystalline forms from which only the selection could be made. Grant of patents in other countries not as a selection patent as argued by R 4, can not be a reason that there can not be any other method of demonstrating inventive step.

We have already observed that the Appellant's alleged invention also satisfies the requirement of inventive step vide sub-paragraph (III) above. Thus, here, the Appellant has demonstrated the inventive step not only by the classical way but also by way of 'selection'. But for determining patentability of pharmaceutical substances mere meeting of novelty and inventive step (and industrial applicability) criteria does

not entitle one to get a product patent. It has to satisfy the requirement of atleast Section 3(d) of the Act which says that a new salt forms, polymorphs etc. or derivatives of a known substance is not patentable unless this form demonstrates significant enhancement of properties with regard to efficacy. We shall discuss the same in the following sub-paragraph.

(V) Section 3(d) of the Act:

R 8 in his impugned orders has held that the Appellant's alleged invention claims only a new form of a known substance without having any significant improvement of efficacy and therefore not patentable under Section 3(d) of the Act. Appellant in its appeals and arguments has challenged the same stating that its invention of beta crystalline form of imatinib mesylate is not a mere discovery of a new form of a known substance but an invention with inventive steps involving human intervention and therefore satisfying the definition of invention and provisions of Section 3(d) do not apply. Even if Section 3(d) of the Act is applied, the subject compound is still patentable as it has shown significant enhancement of known efficacy of the known substance, imatinib, by displaying 30% increased bio-availability Enhancement of 30% of bio-availability in pharmacology is considered very significant and thus the invented compound cannot be held to be same substance as imatinib. Being more bio-available the subject compound with several advantageous properties is far more suitable for the preparation and formation of drugs useable for treatment of cancer as compared with the free base imatinib. Therefore, its alleged invention satisfies Section 3(d) of the Act and is patentable. Respondents vehemently contradicted the arguments of the Appellant. We have very carefully analysed the issue with respect to the various arguments/counter-arguments of the parties (see paragraph 7 supra).

In sub-paragraphs (II), (III) and (IV) above, we have observed that the Appellant's alleged invention satisfies novelty/anticipation and inventive step. There is no dispute about the existence of industrial applicability as required for patentability. But as stated before, an application even if satisfies the definition of invention has to be tested as to whether it falls within any of the categories of inventions which is not patentable as mentioned in Section 3 of the Act. Since the instant subject of invention falls under drugs/pharmaceuticals/pharmocololgy, Section 3(d) of the Act has to be applied.

Section 3(d) of the Act is one of the provisions under Chapter II in the Patents Act, 1970 titled INVENTIONS NOT PATENTABLE.

3. What are not inventions.- The following are not inventions within the meaning of this Act

(a) to (c) XXXXX

(d) 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.

Explanation: For the purposes of this clause, salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance shall be considered to be the same substance, unless they differ significantly in properties with regard to efficacy

Madras High Court in the W.P. No. 24759 and 24760 of 2006 which determining constitutional validity of Section 3(d) of the Act (supra) observed that the amended Section 3(d) of the Act is a comprehensive provision covering all fields of technology, including the field of pharmacology. It further observed that the "explanation" would operate only when discovery is made in the pharmacology field. Thus, we have no doubt that Section 3(d) of the Act has to be applied in the instant case. We find that the "Explanation" to Clause (d) of Section 3 of the Act really gives a clear guideline as to how to apply this section in the field of pharmacology/drugs/pharmaceuticals. According to this provision salts, esters, polymorphs, metabolities, etc. and other derivatives of known substance (say pharmaceutical substance) shall be considered to be the same substance unless they differ significantly in properties with regard to efficacy.

The term "efficacy" has already been defined by the Madras High Court in its decision (supra) as "therapeutic effect in healing a disease or having a good effect on the body" taking into consideration of legislative intent for introduction of this provision in the patent law amended in such a fashion so as to avoid proliferation of

patents around existing pharmaceutical products and to prevent "evergreening" by creeping in a new standard of novelty and inventive step in the patent law for such products attaching a tag of "efficacy". We also respectfully agree with the observation of the Hon'ble Court. However, the experts in the pharmaceutical field know best how to determine therapeutic efficacy of a pharmaceutically active substance. According to the said Section 3(d) of the Act, only those new forms or derivatives would be patentable which could display a significant enhancement in properties with regard to efficacy. The word "significantly" in this section is also not defined. In our view it is not possible to quantify this term by any general formula, so as to establish significant enhancement of known efficacy. In our opinion, it may vary from case to case as per situation. However, we believe in the case of non-pharmaceutical chemical substances where also Section 3(d) of the Act is applicable, the demonstration of significant enhancement of efficacy can not be done in the same way, but may be done by demonstrating significantly "improved power of producing an effect" as per English meaning given to it by the Chambers Dictionary. Examples of diamond form of carbon as argued by the Appellant comes to our mind.

Coming to the present case, we have already observed that the Appellant's alleged invention consisting of claims for the product, beta crystalline form of imatinib mesylate, pharmaceutical composition containing the same and process for preparing beta crystalline form of imatinib mesylate is novel and possesses inventive step. The inventive step is additionally statisfied by way of "inventive selection" as a selection patent as discussed in sub-praragraphs (II), (III) and (IV), respectively (supra). We have also already observed that bio-availability is not the same as therapeutic efficacy [paragraph 9(xviii) supra]. Therapeutic efficacy is different from advantageous property of a drug [paragraph 9(xxi) supra] Appellant can not make its own conclusion on the meaning of efficacy [paragraph 9(x) supra]. Imatinib mesylate as such and its beta form are therapeutically same substances [paragraph 9(xxiv) supra] and also beta form of imatinib mesylate and imatinib are same substances with regard to efficacy [paragraph 9(xxv) supra]. It is also observed that imatinib mesylate is a known substance [paragraph 9 (xvi) supra]. From our above observations we have convincingly come to the conclusion that by demonstrating enhanced bio-availability of 30% which also is obvious, because of increased solubility of the salt in water, the Appellant could not show any actual enhancement of known efficacy for its subject compound with respect to either imatinib or imatinib mesylate as the known substance. Thus, we obviously can finally conclude that Appellant has failed on account of efficacy requirement for its beta crystalline form of imatinib mesylate under Section 3(d) of the Act.

By not satisfying Section 3(d) of the Act would mean that a claim for beta crystalline form of imatinib mesylate and a pharmaceutical composition containing the same as products are not patentable under [Section 3(e)] of the Act because these are all termed as same (known) substances. Here we find that the process for preparing the subject compound beta crystalline form of imatinib mesylate is not affected by the said provisions of Section 3(d) of the Act. We find that Section 3(d) of the Act requires also different standard of protection by demanding stricter inventive step for the products but not so for the process. Thus, a patent on the said process can not be denied to the Appellant. However, we have to mention here that the Appellant has never had any object of improving the efficacy for treating cancer in its impugned specification. Had that been there it would have been a startling discovery and definitely would have been prominently found a place in the specification. Rather, it has discovered the new crystalline form with improved thermodynamic stability, improved flow properties and lower hygroscopicity. These physical properties in a drug are important to formulate the active ingredients in solid dosage forms such as capsules, tablets, etc. but has no contribution to actual therapeutic effectiveness of the drug [Berge article (supra)]. We have already observed in [paragraph 9(xxi) above] that advantageous properties such as thermodynamic stability, and lower hygroscopicity and better flow properties of a drug substance can not be equated with the therapeutic efficacy of the drug. We also have observed in paragraph 9(xvii) above that the Appellant can not also make out a case by adducing new information at a later date turning inventive step into a new direction and establish patentability. The patentability would have to be based on the original disclosure as available in the specification and disclosed on the date of filing. The grant of patents in other jurisdictions is also similarly made. Since India is having a requirement of higher standard of inventive step by introducing the amended Section 3(d) of the Act, what is patentable in other countries will not be patentable in India [See also paragraph 9(xix) above]. As we see, the object of amended Section 3(d) of the Act is nothing but a requirement of higher standard of inventive step in the law particularly for the drug/pharmaceutical substances. This is also one of the different public interest provisions adopted in the patent law at the pregrant level, as we see, are also permissible under the TRIPS Agreement and to accommodate the spirit of the Doha Declaration which gives to the WTO member states including India the right to protect public health and, in particular, to promote access to medicines for all. This is also reflected in the said **Novartis AG v. Union of India and Ors.** (2007) 4 MLJ 1153 decision by the Madras High Court on the Appellant's challenge to the constitutional validity of Section 3(d) of the Act where Hon'ble High Court have remarked in paragraph 19 thereof: "We have borne in mind the object which the amending Act wanted to achieve namely, to prevent evergreening; to provide easy access to the citizens of the country to life saving drugs and to discharge their constitutional obligation of providing good health care to its citizens". We are fully conscious of the Appellant's benevolent GIPAP program for free distribution of GLEEVEC to certain cancer patients. But as per information furnished in its written counter-argument by R 3 that when the Appellant was holding the right as EMR on GLEEVEC it used to charge Rs. 1,20,000/- per month for a required dose of the drug from a cancer patient, not disputed by the Appellant, which in our view is too unaffordable to the poor cancer patients in India. Thus, we also observe that a grant of product patent on this application can create a havoc to the lives of poor people and their families affected with the cancer for which this drug is effective. This will have

disastrous effect on the society as well. Considering all the circumstances of the appeals before us, we observe that the Appellant's alleged invention won't be worthy of a reward of any product patent on the basis of its impugned application for not only for not satisfying the requirement of Section 3(d) of the Act, but also for its possible disastrous consequences on such grant as stated above, which also is being attracted by the provisions of Section 3(b) of the Act which prohibits grant of patent on inventions, exploitation of which could create public disorder among other things We, therefore, uphold the decision of R 8 on Section 3(d) of the Act to the extent that product patent cannot be made available to the Appellant, but the Appellant cannot be deprived of its fruit of research for developing a process for preparing the beta crystalline form of imatinib mesylate. Such process patent compared with a product patent being a lesser degree monopoly, grant of such a patent, in our opinion would not attract any of the provisions of Section 3 of the Act in the instant application and is also expected to limit any possible abuse to ensure that and GLEEVEC should be available at affordable prices.

11. Conclusion

We have observed in paragraph 10 above that the Appellant is not entitled to a product patent for its claims in the impugned application. Thus, claims 1-10 and 14 as the subject compound beta crystalline form of imatinib mesylate and claims 11 and 15 as pharmaceutical composition containing the said substance, being also attracted by Section 3(e), cannot be allowed. The use claims 12 and 16 can not also be allowed as these are outside the purview of the definition of an invention. The Appellant, therefore, is left with only the process claims 13 and 17 for consideration of grant. We, therefore, dispose of the present appeals and remand back the impugned application to the Patent Office (Chennai) with the direction to the Controller to grant a patent expeditiously to the Appellant with the Swiss Convention priority on record subject to the impugned specification being amended by the Appellant restricting the statement of claims to process claims only subject to the office objections raised in the first examination report dated 17th march, 2005 being complied with as per the requirements of the law. The Controller shall also afford an opportunity to be heard to the Appellant, if necessary.

Since the appeals are disposed of, the miscellaneous petition Nos. 1 to 5/2007 do not survive.

Parties shall bear their own costs.