BEFORE CONTROLLER OF PATENTS
THE PATENT OFFICE, DELHI

In the matter of section 25(2) of The Patents Act, 1970 as amended by The Patents (Amendment) Act, 2005

And

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

And

In the matter of: Patent No.254813 (Application No: 558/DEL NP/2003)

APPLICANT: BOEHRINGER INGELHEIM PHARMA GMBH & Co., GERMANY

OPPONENT: CIPLA LIMITED MUMBAI CENTRAL, MUMBAI-400008.

Hearing held on 21st November, 2014

Present in hearing:

Dr.Neeti Wilson, Ms.Archana Shanker (Agents representing the Applicant)
Mr. S Majumdar, Ms.Mythili Venkatesh (Agents representing the Opponent)
Dr.R.Lohia, Dr.Sunil Gautam (Examiner of Patents & Designs)

An application for a patent bearing number **558/DELNP/2003** was filed in Patent Office, Delhi on 16th April, 2003 entitled "CRYSTALLINE TIOTROPIUM BROMIDE MONOHYDRATE AND PROCESS THEREOF" A request for examination under Section 11-B was filed on 30th November, 2005 and was assigned a Request No. 5010/RQ-DEL/2005. As per the provision under Section 11-A of Patents Act, the said application was published on 04th May, 2007.

The said application was examined according to the provisions in force of the Act. A pre-grant opposition was filed by Intermed Labs Pvt. Limited on 05th November, 2007. The said pre-grant opposition was heard by the then Learned Controller Mr.S.K.Roy. The application was recommended for Grant of the Patent on 21st December, 2012 and was allotted the Patent No. 254813. The said Patent was published in the Patent Office Journal U/S 43 (2) on 28thDecember, 2012. The Opponents filed an opposition under Section 25(2) of the Patents Act, 1970 on 08th February, 2013 along with Form-7 and written statement of opposition for the revocation of the said Patent.

Accordingly agent for Patentee has filed petition under Rule 138 of Patents Rules 2003 as amended by the Patents (Amendment) Rules, 2006 on 28thMarch, 2013 for extending the period for submission of the reply statement/ evidence u/r 58 by one month to 08th May, 2013 and submitted the reply statement and evidence on 08th May, 2013.The Agent for opponent filed petition u/r 138 for the extension of time of one month for filing reply evidence under rule 59 on 10th June, 2013. The agent for the opponent filed reply evidence under Rule 59 along with a

permission to file further evidence under Rule 60 on 09th July, 2013.The agent for the patentee further filed a petition under Rule 60 for extending the period for grant of leave along with further evidence of Ms. Wendy Petka and Dr. Markus Johannes Weymann.138 along with the original executed affidavit from the technical expert on 21st May, 2014.

The opposition Board was constituted on 09th June, 2014. The recommendation of the Opposition Board received under Rule, 56 on 09th September, 2014. A notice of hearing along with board recommendations were forwarded to both the parties on 26th September, 2014 & the date of hearing was fixed on 16th October, 2014.

The agent for the Patentee filed a miscellaneous petition on 14th October, 2014 stating that the board recommendations of the opposition board are vitiated & therefore should be expunged as the opposition Board has failed to consider the evidence filed by the patentee/petitioner of Dr. Markus Johannes Weymann (Affidavit No. 2) and Ms. Wendy Petka filed under Rule 60 of the Indian Patents Act on 20th May 2014, which is prior to the reference made by the Controller of Patents under Section 25(3).

After thorough inspection it was found that these evidences remained unconsidered due to technical problem. Realizing the gravity of the situation this evidences were immediately forwarded to the opposition board for consideration & their recommendations on 15th October, 2014 & the scheduled hearing was adjourned. The opposition board carefully considered the

said evidences & submitted their revised report on 10th November, 2014 i.e. after 25 days from the date of referral.

A notice of hearing along with board recommendations were forwarded to both the parties on 11th November, 2014 & the final hearing date was scheduled on 21st November, 2014. After hearing both the parties submitted their written submissions.

Before getting into the details of this opposition I will first decide the Miscellaneous Petition as filed by the agent of the applicant discussed above.

Miscellaneous Petition:

A miscellaneous petition was filed by the Patentee/Applicant before the Controller-General on 14th October 2014, to reconstitute the Opposition Board contending that the Applicant's Evidence submitted under Rule 60 dated 20th May 2014 was not considered by the Opposition Board. The agent for the Patentee in their petition stated that the board recommendations of the opposition board are vitiated & therefore should be expunged as the opposition Board has failed to consider the evidence filed by the patentee/petitioner of Dr. Markus Johannes Weymann (Affidavit No. 2) and Ms. Wendy Petka filed under Rule 60 of the Indian Patents Act on 20th May 2014, which is prior to the reference made by the Controller of Patents under Section 25(3).

The petition was considered meticulously. It was found that these evidences remained unconsidered due to technical problem. Since this matter was at initial stage & no proceedings in this matter has started, realizing the gravity of the situation the Evidence filed under Rule 60 were immediately forwarded to the

opposition board for consideration & their recommendations on 15th October, 2014 & the scheduled hearing was adjourned to the Opposition Board for consideration. The opposition board carefully considered the said evidences & submitted their revised report on 10th November, 2014 i.e. after 25 days from the date of referral. The Revised Opposition Board Recommendations were forwarded to both the parties and the date for final hearing was fixed 21st November 2014.

In the Miscellaneous Petition, the Applicant had relied upon the IPAB order in *Sugen Inc & Anr. v. Controller General of Patents, Design and Trademarks (Order no. 107/2013)* in which the Hon'ble IPAB had "sent the matter back to the Controller on the ground that Cui 2 [evidence] was not furnished, it is necessary that an Opposition Board is constituted again". However, in that case the Hon'ble IPAB had found that the order of the Controller was vitiated as the Patent Office rendered the final decision as the Controller relied upon the defective Opposition Board Recommendation.

In the present case, I corrected the procedural error by referring the said evidences to the opposition board back, for their consideration at the first instance before any hearing proceedings commenced & adjourning the hearing. Only after submission of the revised opposition board recommendations by the opposition Board (i.e. after 25 days after referring for reconsideration) and forwarding to both the parties had the omission removed. Moreover, under the Scheme of Law, the decision under section 25(2) is given solely by the Controller who is "free to agree or disagree with" Opposition Board Recommendations [Sugen Inc. v.

Controller General, Order 107/2013, IPAB, paragraph 20]. In the present case, I have the benefit of a complete Opposition Board Recommendation, unlike the Sugen case, where the Controller did not had the benefit of a complete Opposition Board's Recommendation yet decided the opposition.

In view of these facts, I hereby dispose the miscellaneous petition holding that in the present case the final hearing was yet to be taken and therefore the prayer for change of Controller cannot be allowed as done in the Sugen Inc.3 case where the Controller had rendered his final decision on the basis of the defective recommendation. Also not accepting the prayer of expunging the opposition board recommendations and constituting of a fresh Opposition Board as the board has provided revised recommendations taking into account all the evidences as filed by the Applicant. It was observed that every procedural lapse must lead to reconstitution of Opposition Board is neither supported by the Order of the Hon'ble IPAB nor is acceptable under the Scheme of Law.

Having dealt with the miscellaneous petition I further proceed on the grounds on which the actual opposition is based.

THE CLAIMS UPON WHICH THE PATENT IS GRANTED:

1) Crystalline tiotropium bromide monohydrate characterised by an endothermic peak at230 ± 5°C occurring during thermal analysis using DSC, at a heating rate of l0K/mm.

2) Crystalline tiotropium bromide monohydrate as claimed in claim 1 characterised by an IR spectrum which comprises bands

at wave numbers 3570, 3410, 3105, 1730, 1260, 1035 and 720 cm-1, *inter alia.*

3) Crystalline tiotropium bromide monohydrate as claimed in one of claims 1 or 2, characterised by a single monoclinic cell having the following dimensions: a= 18.0774 *A,* b = 11.9711 *A, c*=9.9321 *A,* p = 102.691°, V = 2096.96 *A3.*

4) Process for preparing crystalline tiotropium bromide monohydrate as claimed in one of claims1, 2 or 3, wherein the said process comprises following steps;

(a) tiotropium bromide is taken up in water,

(b) the mixture obtained is heated, (c) activated charcoal is added and

(d) after the removal of the activated charcoal, tiotropium bromide monohydrate is slowly crystallised with slow cooling of the aqueous solution.

(5) Process as claimed in claim 4, wherein (a) 0.4 to 1.5 kg of water are used per mole of tiotropium bromide put in,

(b) the mixture obtained is heated to more than 50°C,

(c) 10 to 50 g of activated charcoal are used per mole of tiotropium bromide used and after the activated charcoal has been added stirring is continued for between 5 and 60 minutes,

(d) the mixture obtained is filtered, the filtrate obtained is cooled to a temperature of 20-25°C at a cooling rate of 1to 10°C per 10 to 30 minutes and the tiotropium bromide.

(6) Medicament, wherein said medicament contains crystalline tiotropium bromide monohydrate as claimed in one of claims 1 to 3.

(7) Medicament as claimed in claim 6, wherein it is an inhalable powder.

GROUNDS OF OPPOSITION:

Initially the opponent filed the following grounds of opposition U/S 25(2): Following grounds have been relied upon by the opponents

a. U/S25(2)(b): that the invention so far as claimed in any claim of the complete specification has been published before the priority date of the claim

(i) In any specification filed in pursuance of an application for a patent made in

India on or after the 1st day of January, 1912; or

(ii) In India or elsewhere, in any other document;

b. U/S25(2)(d): that the invention so far as claimed in any claim of the complete specification was publicly known or publicly used in India before the priority date of that claim;

c. U/S25(2)(e): that the invention so far as claimed in any claim of the complete specification is obvious and clearly does not involve any inventive step, having regard to the matter published as mentioned in section 25 (2) (b)or having regard to what was used in India before the priority date of the Patentee's claim;

d. U/S 25 (2) (f): that the subject of any claim of the complete specification is not an invention within the meaning of this Act, or is not patentable under this Act;

e. U/S 25 (2) (h): that the patentee has failed to disclose to the Controller the information required by section 8 or has furnished the information which is in any material particular was false to his knowledge.

The chronological order of the Documents filed relating to the opposition by the opponents and the Patentee is mentioned below:

S.No.	Name of the Document	Date of filing
1.	Notice of Opposition under section 25(2) of the patent Act, 1970 and Rule 55A and 57 of the Patent Rules by S. Majumdar& Co. On behalf of Cipla Limited, Mumbai	**08/02/2013**
2.	Notice of opposition received by the patentee's agent on the same date	**08/02/2013**
3.	M/s Anand & Anand agent for applicant has filed petition under Rule 138 for extending the period for submission of the reply statement/ evidence by one month to May 8 , 2013.	**28/03/203**
4.	Reply filed by patentee U/R 58	**08/05/2013**
5.	S. Majumdar& Co. Agent for the opponent has filed petition u/r 138 for the extension of time of one month for filing reply evidence under rule 59	**10/06/2013**
6.	Reply evidence has been filed U/R 59 due to be filed upto09/07/2013	**09/07/2013**
7.	M/s Anand & Anand agent for applicant has filed petition under Rule 60 for extending the period for grant of leave along with further evidence of Ms. Wendy Petka and Dr. Markus Johannes Weymann.	**21/05/2014**

During hearing the applicant highlighted on certain position of law & also filing of evidences. The applicant submitted that

Arguments on Merits

1) Other contention of Patentee

1) Issue: Binding nature of orders of the higher Authorities including Intellectual Property Appellate Board (IPAB).

It is submitted that the orders of the superior courts including the IPAB are binding on the Indian Patent Office as IPAB is a superior forum to the Patent office. In this regard the applicant relies on the following case laws:-

• The Hon'ble Bombay High Court in **CIT vs. Godavari Saraf reported in 119 ITR 539** held that "*until contrary decision is given by any other competent High Court, which is binding on a Tribunal in the relevant State, it has to proceed on the footing that the law declared by the High Court, though of another State, is the final law of the land, which means that once a decision is given by any of the High Courts in the country and there is no contrary decision by any other High Court, on the same issue, then such decision of High Court will be binding on all the administrative authorities and Tribunals/quasi-judicial authorities throughout India" (copy enclosed)*

•The Hon'ble Allahabad High Court by their order dated 27th August 2012, in City Booking Agency vs, State Of U.P upheld and endorsed the finding of the Bombay High Court in CIT vs Godavari Saraf. (Copy enclosed)

2. Issue: Application of Code of Civil Procedure, 1908 (CPC) and Evidence Act in proceedings before the Indian Patents Act:

a. It is submitted that the provisions of CPC and the Evidence Act apply to all Disputes resolving authorities including Tribunals, Quasi-judicial Forums such as the patent office.

b. In this regard, the Patentee relies on Section 77 of the Indian Patents Act which is not being reproduced herein below for the sake of brevity. In accordance with Section 77, the Controller in any proceedings before him under this Act shall have the powers of the Civil Court while trying the suit under CPC.

5. Issue: IN254813 is a valid and subsisting patent.

a. The IN'813 is prima facie valid patent for the following reasons:-

i. The Indian patent office granted a patent after a thorough substantive examination.

ii. The Indian patent office granted a patent after considering and disposing of a pre-grant opposition filed by Intermed Laboratories.

iii. Most of the averments and documents cited in the present proceedings were considered in the pre-grant. A reference in this regard is made to Pages 15 and 16 of the reply statement.

iv. The Controller after duly considering the pre-grant Opposition and the evidence placed before him allowed the patent application to proceed to grant and held the following:

- The monohydrate form claimed is stable under rigorous manufacturing condition and post manufacture.
- This specific form of the compound claimed and its stable particle size distribution make it effective as an inhalable drug.

• The documents which relate to oral administration are irrelevant to the present case.

• D1 and D2 (D3 and D4 in present Opposition) alone or in combination do not motivate or suggest the active presently claimed and therefore the present invention is inventive over them.

• It is this ability of this crystalline monohydrate with its specific stable particle size distribution which make the active show the anticipated efficacy on administration by powder inhalation, whereas, the prior art crystalline form could not reach the targeted site in a given time to show the same efficacy.

v. Several patent applications corresponding to IN'813 have been filed and several such patent applications have been granted in other jurisdictions. Reference in this regard is made to form -3 dated 21st July 2010 filed by the applicant. (Pages 206-210 of the Opposition filed by the Opponents).

6. Issue: Burden of Proof not discharged

a. In the present opposition proceedings, the Opponent has not filed any evidence in support of their post- grant opposition and clearly did not discharge their onus of establishing the invalidity of **IN' 813.**

b. It is a well settled principle in patent law, that it is the challenger who has to discharge the onus through filing of "verifiable evidence" while dealing with invalidity grounds. In this regard, the Supreme Court of India and the IPAB have clearly recognized and held that if evidence has not been filed, the challenger has not discharged their onus. In the absence of any evidence on behalf of the Opponent in the present proceedings, it

is respectfully submitted that the post grant opposition should dismissed *in limine.*

c. The need for evidence is also recognized by the Hon'ble High Court in ***F. Hoffmann-La Roche Ltd. & Anr. V. Cipla Ltd.,*** *2012 (52) PTC 1 (Del) in paras 67 and 70,*

Para 67

"It is also necessary to examine the ***legal aspect of onus of proof*** *involved in the revocation proceedings. It is well settled principle of law that the onus of proof in the revocation proceedings is akin to the principle of onus of proof involved in the civil cases which is on balance of probabilities"*

Para 70

"This discussion on onus of proof in revocation proceedings became necessary in order to delimit the scope of the enquiry as to weighting of the evidence. This is due to the reason that the parties in instant case continue to insist on the anomalies done by each other and also stating the lack of evidence on either side one way or the other. Therefore, it has become necessary to point out that the evidence of the parties are to be tested on the balance of the probabilities…"

d. The evidence-in-reply of Dr. Ganga Srinivasan filed by the opponent cannot be considered as evidence for discharging onus in a post grant opposition. The evidence-in-reply u/r 59 has to be restricted to the evidence filed by the Patentee and is more in the form of a reply (rebuttal evidence) to the evidence of the patentee.

e. It is submitted that in the absence of evidence and the Opponent not having discharged the burden of proof, all

assertions made in the opposition are mere allegations. Grounds such as obviousness, novelty, and insufficiency have to be judged by a person skilled in the art and it is a person skilled in the art, the hypothetical construct, who has to assess the prior art and the patent specification.

f. In the instant case, it is the Opponent who has alleged that the patent is invalid and thus is the "challenger" i.e. the ***burden of proof to prove invalidity lies on them.*** Therefore, the assertions made are simply unsupported allegations which are not proven and thus need to be dismissed *in limine.*

g. The Patentee relies on the following procedures and provisions of law in this regard:

• Sections 101 and 102 of the Evidence Act.

*"**101. Burden of proof.** - Whoever desires any Court to give judgment as to any legal right or liability dependent on the existence of facts which he asserts, must prove that those facts exist. When a person is bound to prove the existence of any fact, it is said that the burden of proof lies on that person.*

***102. On whom burden of proof lies**.- The burden of proof in a suit or proceeding lies on that person who **would fail if no evidence** at all were given on either side."*

•In F & H v. Unichem (AIR 1969 BOM 255 (V 56 C40) (Para 13), the following was held :

"13. .....[I]t may be stated that the onus in regard to all objections to validity lies on the defendant (Halsbury, (3rd ed.) Vol. 29 p. 106 paragraph 218).

• **In The Travancore Mats & Matting Co. v The Controller of Patents and Ors in ORA/44/2009/PT/CH,** the Hon'ble IPAB in para 13 held:

"The Petition and the Miscellaneous Petition accompanying the same do not contain any substantial objections nor are supported by any relevant documentary proof or evidence Thus, the onus of establishing invalidity of a Patent lies on the party seeking to revoke the patent and this has been laid down in several cases. The Petitioner has not put forth any valid submissions in support of his petition for revoking the Patent. The onus lies on the Petitioner to validate its contentions and it has failed to do the same".

h. Further, Rule 57 of the Patent Rules 2003 requires the opponent to file a written statement which is akin to pleadings setting out the nature of opponent interest, the facts upon which the basis is caused and relief which he seeks and evidence, if any, along with the notice of opposition.

The Courts in India have clearly interpreted the provision relating to invalidity of the patent and held that in any invalidity proceedings the burden of proof is always on the opponent. The said burden of proof can only be discharged through evidence.

i. Rule 57 of the Patents Rules 2003 clearly provides a distinction between "pleadings" and "evidence". Pleadings such as the written statement have to contain "**material facts"**. The Opponent has to file a written statement which sets out the nature of Opponent's interest. Rule 57 further provides that along with written statement, evidence needs to be filed.

j. Under Section 79 of the Indian Patents Act, evidence before the Controller **shall** be given by way of affidavit. This is a mandatory provision and shall cannot be interpreted as **"may"** .

k. Rule 57 read with Section 79 which is substantive provision of law requires that evidence shall in any proceedings under the Indian Patents Act be given by way of an affidavit. Therefore, no amount of documents that are not accompanied with any affidavit of an expert to prove invalidity grounds of a patent can be allowed and the opposition be proceeded with based on legal surmises and conjectures of a legal counsel.

l. This is particularly important in view of the fact that IN'813 is already established and proved to be a valid patent after having gone through the several rounds of examination before the Indian Patent Office.

m. In so far as how evidence is lead, reliance is placed on Rules 126(2) and

(3) of the Indian Patent Rules, which we are reproducing herein below:-

126. Form, etc., of affidavits.—(1) The affidavits required by the Act or these rules to be filed at the patent office or furnished to the Controller shall be duly sworn to in the manner as prescribed in sub-rule (3)

(2) Affidavits shall be confined to such facts as the deponent is able, of his own knowledge, to prove except in interlocutory matters, where statements of belief of the deponent may be admitted, provided that the grounds thereof are given.

(3) Affidavits shall be sworn to as follows:—

(a) in India—before any court or person having by law authority to receive evidence, or before any officer empowered by such court as aforesaid to administer oaths or to take affidavits;

(b) in any country or place outside India—before a diplomatic or consular officer, within the meaning of the Diplomatic and Consular Officers (Oaths and Fees) Act, 1948 (41 of 1948) in such country or place or before a notary of the country or place, recognized by the Central Government under section 14 of the Notaries Act, 1952 (53 of 1952), or before a judge or magistrate of the country or place.

7. Issue: No Evidence Filed/Opponent's Documents Cannot Be Treated As Evidence In View Of Section 79 Of The Indian Patents Act

a. It is submitted that the Opponent has not filed any evidence to establish the grounds of challenge and the exhibits filed by the Opponent cannot be considered as being 'evidence' particularly under Section 79 of the Indian Patents Act for the following reasons:

b. A post-grant opposition is a proceeding under the Indian Patents Act.

Therefore the nature of evidence that is admissible before this Hon'ble Controller will also be determined and governed by the provisions of the Act.

c. Section 79 of the Indian Patents Act (which is a **substantive provision and not a subordinate legislation)** clearly requires that the evidence in any proceedings under the Indian Patents Act before the Controller **shall be** given by way of an affidavit in the absence of directions by the Controller to the contrary.

d. The exhibits filed by the Opponent cannot be treated as evidence as they were not filed by way of an affidavit as required under Section 79 of the Indian Patents Act and therefore all pleadings and arguments based on the exhibits cannot be considered or taken into account.

e. The patentee in this regard would like to direct the attention of the learned controller to the following cases:

- ***ORA/8/2009/PT/CH,*** the Hon'ble IPAB in para 42 held, *"42. Obviousness has been accepted to be a statement of policy.....we may need an expert to say what would be obvious considering the state of the art in say genetic technology"*

- In TRA/3/2007/PT/DEL, **LML Limited Vs. Bajaj Auto Limited** the Hon'ble IPAB held in para 57 the following**:**

"We also find the specification has disclosed the invention sufficiently and fairly. In absence of any evidence of the applicant to the contrary we are inclined to disagree with the argument of the applicant in respect of insufficiency. This ground therefore also fails."

- In **Ajay Industrial Corporation Delhi v. Shiro Kanau, 1983 PTC 245,** page 264 the Court held:

In the absence of any technical or expert evidence either indicating that these statements are wrong or that the article produced incorporates no new – devices to get over these defects, it cannot be held that the patent embodies no new discovery or invention"

- **ORA/21/2011/PT/KOL in Order no. 173 of 2013 passed by the IPAB,** it was held: *"Having found that the invention is obvious, we must state that it is the duty of the applicant [of the*

opposition/ revocation] to adduce evidence to prove obviousness. In pharmaceutical patent revocations it may not always be possible to rest on just prior arts…….This may not be so clear in other cases. We do not know why the affidavit originally filed was withdrawn. We reiterate as we have done in other cases before that the applicant must plead and prove his case."

f. Therefore the post-grant opposition should be dismissed *in-limine* in the absence of evidence not being filed by the Opponent in accordance with Section 79 of the Indian Patents Act.

8. Issue: Legal Arguments Of The Counsel Cannot Take Place Of Evidence

a. Rule 57 of the Patent Rules (Pleadings and Evidence): To discharge the burden of proof, arguments or rebuttal evidence cannot be considered. Rule 57 of the Patents Rules 2003 clearly provides a distinction between "pleadings" and "evidence". Pleadings such as the written statement have to contain "**material facts"**. The Opponent has to file a written statement which sets out the nature of Opponent's interest. Rule 57 further provides that along with written statement, evidence needs to be filed. Under Section 79 of the Indian Patents Act, evidence before the Controller shall be given by way of affidavit.

b. In the absence of having filed evidence by way of affidavit, the oral arguments made by the Opponent's legal counsel before the Learned Controller at the hearing, cannot take the place of evidence or pleadings.

c. Mere allegation and legal counsel arguments is not sufficient to dislodge a validly granted patent.

d. In ***para 17 ORA/44/2009//PT/CH in The Travancore Mats & Matting Co v Controller of Patents and Ors,*** *the Hon'ble IPAB held:*

- *"17. It is trite law that person who seeks revocation must prove it. The onus of proving invalidation of a patent is on the applicant [opponent, not to be confused with patent applicant]. The applicant in this case failed miserably to prove his case****. Mere allegation is not sufficient to dislodge a validly granted patent****."*

- ***Application of Klaus Schulze [346 F.2d 600], United States Court of Customs and Patent Appeals,*** at page 3:

"…. Argument in the brief does not take the place of evidence in the record.

- ***In re Michael GEISLER, Rudolf Kotter-Faulhaber, Susanne Wuerz and Michael Jung****.[116 F.3d 1465], the Federal Circuit at second column page 6, held that: "…("mere lawyers' arguments unsupported by factual evidence are insufficient to establish unexpected results")."*

9. Issue: Dr. Srinivasan's affidavit and annexure 2 annexed thereto inadmissible

a. Rule 59 deals with the filing of reply evidence by Opponent and states as follows:

"The opponent may, within one month from the date of delivery to him of a copy or the patentee's reply statement and evidence under rule 58, leave at the appropriate office ***evidence in reply strictly confined to matters in the patentee's evidence*** *and shall deliver to the patentee a copy of such evidence."*

b. In view of Rule 59, it is submitted that the evidence in reply (rebuttal evidence) has to be confined only to matters present in the Patentee's evidence.

c. Dr. Ganga Srinivasan in her evidence has gone beyond the mandate of Rule 59 and has relied on a new document, Annexure 2 in her evidence in-reply.

d. In view of the above, the evidence in-reply cannot cure the lack of evidence required to support filing of the opposition.

e. In this regard, we submit that even the Hon'ble IPAB has ruled that if the evidence in reply travels beyond the Patentee's evidence, the Controller has the discretion to "disregard such evidence" or "only rely on those parts of the evidence in-reply which specifically refer and addresses the patentee's evidence".

f. In this regard, we wish to rely on the Hon'ble IPAB order dated 13th May 2013- ***Sugen vs. CIPLA, IPAB*** in para 17 held: *"..the evidence filed under Rule 59 not being strictly confined to matters in the Patentee's evidence. According to the appellant the evidence filed by the respondent including the affidavit of Dr.Rao had not been confined to the evidence that they had filed under Rule 58. If so, they are not prejudiced by the contents of the respondent's evidence. Even otherwise* ***it is open to the appellant to point out the matters which are extraneous at the time of hearing, and the Controller will decide the question in accordance with law****."*

10. Issue: Dr. Srinivasan is not an expert in the field of inhalative formulations

a. As stated above, the evidence/declaration of an expert is a critical document in an opposition proceeding.

b. The patentee had filed evidence of expert in the field of technology. The patentee had in fact filed the evidence of the inventor and as held by Roche Vs. Cipla the inventor is the best expert to depose a declaration in the field of technology of the subject matter in question: *As per the Supreme Court judgment Bishwanath Prasad vs. Hindustan Metal [1979] 2 SCC 511 paras 21, 36, 43 to 50, the inventor would have been the best witness.*

c. The Opponent on the other hand, did not file any evidence with the opposition. Further, the evidence in reply filed by the opponent was only as reply evidence (rebuttal argument). Also Dr. Ganga Srinivasan who deposed the evidence in reply while is a highly qualified professional; she is not an expert in the field of inhalative formulation, the field of technology of the present patent.

d. The issues relating to inhalative formulations are very critical, and different from other modes of drug-delivery for instance trans-dermal delivery. None of the research publications of Dr. Ganga Srinivasan relate to inhalative formulations, or the field of technology of the present invention.

e. We also wish to rely upon the decision of the Hon'ble High Court in Vringo Infrastructure vs. ZTE Telecommunication (copy enclosed). The Hon'ble Court in this case gave its finding on who could qualify as an expert. It held that if an expert does not have a qualification of science or technical law as prescribed under Section 115 of the Indian Patent Act, he could not be termed as an expert.

f. We also rely upon Section 45 of the Evidence Act which we reproduce herein below:

"When court has to form an opinion upon a point of foreign law or of science or art, or as to identify of handwriting (or finger impressions) the opinions upon that point of persons specially skilled in such foreign law, science or art (or in question as to identity of handwriting) (or finger impressions) are relevant facts. Such persons are called experts."

Opponent's reply to the contention of the patentee for:

Requirement of evidence in post grant opposition procedures:

The Opponent contended that the controller is a creature of the patent law and the expert affidavit is not necessary if sufficient documentary evidence has been provided under each ground of section 25(2). It is important to note that under Evidence Act, both documentary evidence and oral testimony are considered as evidence. The members of the opposition board essentially possess scientific degree (s) with skills to understand the scientific principles and filing of expert affidavit is not mandatory in each case and the matter is case specific. Rule 57, specifically makes clear that filing of evidence is not a mandatory, rather it is optional and the decision about its filing is left to the opponent and the merits of the documentary evidence supporting the written statement. The prior art forming part of the pleadings present the state of art and matters of common general knowledge. The Controller having being appointed to the

position due to his technical qualifications is required to possess the capacity to appreciate the technical contents of an invention and the prior art and to determine whether falls out of the track of the teachings of the prior art and is not obvious to a person skilled in the art. If the Controller does not such capability then the entire scheme of the patent examination would fall apart. The Controller under the provisions of sections 12-15 of the Act finally determines the patentability of an invention without hiring the services of an expert and therefore pressing an expert into action in opposition proceedings is the scheme of the law and the same is borne out of several decisions of the Controller on the basis of prior art alone.

Grounds of Opposition

1) Grounds under Section 25(2) (b) and under Section 25(2) (d), i.e. the ground of prior public knowledge and prior public use

Opponents Submission

Though the Opponents had earlier filed the above mentioned grounds of opposition, but during the hearing the opponent did not **pressed on the following grounds:**

a. **U/S 25 (2) (b):** that the invention so far as claimed in any claim of the complete specification has been published before the priority date of the claim

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

(ii) In India or elsewhere, in any other document.

b. **U/S 25 (2) (d):** that the invention so far as claimed in any claim of the complete specification was publicly known or publicly used in India before the priority date of that claim.

Applicants / Patentees submission

The opponent gave up the grounds under Section 25(2) (b) and under Section 25(2) (d), i.e. the ground of prior public knowledge and prior public use respectively at the hearin

2) Inventive Step /Obviousness {Section 25(2)(e)}

Opponents Submission

Arguing on this ground, the opponent took the Ld. Controller through the complete specification where the field of the specification states that the invention is related to the crystalline monohydrate of Tiotropium bromide, its process of preparation and use in pharmaceutical composition.

The specification in its background section discloses that Tiotropium Bromide was well known in the art at the time when this patent application was filed. Admittedly, therefore, the contribution of the patentee was limited to crystalline monohydrate form of Tiotropium Bromide.

The monohydrate crystals of Tiotropium Bromide are the subject matter of presently granted claims of the impugned patent and thus are under scrutiny for the matter of the presently filed opposition in terms of verifying whether they suffice the patentability requirement i.e. novelty, inventive step, industrial applicability and overcoming the objection under

section 3(e) and 3(d) as prescribed by the Indian Patent Act.

The specification on page 3 states that the aim of the invention is to provide or prepare a stable crystalline form of the compound tiotropium bromide. Admittedly Tiotropium bromide is known in the art and thus the applicant is intending to prepare a stable crystalline form of a known compound.

Thus, the teaching flowing from the specification is that the active medicament which renders the therapeutic benefits (i.e. tiotropium bromide, which was though known in the art) here remains same, and the applicant is exploring around the stable form of the same. The technical problem as highlighted in the specification on page 3 is to increase/enhance the shelf life of the pharmaceutically active substance (i.e. tiotropium bromide) so that the physical and physiological property remains active under storage condition. Therefore admittedly the case of the petitioner was to achieve this stability, and for such purpose applicant treated the active substance through crystallization process.

On the same page, in paragraph 3, the applicant states that any change to the solid state of a pharmaceutical composition which is capable of improving its physical and chemical stability gives a significant advantage over less stable forms of the same medicament. Further, in the second last paragraph, the applicant admits that the surprising feature found by them is that the monohydrate tiotropium bromide can be obtained in crystalline form by choosing specific reaction condition, solving the problem on which the present invention is based and

accordingly the invention provides crystalline tiotropium bromide monohydrate.

The opponent further stated that in view of the aforesaid, it is important here to answer the following 3 essential questions, based on which the inventive step of the invention has to be decided:

Question 1: Whether the crystallization of a medicament for improving its physical and physicochemical properties was known in the art?

Question 2: Was there any motivation for solving the problem in the same way as that adopted by the patentee?

Question 3: Whether there is any data in the specification which shows the improvement of any beneficial properties to the active substance other than shelf life of the medicament?

The answers to the above questions will help in gazing out the clear picture of the inventive step of the invention.

D1	Tiotropium (Spiriva): Mechanistical Considerations and Clinical Profile in Obstructive Lung Disease by Disse et al published in 1999.
D2	Long-Acting Bronchodilation with Once-daily Dosing of Tiotropium (Spiriva) in Stable Chronic Obstructive Pulmonary Disease" by Littner et al published in April 2000 in The American Journal of Respiratory and Critical Care Medicine

D3	US5610163; published on March 11, 1997 alongwith the Espacenet INPADOC family list.
D4	US 5468758; published on November 21, 1995. D4 relates to Crystalline and pharmacologically active monohydrate forms of drugs.
D5	US3634582 published on January 11, 1972.
D6	US5478578 published on December 26, 1995.
D7	US5354760 published on October 11, 1994

The opponent stated that each of the above referred document(s) has different implication as well detailed in the Written Statement and further relied on the prior art document, D3 (i.e. EP 418716 while its US corresponding is US 5610163), which is an acknowledged prior art by the patentee in its complete specification. D3 essentially teaches Tiotropium Bromide. The abstract of D3 expressly discloses that Tiotropium Bromide is used as anticholinergic and suggests its administration through inhalation, useful for the treatment of chronic obstructive bronchitis, asthma etc. D3 further suggests that the drug may be administered through the intravenous or oral routes as well.

The opponent states that the admitted position flowing from the teachings of D3 is that the Drug i.e. Tiotropium Bromide is known in the art, its mode of administration i.e. through inhalation, is known along with its pharmacological property. Further, example 4 of D3 provides preparation of crystals of

Scopine di-(2-thienyl) glycolate methobromide which actually represents tiotropium bromide. The same paragraph line 13 also discloses about the white crystals of Scopine di-(2-thienyl) glycolate methobromide which represents tiotropium bromide which are prepared by using solvents like methanol/acetone having melting point of 217 to 218 degree Celsius after drying at 111 degree Celsius.

Similarly, page 6 of the specification, mentions that the crystalline tiotropium bromide monohydrate is characterized to have an endothermic peak at temperature ranging from 225 to 235 degree Celsius at a heating rate of 10K/min.

The opponent stated that the crystal structure of D3 and the tiotropium bromide monohydrate of impugned patent has similar crystal structure which is evident from the last example of the impugned patent wherein the crystals are prepared using acetone as solvent as similar to the teachings of example 4 of D3.

Further, the opponent stated that the Evidence by Way of Affidavit of Dr. Michael Trunk in paragraph 10.4 states that there was only one process for manufacturing Tiotropium Bromide before this patent application was filed and which was covered by D3. The expert has admitted that D3 is the basic patent disclosing Tiotropium Bromide and its synthesis. He has acknowledged that the final step of synthesis of tiotropium bromide is described in the example 4 of D3 and a skilled person by following this procedure would be able to obtain the crystalline modified form of tiotropium bromide.

Furthermore, the opponent took support from Dr. Weymann's affidavit which in paragraph 40 clearly states that D3 covers

and protects Spiriva handihaler product. Furthermore, D3 claims and protects tiotropium salts regardless of their physicochemical appearance and characteristic.

Reading the affidavit of applicant's experts (Dr. Trunk and Dr. Weymann), it is clear that D3 taught about tiotropium salt regardless of physiochemical properties and the example 4 of D3 taught about the process for obtaining crystalline modification of Tiotropium bromide.

Thus, it is possible to obtain the monohydrate crystal of Tiotropium bromide starting from the teaching of example 4. The opponent states that the monohydrate of Tiotropium bromide is evidently the part of the teaching of D3 though not characterized. The Patentee ought to have furnished comparative test data in terms of product property, stability and performance. In other words the onus is on the Patentee to prove that the allegedly claimed product is technically advanced as compared to the known product viz D3.

Further, the opponent relies on D4 (i.e. US 5468758) which has a publication date prior to the priority date of the Patentee's specification.

D4 addresses the technical problem of providing physical and chemical stability faced by a person skilled in art, difficulties in prior art like moisture absorption tendency of a drug, stability problems of an active ingredient due to polymorphic modifications, variation in crystal lattice during milling (Column 1 and Column 2). The technical problem addressed by D4 is same as that of the technical problem addressed in the specification of the impugned patent as page 2 of the

specification which states that uniform distribution of the medicament in the formulation is a critical factor particularly when the medicament has to be given in low doses and in order to obtain the active substance of a corresponding particle size, a grinding process is again required. Thus, the active is expected to be sufficiently stable during the grinding process. The opponent states that the problem to be solved both in the present specification and D4 is to provide uniform distribution of the medicament in the formulation. D4 provided that the physical and chemical stability problems of an active ingredient faced by a person skilled in art may be addressed by using monohydrate form of an active ingredient in Column 3, Lines 13 to Lines 25.

The opponent states that D4 also demonstrates the effect of milling studies and the uniformity content in the 2a and 2b monohydrate forms at columns 11 and 12. It is pertinent to note that in both the accelerated stability tests and normal stability tests, it is observed that the novel monohydrate forms 2a and 2b show better stability than 1a and 1b which are the anhydrous forms of the prior art.

The advantages of monohydrate crystalline forms in pharmaceutical preparations are mentioned in D4 with regard to hygroscopicity, physical and chemical stability during manufacturing process and during storage in form of pharmaceutical preparations. D4 teaches the tolerance of a particular polymorphic form to micronization stress. Irrespective of the dosage form in which the micronized active is going to be utilized, one needs to gather that a direction for preparing a different polymorphic form prior to micronization is provided in

D4.

Thus, D4 provides motivation for addressing the technical problem of achieving uniform distribution of a compound, which is also stable during the milling process. Since the technical problem and the solution to it as addressed in D4 is same to that of the present invention, thus the statement of expert Mr. Weymann that D4 is not related to the present patent does not stand valid in this context.

Having regard to the teachings contained in D4, it would be obvious to a person skilled in the art to address the problems faced by the Patentee to be in the use of the monohydrate salt form of tiotropium bromide, which was already known in the art through D3, as even admitted by the Patentee in its specification.

The opponent states that D4 clearly endorses the fact that when one faces a problem with a particular form of a drug substance then the same may be converted to another polymorphic form which will exhibit stability while processing i.e. during the milling process and show uniform content in the final dosage form.

In fact, D3 and D4 (both owned by the patentee of this patent) had research going on parallely as the patent applications for D3 and D4 were filed almost at the same time.

The opponent further relies on D5 i.e. US 3634582. D5 is the counterpart of the patent DE-A-1792207 acknowledged in the specification of the impugned patent. D5 in particular teaches a pharmaceutical powder composition for inhalation comprising a mixture of a solid finely divided medicament having an effective

particle size in the range 0.01 to 10 microns and a solid pharmaceutically acceptable water-soluble carrier having an effective particle size in the range 30-80 microns.

D5 teaches that ***"Medicaments 'for 'administration by inhalation should be of a controlled particle size in order to achieve maximum penetration into the lungs; a suitable particle size range being 0.01 to 10, usually 1-10, microns".***

The opponent states that in the event where D3 discloses basic Tiotropium Bromide(basic patent), D4 discloses that monohydrate can be prepared for overcoming issues faced during the milling process along with D5 disclosing the prescribed particle size useful for the inhalation formulation, the invention of the impugned patent lacks inventive step.

Particularly, the following information flows from the prior art:

I.Tiotropium bromide is an effective anti-cholinergic agent thereby capable of providing therapeutic benefit in the treatment of COPD;

II.Polymorphs have different stabilities and may spontaneously convert from a metastable form (unstable form) to the stable form;

III.Particle size of active in the range of 0.01 – 10 micron for effective lung penetration for drugs which are administered by the inhalation route;

IV.Crystalline monohydrate been stable to micronization and grinding.

The availability of the aforesaid information required no extraordinary efforts on the part of the patentee. Preparing the monohydrate form allegedly claimed as a stable crystalline form

which meets the stringent requirements imposed on pharmaceutically active substances is a matter of routine experimentation and does not involve any inventive ingenuity in doing so.

Essentially, all the features contributing towards the inventive step as allegedly claimed by the patentee are present in the teachings of D3, D4 and D5 read in combination with each other.

The opponent further relies on D6 i.e.US5478578. D6 in particular is directed to inhalation powders and their desired particle size. ***The term 'inhalable' as per D6 means those particles which are transported deep into the branches of the lungs when inhaled with the inspired air. The particle size required is less than10 µm, preferably less than 6 µm. D6 thus teaches that the particles size of less than 10 µm is the basic requirement for powder for inhalation to elicit a therapeutic response.***

The opponent states that it is important to find out whether a skilled person can follow the thread of prior art to reach the claimed invention?

And

Whether the claimed invention lies so much 'out of track' that it must not be obvious of what was previously known?

The opponent states that, it is evident that the product allegedly claimed in the impugned application is obvious and lacks inventive merit on the face of the teachings of:

i. D1;

ii. D2;

iii. D3;

iv. D3 in view of D4;

v. D3 in view of D4 and D5;

vi. D4 in view of D3 and D5;

vii. D3 in view of D4 and D6;

viii. D4 in view of D3 and D6.

Thus, the assertion of applicant for having "magic" in the particle size of actives allowing to be used for inhalation becomes obvious based on the combined teachings of documents.

The opponent further relied on Annexure 2 referred in Evidence in reply of the opponent of Dr. Ganga Srinivasan. Annexure 2 teaches that the monohydrate polymorphic form is stable after micronization, during formulating of the inhalable drug product and even after storage for extended periods which is also the solution to the stability issue of tiotropium bromide adopted by the impugned patent. The opponent stated that Annexure 2 is a motivating document to reach to the impugned patent.

The opponent also referred to the definition of person skilled in the art through IPAB decisions. The Hon'ble IPAB quoting Hon'ble High Court of Delhi and Hon'ble Supreme Court in *Fresenius Kabi Oncology v. Glaxo Group Limited,* stated that "it is definitely not necessary nor proper for us to dumb down the Person Skilled in the Art, nor make him so ignorant of anything that is happening elsewhere or presume he is ignorant of even common text books unless proved otherwise. In fact this hypothetical person is presumed to know all the prior arts as on that date, even non-patent prior art in theory available to public. He has knowledge of the technical advancement as on that date, and the skill to perform experiments with the knowledge of state of the

art."

In *Enercon India v. Aloys Wobben*, Hon'ble IPAB stated that "Indian law expects the non- obviousness to be tested against this person and not the person who is the touchstone in U.S. Law. She is Ms. P. Sita (Person Skilled in the Art) and not Mr. Phosita or Mr. Posita who are both ordinary by definition!" Hon'ble IPAB has also noted that Ms. P. Sita should be understood "as working in [her] shop with the prior art references . . . hanging on the walls around [her]" This is a very evocative scene and does help us in figuring out what the hypothetical person: the Person Skilled In The Art will do"(known through paragraph 56).

Hence, Person skilled in the Art would pursue these options as it is a obvious solution to administer Tiotropium Bromide and hence, the product is outcome of ordinary skill and common sense.

From the aforesaid, it is evident that the claimed invention does not lie "out of track".

The Opponent pointed out to

Recommendation of Opposition Board:

The Opposition Board recommends that the "unexpected surprising advantageous technical effect had been achieved by the claimed crystalline Tiotropium bromide monohydrate compound as based on Patentee in his admission, the purity and stability (among the unexpected effects) could not be predicted by one person skilled in the art over the cited document D3-D6. Thus the Board opinioned that the present patent invalid in lack of inventiveness over the disclosure made

in documents D3-D6, because one person skilled in the art would readily arrive at the invention based on the above teaching. Relying on such an originally filed document, the applicants failed to provide sufficient comparative data for any unexpected surprising advantageous technical effects verified in the description over the closest prior."

As explained above, documents D3-D6 guides a skilled person to arrive at the claimed invention without requiring any inventive ingenuity. The Opponent is 'for' the recommendations of the Board.

The Opposition Board has observed that "Claim 4 and Claim 5 of document D3 disclose the molecule Tiotropium bromide. Further D3 teaches anticholinergic drugs administered by inhalation and used in the treatment of chronic obstructive bronchitis or slight to moderately severe asthma."

This provides the starting point for manufacturing the claimed invention. The skilled person is motivated to use Tiotropium Bromide in inhalative formulation to treat COPD. It is to be noted that D1 and D2 further would strengthen such a choice as they disclose use of inhalative formulation of Tiotropium Bromide as yielding beneficial results vis-à-vis treatment of COPD. The Opponent is 'for' the recommendations of the Board.

The Opposition Board has also pointed out that the when the skilled person would know that Tiotropium Bromide is to be used as inhalative formulation, he would be motivated to arrive at powdered form within the range of 0.01 to 10 microns and to do so he would be motivated to rely upon crystalline monohydrate form.

The Opposition Board observes that the specific advantages of monohydrate crystalline forms in pharmaceutical preparations are known, especially its tolerance to micronization. The Opposition Board states "Document D4 on column 4, discusses the specific advantages of monohydrate crystalline forms in pharmaceutical preparations with regard to hygroscopicity, physical and chemical stability during manufacturing process and during storage in form of pharmaceutical preparations. D4 teaches that the monohydrate forms show better stability than the anhydrous from of the prior art compound. Further D4 teaches the tolerance of a particular polymorphic form to micronization stress. In view of aforesaid teaching, it is observed that if any of the references D1 to D3 is combined with D4, the combination provides clear motivation and reasonable expectation of success for a person skilled in the art to prepare the crystalline hydrate form of Tiotropium bromide as claimed in the impugned patent with enhanced properties."

The Opposition Board observes that the particles in size range of 0.01 to 10 microns are effective as inhalative formulation is prior knowledge in light of D5. The Opposition Board notes, "D5 teaches that particles in the size range of 0.01 to 10 microns alone are effective for penetration into the lungs and that the composition should contain a coarser solid diluents or carrier for ready fluidization in other words ease of inhalation of the composition and D6 relates to powder for inhalation and is specifically directed to inhalation powders and the desired particle size. It is observed from the disclosure of D5 and D6 reveals that the alleged invention is merely a combination of

known features from the prior art and is a product of mere trial and error and does not involve any inventive skill."

The Opponent is for the Recommendations of the Opposition Board.

The opponent relied on the following case laws for Inventive step:

a) In the decision of opposition filed for 2899/Delnp/2005, the Ld. Controller on page 10, paragraph 15.18 clearly stated that where specification does not demonstrate the betterment of the properties of the claimed subject matter (i.e. Composition) as compared to the already existing piece of information in prior art(s) and thus in such a case the invention would lack inventive step.

The relevant text is reproduced below:

> 15.18 I observe that the applicant has failed to provide any evidence of improved unexpected properties of the claimed composition. Moreover the specification does not demonstrate betterment of properties of the claimed composition with the lower amount of albumin (4.5:1-albumin: active) as against the high amount of albumin (27:1 or 18:1 – albumin: active). Going through the teachings of the cited references, a person having ordinary skill in the art would have sufficient teachings/ suggestions and motivation to reach at each and every element of the claimed composition.
> Therefore, the amended claims 1 to 12 lack inventive step.

Further, paragraph 15.19 of the same decision, refers to an EP case law which expressly states that for demonstrating inventive step on the basis of an improved effect, the comparative test should be with the closest prior art.

15.19 I observe that in Case Number: T 0059/04 - 3.3.02 (Date of decision: 23 November 2006), the EPO Board of Appeals held that

'It is true that the patent in suit contains comparative tests (clinical trial A) which demonstrate a lower incidence of diarrhoea for the ratio 7:1, but as the opposition division had already correctly pointed out in the decision under appeal, these tests cannot be taken into consideration, as the comparison was made with a 4:1 t.i.d. regimen which does not represent the closest prior art. In this context, it is emphasized that it has been established case law at the EPO that if comparative tests are chosen to demonstrate an inventive step on the basis of an improved effect, the nature of the comparison with the closest state of the art must be such that the said effect is convincingly shown to have its origin in the distinguishing feature of the invention (T 197/86, OJ 1989, 371).

The Hon'ble IPAB in *CIMA LAB v. Controller* (Order no. 60/2013), rejected an application for patent claiming a dosage formulation relating to orally disintegrable/dissolvable effervescent opiate where the patentee claimed that the inventiveness lay in addition of starch glycolate to the formulation. However, the Hon'ble IPAB rejected the argument in view of prior art which disclosed the formulation as well as the property of starch glycolate being a super disintegrant. The Hon'ble IPAB concluded that this being in knowledge of the person skilled in the art would not qualify as being inventive and hence, refused to overturn the Controller's rejection.

Order in the counterpart Chinese patent

Boehringer Company appealed the decision of lower Court of China which had rejected the patent over crystalline tiotropium bromide monohydrate. The Supreme People's Court of People's Republic of China upheld the invalidity of Boehringer's crystalline tiotropium bromide monohydrate patent application

reasoning that it lacked 'unexpected technical effects' and hence was not 'creative'.

The Court relying upon the Review Guidelines which state "a compound that has the similar structure of known compounds, must have the differentiated use or effect" stated that if the molecule or compound has a similar core structure as another known compound, then the determination of 'creativity' depends on whether "the crystal has the unexpected technical effects or not". The Court further stated that this "differentiated use or effect can be different from the known uses of the know compounds; or it has substantial improvement or modification to a known effect of the compounds know; or it has usage or effect that is not clear".

The Court found that the claimed subject-matter of the patent, monohydrate tiotropium bromide monohydrate had the similar core structure like the known compound 'tiotropium bromide'. The Court then stated that the original patent lacked any data to establish unexpected technical effect and hence, the holding of the lower Courts that the patent was invalid was correct.

Compared to the same drug formulation that is relatively unstable, the solid state change of any physical and chemical stability drug composition that can improve the pharmaceutical composition can provide significant advantages. The said technical effect is recorded in the patent, but there is no evidence to prove that the patent has the technical effect.

Applicant /Patentees Submission

a) On the ground of inventive step, the patentee submits the following:

I.The opponent is incorrect in stating that the inventive step of the present invention lies in the particle size of the active.

II. It is respectfully submitted that the problem underlying the invention is not to determine the effective particle size range but lies in identifying and finding a novel pharmaceutical substance that can be converted into the particle size range which is effective in entering the lungs when administered by inhalation.

III. It is a well established legal principle that in any obvious enquiry the problem underlining the invention has first to be analyzed.

IV. This has not been done by the opponent in the first case, in fact the opponent has incorrectly identifying and applying the problem underlying the invention.

V. Polymorphism is a complex field and different polymorphs of different compound could have different properties. The physical, chemical properties of any polymorph can be very complex and unpredictable. A drug substance can exist in various crystalline forms which cannot be predicted. Further, the polymorph form can have un- predictable physical and chemical properties like volume, density, viscosity, crystalline shape, stability etc. and associating any property with a polymorphs can only be done in hindsight which is not allowed non-obviousness enquiry.

b) Document D3 (US5610163)

i. It is submitted that the opponent is misleading the Learned Controller by stating that the crystalline form in example 4 of D3 is the same as the claimed tiotropium bromide form.

Ii.The patentee has already submitted comparative analysis with regard to the prior art form disclosed in D3 and the monohydrate form presently claimed. Dr. Weymann in his affidavit clearly proved that the two forms are different. Every tiotropium salt, solvate, solvates of salt may exist in crystalline form, this does not imply that the crystalline form of D3 is the same as the present invention. (**Para 12 of his evidence – Page 143 of the reply statement**)

iii.D3 is a basic compound patent for tiotropium which was granted in the year 1997. Document D3 has been dealt with by the patentee in their patent specification. For the purpose of inventive step a person skilled in the art based on the teaching of the said **document as a whole** should be able to arrive at the impugned patent without any inventive ingenuity. This is a law which has been held for several Courts in India and overseas.

iv. Document D3 in columns 3 & 4 merely refers to the use of novel active ingredients including tiotropium for respiratory tract diseases. In fact, column 3 line 39 and column 4 lines 1 to 10 teaches the following for the purpose of inventive step:

- That the novel active ingredients in accordance with US'163 are recommended for respiratory tract diseases.
- For administering the active ingredients of US'163 they have to be mixed or processed with known auxiliaries and/or

excipients to give conventional galenic preparation for example inhalation solutions, suspensions in liquified propellants, etc. In other words, if the active ingredients according to US'163 have to be administered by inhalation, they necessarily have to be mixed with auxiliaries and/or excipients.

• Further in Example 2 of US'163, the active is a hydrochloride salt and not a bromide salt. Example 2 does not make any reference to a solvate. This document, therefore, alone does not render the subject invention as lacking an inventive step.

• It is submitted that a person skilled in the art would know of tiotropium bromide from D3, he would not know which salt and then which form of crystalline form of tiotropium would exist in anhydrous form and in any of the solvated form such as mono, di, tri etc. Further, even if it is assumed that a person skilled in the art knew of the monohydrate tiotropium bromide, he would not know the valuable physio-chemical property associated with the form.

• **There is no teaching or motivation in D3 to arrive at a tiotropium bromide monohydrate form**

c. Annexure – D, an application for extension of patent term in US is immaterial to the present proceedings as patent term extension concepts are unique to the US law. Notwithstanding the above, that the said document is dated 15.03.2004, after the priority date of the present application.

d. Similarly **Annexure – E**, is a patent certification granted under the US law and is also dated after the priority date of IN'813.

e. Annexure – F is an approval letter and is not a relevant piece of document and is also undated document.

f. Document D4 (US5468758), relates to crystalline forms of active monohydrates of hydrochloride salt of Endo-2, 3-Dihydro-N-(8- Methyl)-8-Azabicyclo {3.2.1} Oct-3-yl)-2-Oxo-1H-Benzimidazole-1-Carboxamides.The reason why the Opponent seems to have cherry- picked this document is only with a view to identify a document that discloses monohydrates. Document D4 is not relevant for the following reasons:

a. The said document relates to crystalline pharmaceutical active monohydrate of Endo-2, 3-Dihydro-N-(8-Methyl)-8-Azabicyclo{3.2.1}Oct-3-yl)-2-Oxo-1H-Benzimidazole-1 Carboxamides.

b. The said compound is used as an anti-anxiety agent.

c. The monohydrate disclosed is a hydrochloride salt of a different active. There is no disclosure of the said drug being administered through the inhalation route and therefore, the issue of the active being stable with a particle size within the range necessary for inhalation product is not even dealt with.

d. In fact, in column 13 lines 20 to 30, it is submitted that pharmaceutical composition according to US'758 is used either for oral or rectal administration.

e. This being a non analogous art, a person skilled in the art looking at a problem of achieving stable active ingredients with a particular particle size for being used as inhalation product will not look at active ingredient such as those disclosed in US'758 which is a hydrochloride salt and is

used as antipsychotic agent, preferably administered by oral or rectal routes.

f. Further, without prejudice to the above, even if a person skilled in the art uses the process disclosed in D4 and applies it to Tiotropium Bromide, it would not lead to the claimed monohydrate crystalline form as alleged by the Opponent and contradicted by the inventor of the present patent.

g. D4 is therefore nothing more than a conscious pick and choose exercise by the opponent, to find documents related to monohydrate in hindsight.

g. Document **D5 (US3634582)** is a document of 1972. This document is generally relates to pharmaceutical composition with an effective particle size of 0.01 to 10 microns. There is no mention of tiotropium bromide in the said document, let alone a monohydrate form of tiotropium bromide. In fact, the teaching of this document suggests to a person killed in the art that in order to prepare a powder composition for inhalation a solid pharmaceutical acceptable water soluble inhalation powder carrier having an effective coarser excipient of particle size in the range from 30 to 80 microns be used. In fact, as stated above, the patentee has not made any claim for particle size and the Opponent's understanding of the invention is incorrect and flawed.

h. In so far as **document D6 (US5478578)** is concerned, this document is of Patentee themselves of the year 1992. US'578 in fact is directed to the use of auxiliaries consisting of **mixture of coarser particle, average particle size of greater than 20 microns** and fine particle average size less than 10 microns.

Column 1 line 45 of the said document states that the inhalable portion of active substance of inhalable powders can be controlled by mixing the active with excipient which is a mixture of coarser and fine particles. Again, there is nothing in this document which talks about monohydrate form of tiotropium bromide. In fact, as stated above, the patentee has not claimed any claim for particle size and the Opponent understanding of the invention is incorrect and flout.

i. **Document D7 (US5354760)** is irrelevant non-analogous prior art document for the following reasons:

- o The active is tiagabine which is a hydrochloride salt.
- o Tiagabine is used as an anti-epileptic agent
- o used for oral administration

j. It is further submitted that the opponent has withdrawn the ground of anticipation thereby clearly acknowledging the novelty of the claimed product. Considering that tiotropium bromide monohydrate crystalline form is novel, the process for manufacturing the same cannot be considered as obvious and therefore the patentability of claim 4 and 5 is acknowledged and accepted by the opponent.

K.In relation to **non-analogous art** being irrelevant in an obviousness analysis we wish to rely upon In **re Arnold G. Klein (Serial No.10/200,747)** which defines an analogous art as below:

A reference qualifies as prior art for an obviousness determination under § 103 only when it is analogous to the claimed invention. Innovation Toys, LLC v. MGA Entertainment, Inc., No. 210-1290,

slip op. at 12 (Fed. Cir. Mar. 21, 2011); In re Bigio, 381 F.3d 1320, 1325 (Fed. Cir. 2004); In re Clay, 966 F.2d

656, 658 (Fed. Cir.1992). "Two separate tests define the scope of analogous prior art: (1) whether the art is from the same field of endeavour, regardless of the problem addressed and, (2) if the reference is not within the field of the inventor's endeavour, whether the reference still is reasonably pertinent to the particular problem with which the inventor is involved."

l. On hindsight **being inadmissible in an obviousness analysis**, the patentee would like to rely on the following cases:

F.H & B. Corpn. V. Unichem Laboratories reported in AIR 1969 Bombay 255 held in:*"Was it for practical purposes obvious to a skilled worker, in the field concerned, in the state of knowledge existing at the date of the patent to be found in the literature then available to him, that he would or should make the invention the subject of the claim concerned?" (Page 268)*

Ortho-McNeil Pharmaceutical, Inc. Vs. Mylan Laboratories, Inc. reported in 520 F.3d 1358 held in page 11

"the subject matter as a whole" to ascertain if it "<u>would</u> <u>have been obvious at the time the invention was made</u>." 35

U.S.C. § 103(a) (emphasis added). In retrospect, Dr. Maryanoff's pathway to the invention, of course, seems to follow the logical steps to produce these properties, but at the time of invention, the inventor's insights, willingness to confront and overcome obstacles, and yes, even serendipity, cannot be discounted."

In paras 43 and 44, ORA/08/2009/PT/CH, the Hon'ble IPAB held *Para 43 "The mere existence in the prior arts, of each of the elements in the invention, will not ipso facto mean*

obviousness. For after all most inventions are built with prior known puzzle-pieces. There must be a coherent thread leading from the prior arts to the invention, the tracing of the thread must be an act which follows obviously. We must apply this reasoning to test if indeed it is obvious, or if it seems to us to be obvious to the person skilled in the art because of what we know now. If it is the latter, it is hindsight deduction and is not acceptable, but if it is the former, then the patent must go.

Para 44. "We will examine if the person with skill and knowledge, as per our own law, would have arrived at the invention with the benefit of the prior arts. While we look at prior arts and the decisions on how prior arts must be applied, we must never lose sight of the invention in question……."

In OA/8/2009/PT/CH, the Hon'ble IPAB passed the order dated 2nd November 2012 in Sankalp Rehabilitation Trust Vs. F. Hoffmann-La Roche AG

Para 40 ".....While the Indian law does not create a statutory presumption of validity of the patent, we must be loath to set aside the grant, as hindsight bias is a trap into which one might easily fall and thereby deny to a deserving inventor the fruits of the invention."

The ground of lack of inventive step should therefore be dismissed.

3) Ground of Section 3 (d) i.e. the subject-matter of IN 254813 is not an invention within the meaning of section

Arguing on this ground, the Opponent states that the claimed invention falls under the prohibition of section 3 (d) as crystalline tiotropium bromide monohydrate is a polymorph of Tiotropium bromide and the active ingredient Tiotropium Bromide was already known through the document D3. It is, therefore, incumbent upon the Patentee to establish enhancement of therapeutic efficacy of the claimed invention over the known substance, that is, Tiotropium Bromide.

Tiotropium bromide monohydrate is the active principle used in tiotropium bromide preparation commercialized or marketed in the name of "Spiriva." The opponent therefore states that the claimed impugned patent application is a new form of a known substance. The patentee has been granted a claim over the crystalline monohydrate form of Tiotropium Bromide without showing any therapeutic efficacy. It is also to be noted that the Controller's decision in Pre-Grant Opposition did not have the benefit of the Hon'ble Supreme Court of India's judgment in *Novartis AG v. Union of India* 2013 (54) PTC 1 (SC) where the application of section 3(d) was clarified. It is to be noted at the outset that there is nothing in the specification nor any data has been adduced by the applicant which goes to demonstrate any enhancement in the therapeutic efficacy of crystalline tiotropium bromide monohydrate over Tiotropium Bromide.

The subject-matter of IN 254813 being a new form of known substance, can be granted patent only and only, if the patentee establishes by way of comparative data, that the new form has resulted in enhancement of therapeutic efficacy over the known

substance.

The new form does not elicit any enhancement in the therapeutic efficacy of the drug and the so called "physical stability" under milling stress cannot be considered sufficient to fulfill the requirement of therapeutic efficacy as mandated by section 3(d) of the Patents Act.

In Novartis AG v. Union of India, Hon'ble High Court of Madras was confronted by the Appellant to declare section 3(d) unconstitutional as it was vague and arbitrary. However, the Madras High Court rejected the argument of the Appellant and stated that the term 'efficacy' as mentioned in section 3(d) "in the field of pharmacology [means] the ability of a drug to produce the desired therapeutic effect" and that "efficacy" is independent of potency of the drug.[2]

The Supreme Court of India upheld the interpretation given by the Madras High Court and succinctly summarized that[3]:

1. Efficacy means only Therapeutic Efficacy: That there has been enhancement of "therapeutic efficacy" over the known substance and that not all advantageous or beneficial properties would be considered for establishing enhancement of "therapeutic efficacy" of the derivative/new form. (paragraph 180)

2. No Physical Attributes can be considered: That physical attributes (like greater stability, etc) could not be considered for assessment of section 3(d) (paragraph 173 and 187)

3. Duty of Applicant/Patentee to furnish Comparative Data: That the applicant for patent is under duty to establish an

enhanced or superior therapeutic efficacy by providing comparative data and analysis between the known substance and the derivative substances. (Paragraph 189)

The Hon'ble Supreme Court further stated that if the applicant claims that the derivative substance displays increase in certain properties, even then, the applicant must show that there has been an enhancement in therapeutic efficacy. The Hon'ble Supreme Court concluded by stating that "No material has been offered to indicate that the beta crystalline form of Imatinib Mesylate will produce an enhanced or superior efficacy (therapeutic) on molecular basis than what could be achieved with Imatinib free base in vivo animal model" and hence, conclusively rejected the claim of the Appellant that increase in bioavailability suffices to show enhancement of efficacy.

Therefore, the term "efficacy" as provided within section 3(d), means only "therapeutic efficacy" and it does not include any advantageous or beneficial property. Moreover, "physico-chemical" properties/attributes are completely excluded from the consideration of section 3(d).

The Hon'ble IPAB in *Fresenius Kabi Oncology v. Glaxo Group and Anr*[4], the Respondent- patentee stated that the derivative substance displayed "improved water sorption properties and improved stability". The Respondent-patentee had also stated that the derivative substance can "sorb much lower amounts of water when exposed to broad range of humidities and can be prepared in a stable crystal form" and that "due to the improved

moisture sorption properties of these compounds and increase in stability they exhibit enhanced efficacy". However, the Hon'ble IPAB rejected the argument of the Respondent-patentee and citing the Hon'ble Madras High Court decision in *Novartis Ag v. Union of India* and the Supreme Court decision in *Novartis Ag v. Union of India* restated that *"only those properties that are directly related to efficacy are relevant to section 3(d) and not all advantageous or beneficial properties….and the words "therapeutic efficacy" must receive a narrow and strict interpretation"*

The Hon'ble IPAB further concluded that *"the net cannot be widened to bring in other non therapeutic advantages"* and that *"physico-chemical properties have nothing to do with therapeutic efficacy"*.

In the present case, the Applicant-Patentee has admitted that the technical advance lies in "the active substance should always have the same crystalline morphology, stability and the properties of the crystalline substance under various manufacture and storage conditions be maintained"[5].

It is also important to note that the additional data is merely in respect of 'physico-chemical' properties pertaining to stress stability under milling process. Hence, the same cannot in itself be considered having established the requirement of 'therapeutic efficacy' as laid down by the Hon'ble Supreme Court and Hon'ble IPAB. Further, the Applicant has failed to provide any comparative data or analysis establishing the enhancement of therapeutic efficacy of the claimed invention over the known substance (Tiotropium Bromide) either because

of greater stability or otherwise.

Has Patentee established the enhancement of therapeutic efficacy in the claimed substance?

The Hon'ble Madras High Court in *Novartis AG v. Union of India*[6], stated that the Applicant- Patentee is under burden "to show by giving ***necessary comparative details*** based on such science that the discovery of a new form a of known substance had resulted in the enhancement of the known efficacy of the original substance and the derivative so derived will not be the same substance, since the properties of the derivatives differ significantly with regard to efficacy."

Further, Hon'ble Supreme Court in *Novartis AG v. Union of India* concretized this principle by stating that "In this case, there is absolutely nothing on this score [leading to an enhancement of therapeutic efficacy] apart from the adroit submission of the counsel. No material has been offered to indicate that the beta crystalline form of Imatinib Mesylate will produce an enhanced or superior efficacy (therapeutic) on molecular basis than what could be achieved with Imatinib free base in vivo animal model". Even though, the Appellant-Patentee in that case had adduced data with regard to bioavailability, the Hon'ble Court specifically asked the Appellant-Patentee to adduce comparative data with respect to 'enhanced therapeutic efficacy'. The Hon'ble Supreme Court had categorically rejected the submissions of the Appellant-Patentee where he showed increase in physico-chemical attributes and bioavailability and stated that the test under section 3(d) is narrow and strict which could only be cleared by adducing specific data on

therapeutic efficacy.

The Patentee in the present case has provided data with respect to stability under conditions of micronization but such data in itself does not fulfill the requirement of comparative analysis within the meaning of section 3(d). The Patentee has failed to show any enhancement of therapeutic efficacy and hence, the present application does not meet the requirements of section 3(d).

The Opposition Board Recommendations

The Opposition Board has concluded that the claimed invention does not display enhanced therapeutic efficacy in relation to tiotropium bromide as cited in D3.

The Board observed that "the impugned patent has provided the crystalline tiotropium bromide monohydrate which is a polymorph of tiotropium bromide and the specification of impugned patent does not demonstrate any enhancement in efficacy of the crystalline tiotropium bromide monohydrate as compared to its structurally similar compounds i.e. tiotropium bromide as cited in D3. Thus, the impugned patent claims only a new form of a known substance without having any significant improvement of efficacy and attracts the provision of Section 3(d) of the Indian Patents Act. Patentee arguments that crystal of Example 4 (prior art) in D3 are different from crystalline form presently claimed and the stability tests provided in the reply statement clearly prove the superior properties of the Monohydrate form in comparison with the prior art form (Example 4 of D3) does not appear convincing as the data relating to stability does not have any relation with the

therapeutic efficacy(as defined by the Hon'ble Supreme Court in Novartis AG Vs UOI in CA No2706-2716 of 2013, from paragraph 180 to 192)."

The Opposition Board has also observed that better physical properties are not sufficient to clear the hurdle posed by section 3(d). The Board observed, "Board agree with arguments of Dr. Ganga submitted in the form of affidavit that efficacy is not related to 1) particle size, 2) Stability of the polymorphic form of the drug substance during or after micronization or grinding 3) Stability of the polymorphic form during formulation of the inhalable product 4) Drug product to reach the targeted size to treat the disease. Since these factors will have influence on the bioavailability of the drug rather than the therapeutic efficacy of the drug. The physical stability of the compound during formulation cannot be considered as a sole factor for improvement of therapeutic efficacy of the drug under as required under section 3 (d) of the Indian Patent Act."

The Opponent is for the recommendations of the Opposition Board.

Case laws relied by the opponent for Section 3(d):

a) In the decision of opposition filed for 2485/Del/1998, the Ld. Controller stated that the specification was lacking for the data to show that improved particle size stability translates into better therapeutic effect. The relevant text is reproduced below:

F*rom [page 12]: "There is no data upon which one can conclude*

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

F*rom [page 13]:*

> 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. Novartis, Annexure 1 at para 13. Improved particle size stability, at most, means that someone who chooses to manufacture nevirapine in an aqueous solution would benefit from being able to store the medicine for longer periods of time. However, the therapeutic effect of nevirapine, whether in hemihydrate form or anhydrous form, or whether administered in aqueous, tablet, parental or any other dosage form, would remain unchanged. The applicant has failed to place on record any evidence to show that the therapeutic effect of nevirapine hemihydrate in aqueous solution is significantly enhanced over other known forms of nevirapine. As such, Claims 1, 2, and 5 are invalid and fall under Section 3(d).

In *Boehringer Ingelheim International GMBH*, 924/DELNP/2006, the Controller rejected the grant of patent on the ground of absence of filing of any experimental proof of enhancement of properties vis-à-vis the known substances, "i.e.,, to say no comparagraphtive experimental data is available in the specification to prove the improvements are significant and the new form is efficacious than the earlier one" (page 13). The Controller in page 12 stated that "Section 3(d) emphasizes that a new form of a known substance is patentable unless the new form shows enhancement in the known efficacy of the known substance….Efficacy of a pharmaceutical, in pharmacology, as defined in Dorland's Illustrated Medical Dictionary is the ability of a drug to produce the desired therapeutic effect and it is independent of potency".

The patentee is can be seen from foregoing is under burden of proof to adduce 'comparagraphtive data and analysis' comparing the therapeutic efficacy of the claimed invention vis-à-vis the known substance, Tiotropium Bromide and show that there was an enhancement thereof. This principle has been applied by the Hon'ble IPAB in *Fresenius Kabi Oncology* (Order 161/2013), the decisions of the Patent Office and the recommendations of Opposition Board.

Further, the Patentee contended that the onus of proof was not discharged by the Opponent as no evidence was filed at the time of filing of Notice of Opposition and that the documentary evidence cannot be looked into as they were not accompanied with Expert Evidence. Relying upon *Travanacore Mats & Matting Co. v. Controller of Patents* (Order no. 47/2012) (paragraph

17); *Farbewerke Hoechst v. Unichem Laboratories* AIR 1969 Bom 255 (paragraph 13); *Roche v. Cipla* (CS(OS) 89/2008 and CC 52/2008); *Ajay Industrial Corporation v. Shiro Kanao of Ibaraki City* (AIR 1983 Del 496) contended that the Opponent has failed to discharge the burden of proof. However, the reliance on each of these decisions is misplaced – *Travanacore Mats & Matting Co.* stated that "mere allegation is not sufficient to dislodge a validly granted patent" as the Petitioner in that case had not furnished any evidence, documentary or otherwise; *Frabewerke Hoechst* considered the question of validity of the patent and merely clarified that the 'onus of proof' lies on the Opponent/Challenger; *Roche v. Cipla* clarified that the burden of proof on the Defendant [party

challenging the validity of patent] is that of balance of convenience and not that of criminal suit, requiring, proof beyond reasonable doubt [paragraphs

67-69] and *Ajay Industrial Corporation* stated that a challenge to long-established validly granted patent cannot be dislodged by mere reliance on oral testimony and hence, a Post-Grant Opposition cannot be said to have been after a long period of time. However, none of these cases help the case of the Patentee because in each of the case, the challenging party had not provided any evidence and expert affidavit till the date of hearing.

Moreover, the patentee is attempting to rigidly construe the Patents Act and the rules made there under so as to complete negate the Law's purpose by contending that each evidence ought to be accompanied by expert evidence. This would defeat the Scheme of Law as it would render every FER without force of law. The procedure of every law is handmade to attain the remedies and rights provided under that law and cannot be stunted or interpreted in such a manner that the remedies and rights are defeated.

Order in the counterpart Chinese patent

Boehringer Company appealed the decision of lower Court of China which had rejected the patent over crystalline tiotropium bromide monohydrate. The Supreme People's Court of People's Republic of China upheld the invalidity of Boehringer's crystalline tiotropium bromide monohydrate patent application reasoning that it lacked 'unexpected technical effects' and hence was not 'creative'.

The Court relying upon the Review Guidelines which state "a compound that has the similar structure of known compounds, must have the differentiated use or effect" stated that if the molecule or compound has a similar core structure as another known compound, then the determination of 'creativity' depends on whether "the crystal has the unexpected technical effects or not". The Court further stated that this "differentiated use or effect can be different from the known uses of the know compounds; or it has substantial improvement or modification to a known effect of the compounds know; or it has usage or effect that is not clear".

The Court found that the claimed subject-matter of the patent, monohydrate tiotropium bromide monohydrate had the similar core structure like the known compound 'tiotropium bromide'. The Court then stated that the original patent lacked any data to establish unexpected technical effect and hence, the holding of the lower Courts that the patent was invalid was correct.
Compared to the same drug formulation that is relatively unstable, the solid state change of any physical and chemical stability drug composition that can improve the pharmaceutical composition can provide significant advantages. The said technical effect is recorded in the patent, but there is no evidence to prove that the patent has the technical effect.

Applicants /Patentee Submission

a. The Patentee respectfully submits the following:-

i. Section 3(d) of the Indian Patent Act, permits grant of

patents even to a discovery.

ii. The invention claimed in IN254813 is not mere discovery and therefore, Section 3(d) would not apply.

iii. Even if Section 3(d) is applied, the patentee has shown increase in pharmaceutical properties and therapeutic efficacy of claimed form vis- à-vis a closest known compound tiotropium bromide disclosed in D3.

iv. The intent of the legislature behind Section 3(d) was to protect incremental inventions and to promote the same, if the criteria is laid down by Section 3(d) are satisfied.

v. The Hon'ble Supreme Court in Novartis case held that patents under Section 3(d) can be granted if the applicant/patentee is able to demonstrate an improvement in properties that have a bearing on therapeutic efficacy.

vi. The following paragraphs of the *Novartis* case are relevant for Section 3(d) determination:

Paragraph 180: *What is "efficacy"? Efficacy means "the ability to produce a desired or intended result". Hence, the test of efficacy in the context of Section 3(d) would be different, depending upon the result the product under consideration is desired or intended to produce. In other words, the test of efficacy would depend upon the function, utility or the purpose of the product under consideration. Therefore, in the case of a medicine that claims to cure a disease, the test of efficacy can only be "therapeutic efficacy". .....It may be noted that the text added to Section 3(d) by*

the 2005 amendment lays down the condition of "enhancement of the known efficacy". Further, the explanation requires the derivative of "differ significantly in properties with regard to efficacy". What is evident, therefore, is that not all advantageous or beneficial properties are relevant, but only such properties that directly relate to efficacy, which in case of medicine, as seen above, is its therapeutic efficacy.

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

Paragraph 189: *Whether or not an increase in bioavailability leads to an enhancement of therapeutic efficacy in any given case must be specifically claimed and established by research data.*

Paragraph 191: *We have held that the subject product, the beta crystalline form of Imatinib Mesylate, does not qualify the test of Section 3(d) of the Act but that is not to say* ***that Section 3(d) bars patent protection for all incremental inventions of chemical and pharmaceutical substances. It will be a grave mistake to read this judgment to mean that Section 3(d) was amended with the intent to***

undo the fundamental change brought in the patent regime by deletion of Section 5 from the Patent Act. *That is not said in this judgment.*

vii.The efficacy for inhalative formulation requires that the active ingredient reaches the target side in the lung. In order to achieve the objective, it required that the active is of a specific particle size and remains stable in that particle size. The stability of the active therefore has a bearing on the efficacy of the claimed compound as also affirmed by the experts Dr. Markus Weymann and Dr. Michael Trunk. **(Para 16 onward of Dr. Weymann's evidence and Para 10.19 of Dr. Trunks evidence)**

Viii.Further crystal growth and increase in size have a negative impact on the particle deposition in the alveolar of the lungs. It is reasonable to conclude that the lower crystalline growth tendency of the claimed form has a bearing, on the therapeutic efficacy of the drug.

ix. The stability tests relied upon by the experts Dr. Michael Trunk and Dr.Markus Weymann clearly prove the superior properties that have a bearing upon the therapeutic efficacy of the crystalline form claimed in the present patent in comparison to the prior art form.

x.Efficacy of the drug has to be interpreted on case to case basis specifically for respiratory diseases in which the efficacy of the drug is measured in terms of FEVI or forced expiratory volume of the lungs within one second, which depends on the drug reaching to the desired location of the lung. The claimed crystalline form reaches the

desired location of the lung, has improved FEVI and therefore has improved therapeutical efficacy.

b. With regard to acceptance of additional data that has been raised in the Opposition Board recommendations, it is respectfully submitted that:

I.The data relied upon by the Patentee in the Post grant opposition is not new additional data, but the data that was relied during the prosecution of the patent application that lead to the grant of IN254813.

II.The present patent in application filed prior to the 2005 amendment of the act (by which section 3(d) was introduced in the act) and the data was filed to support the patentability of the case and reply to the objections of the Learned Controller.

III.With regard to acceptance of additional data, it is submitted that the EPO Guidelines state the following:

"The extent to which such reformulation of the technical problem is possible has to be assessed on the merits of each particular case. As a matter of principle any effect provided by the invention may be used as a basis for the reformulation of the technical problem, as long as said effect is derivable from the application as filed (see T 386/89). It is also possible to rely on new effects submitted subsequently during the proceedings by the applicant, provided that the skilled person would recognize these effects as implied by or related to technical problem initially suggested (see G-VII, 11 and T 184/82)."

Example of such a new effect:

The invention as filed relates to a pharmaceutical composition having a specific activity. At first sight, having regard to the relevant prior art, it would appear that there is a lack of inventive step. Subsequently, the applicant submits new evidence which shows that the claimed composition exhibits an unexpected advantage in terms of low toxicity. In this case, it is allowable to reformulate the technical problem by including the aspect of toxicity, since pharmaceutical activity and toxicity are related in the sense that the skilled person would always contemplate the two aspects together.

iv. Reference is also made to **T386/89, wherein on page 9, para 4.3, the Board of Appeal**, held that:*"It belongs to the well-established jurisprudence of the Boards of Appeal that where a specific problem is identified in the description, the applicant or patentee may be allowed to put forward a modified version of the problem particularly if the issue of inventiveness has to be considered on an objective basis against a new prior art which comes closer to the invention than that considered in the original patent application or granted patent specification. Reference is made in this respect to the decision T 184/82 (OJ EPO 1984, 261) where the Board allowed a re-definition of the problem to such an extent that the skilled person "could recognize the same as implied or related to the problem initially suggested" (see point 5 of the reasons)."*

v.Knoll Pharmaceutical Company,**Inc.Vs.Teva Pharmaceuticals USA, Inc. reported in 367 F.3d 1381**

held that *"obtain additional support consistent with the patented invention, to respond to litigation attacks on validity; there is no requirement that an invention's properties and advantages be fully known before the patent application was filed, or that the patent application contains all of the work done in studying the invention, in order for that work to be introduced into evidence in response to litigation attack nor is it improper to conduct additional experiments and provide later-obtained data in support of patent validity."*

3) Opposition under U/S 25 (2) (h): that the patentee has failed to disclose to the Controller the information required by section 8 or has furnished the information which is in any material particular was false to his knowledge.

Opponents' submission

For this ground the opponent submitted that the patentee has failed to furnish information regarding the foreign filings (u/s 8(1)). The Applicant by admission, acknowledges, that Form 3 was filed only on three instances, viz., 16th April, 2003 [disclosing the German and PCT application]; 20th November 2007 [disclosing two US patents and one EU patent] and 21st July 2010 [disclosing some 109 applications].

To be noted: The first two submissions are mere eye-washes as the perusal of the third filing shows that a substantial number of applications that existed at the time of filing of the first two Form 3 were never disclosed to the Controller.

Also, section 8(1) requirements were not observed even after the

third filing was made, that is for two years between 2010 and 2012.

What does the law say for requirement under section 8(1):

Every Applicant-Patentee is under duty to inform Controller in writing from **time to time** regarding filing of foreign patent applications. The Hon'ble High Court of Delhi in *Chemtura Corporation v. Union of India,* MANU/DE/1880/2009, paragraph 37 clarified the meaning of the term 'time to time' to mean "a periodicity of furnishing information akin to updating the Controller on the current status of the application filed in other countries". The Hon'ble Court further reiterated that requirement under section 8(1) "does not hinge on the Controller asking for particulars". The above position is also upheld by the Hon'ble IPAB[8].

The term 'time to time' is understood under Patents Act, 1970 to be a maximum period of six months from the date of coming into existence of the corresponding foreign application. This is by virtue of Rule 12(2), which after amendment states, "The time within which the application for a patent shall keep the Controller informed of the details in respect of other applications filed in any country in the undertaking to be given by him under clause (b) of sub-section (1) of section 9 shall be six months from the date of such filing." This duty is placed under section 8(1) read with rule 12(2) and is inescapable.

It is to be noted that section 8(1) and rule 12(2) have remained unchanged since 1st January 2005 and hence, the Applicant cannot claim ignorance of the law for a period extending over six years.

Does one time stray filing satisfy the strictures of section 8(1)?

Compliance under section 8(1) is a continuing one, that is, the Applicant-Patentee is required to disclose details at regular intervals so as to keep the Patent Office abreast.

The scheme of law requires that the Patent Office is kept aware of any foreign filing within six months of such filing. Hence, rule 12(2) dictates the six month period within which the Applicant-Patentee has to discharge its duty.

The Applicant-Patentee has creatively attempted to escape liability under section 8(1) by furnishing the required details at the last moment, thereby, diluting the express provision of law as well as the object of the law. Hence, one time stray filing cannot be held to have satisfied the requirement of section 8(1). Further, the Ld. Controller cannot permit such a conduct so as to dilute the requirements under section 8.

Hon'ble IPAB has warned against any dilution of compliance requirements under section 8: Hon'ble IPAB has in series of decisions has issued strict guidance that the requirement under section 8 cannot be diluted by the Ld. Controller (*Ajanta Pharma v. Allergan Inc.*, Order 173/2013; *Tata Chemicals v. Hindustan Unilever*, Order 166/2012; *Fresenius Kabi Oncology v. Glaxo Group* Order 161/2013). If the present conduct of the Applicant-Patentee is condoned then it would concede that one time filing, rather than periodic six month filing, under section 8(1) is sufficient. Further, it would amount to surrendering the compliance demanded of the Applicant- Patentees under section 8. This would be against the scheme of law.

The conduct of the Applicant defeats the object of the law:

The Applicant-Patentee furnished the third Form-3 much after FER was released. A bare perusal of the 2010 filing shows that over thirty applications/patents ought to have been disclosed in 2007 filing. Hence, the previous two filings concealed the information from the Controller and only after FER was issued, the information was provided by the Applicant-Patentee.

The opponent stated that the Applicant-Patentee cannot cure non-compliance of the law by a single stray filing nor can ask the Ld. Controller to rely upon internet. Hence, the Applicant-Patentee has violated the requirements under section 8.

Applicants /Patentee Submission

Issue: Whether the Opponent can raise a ground under Section 25(2)(h) without pleading and proving the same. A ground wherein material facts have not pleaded is unsustainable in law.

a. With regard to the ground of Section 8 **(Section 25(2)(h))**, the Opponent submitted that in case the Applicant had filed a petition u/r 137 for correction of irregularity and the Ld. Controller had condoned the irregularity, the opponent would not press on the grounds of section 8. As the Patentee had indeed filed a petition, and the Ld. Controller in deciding the pre-grant had condoned the irregularity, this ground too does not stand. The Patentee would however without prejudice, present arguments on this ground as well.

b. Having said this, it is submitted that it a fundamental

principle of Civil Procedure Code and the law on pleadings that all proceedings have to be based on pleadings and in the absence of pleadings and material facts having been pleaded, a ground and evidence produced in relation thereto is unsustainable in law. The purpose of pleadings is also to ensure that the applicant can lead evidence and rebut the objections or grounds taken by the Opponent.

c. On pleading of material facts, the Hon'ble Supreme Court in **Kalyan Singh Chouhan Vs. C.P. Joshi. [(2011)11 SCC 786]** held that;*"This Court in Bachhaj Nahar vs. Nilima Mandal and Ors. AIR2009 SC 1103, held as under: purpose of pleadings and issues is to ensure that the litigants come to trial* ***with all issues clearly defined and to prevent cases being expanded or grounds being shifted during trial****. ..... When the facts necessary to make out a particular claim, or to seek a particular relief, are not found in the complaint, the Court cannot focus the attention of the parties, or its own attention on that claim or relief, by framing an appropriate issue****.....*** *Thus, it is said that* ***no amount of evidence****, on a plea that is not put forward in the pleadings, can be looked into to grant any relief."*

"18. In Gajanan Krishnaji Bapat v. Dattaji Raghobaji Meghe13 this Court held that the ***court cannot consider any fact*** *which is* ***beyond the pleadings*** *of the parties. The* ***parties have to take proper pleadings and establish by adducing evidence*** *that by a particular irregularity/illegality the result of the election has been materially affected."*

"19. Pleadings and particulars are required to enable the court to decide the fights of the parties in the trial. Thus, the pleadings

*are more to help the court in narrowing the controversy involved and to inform the parties concerned to the question in issue, so that the parties may adduce appropriate evidence on the said issue. It is settled legal proposition that "**as a rule relief not founded on the pleadings should not be granted**". Therefore, a decision of a case cannot be based on grounds outside the pleadings of the parties. The pleadings and issues are to ascertain the real dispute between the parties to narrow the area of conflict and to see just where the two sides differ…"*

"28. Therefore, in view of the above, it is evident that the party to the election petition must plead the material fact and substantiate its averment by adducing sufficient evidence. ***The court cannot travel beyond the pleadings and the issue cannot be framed unless there are pleadings to raise the controversy on a particular fact or law. It is, therefore, not permissible for the court to allow the party to lead evidence which is not in the line of the pleadings****. Even if the evidence is led that is just to be ignored as the same cannot be taken into consideration."*

d. Union of India v. Ibrahim Uddin & Anr, the Supreme Court in para 62 held:-*"This Court…held that relief not founded on the pleadings cannot be granted. A decision of a case cannot be based on grounds outside the pleadings of the parties. No evidence is permissible to be taken on record in absence of the pleadings in that respect. No party can be permitted to travel beyond its pleading and that all necessary and material facts should be pleaded by the party in support of the case set up by it. It was further held that where the evidence was not in the*

line of the pleadings, the said evidence cannot be looked into or relied upon."

e.*F. Hoffmann-La Roche Ltd. & Anr. V. Cipla Ltd.,* *2012 (52) PTC 1 (Del)* para 70 *[T]herefore, it has become necessary to point out that the evidence of the parties are to be tested on the balance of probabilities. Though, the defendant had raised almost all the grounds available in Section 64 of the Act However, this Court inclines CS (OS) No. 89/2008 Page No.68 of 275 to* ***discuss only those grounds on which specific pleadings and evidence adduced by the counter claimant****.*

f. On perusal of the pleadings, it is respectfully submitted that there are no material facts that have been pleaded by the opponent in relation to the violation of Section 8 of the Indian Patent Act by the Patentee.

g. Rule 57 of the Patent Rules 2003 requires the opponent to file a written statement which is akin to pleadings setting out the nature of opponent interest, the facts upon which the basis is caused and relief which he seeks and evidence, if any, along with the notice of opposition. Rule 57 of the Patents Rules 2003 clearly provides a distinction between "pleadings" and "evidence". Pleadings such as the written statement have to contain "**material facts"**. The Opponent has to file a written statement, which sets out the nature of Opponent's interest.

h. At the hearing the opponent relied upon one Chinese decision. Before dealing with this document and ground, it is submitted that at the very outset, this document cannot be

taken on record as the opponent has neither pleaded nor proved the violation under Section 8 of the Indian Patent Act based on this document in the written statement filed by the Opponent.

i. This is mandatory in view of the several Hon'ble Supreme Court orders including the Hon'ble IPAB order in Fresenius **Kabi Oncology Limited vs. Glaxo group limited, wherein** the Hon'ble IPAB on Section 8 clearly held in **Para 49** that the invalidity ground on Section 8 is not maintainable unless the opponent pleads and proves the said violation.

j. The Chinese document that is now been allowed in the oral hearing cannot be permitted and allowed as for the following reasons:-

- There is no whisper of the said document in the written statement filed by the opponent. No material fact in relation to the said document was included in the written statement. At the stage of the hearing, such documents cannot be entertained;
- That the Patentee has already complied during the prosecution of the application under Section 8(1) and 8(2).
- That the Controller by virtue of discretionary power vested under Rule 12 allowed the application to proceed to grant only after he was satisfied of the Patentee having complied with the requirement under Section 8(2).
- Hearing under Section 14 took place on 3rd November 2008 and on the pre-grant opposition on 22nd July, 2010 and

the Chinese decision is dated 6th December, 2011. Therefore, the Chinese application has no bearing whatsoever.

- Further it is submitted that Patents have been granted on this invention by approximately 100 countries, which clearly establishes that the said invention is worthy of being granted and sustained.
- Even during the pre-grant opposition the Learned Controller held the subject invention as being valid.
- Notwithstanding the above the patentee also relies upon the recent order of the Division Bench of the Hon'ble Delhi High Court Koninklijke Philips Electronics ... vs. Maj. (Retd) Sukesh Behl & Anr that held the following:

  i) That the power to revoke a patent is discretionary and not automatic;

  ii) The Court has to first examine whether the applicant furnish the information as deliberate or intentional or accidental/clerical on account of *bonafide error.*

  iii) The Court will have to examine the evidence for willful omission of the documents and cannot revoke the patent on the ground of non-compliance of Section 8.

k. In view of the above, the ground under Section 25(2)(h) should be dismissed ***in limine***.

Conclusions:

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

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

The grounds of section 25(2) (b) and 25(2) (d) were not pressed by the opponent and accordingly these grounds are treated as withdrawn and therefore I am not going into these grounds.

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

Regarding the patentees contention that the documents filed by the opponent cannot be considered as evidence since they have not been filed as an affidavit as mandated by section 79 of the Patent Act, it is a settled position that lack of novelty has to be judged only on the basis of prior publication and/ or use, whereas inventive step has to be looked into on the basis of prior art in combination with the common general knowledge. Moreover, rule 57 of the Patents Act requires the filing of the written statement and the facts on which the opponent makes out his case. The requirement of evidence to be filed is optional. If the opponent is successful in proving obviousness on the basis of documents in combination with the common general knowledge, then additional evidence may not be required. Section 79 does not appear to have any relevance in the present case where no evidence is filed. When evidence is filed then Section 79 has to be looked into. IPAB order 173 of 2013 relied upon by the Patentee clearly requires that the applicant has to plead and prove his case. In this regard, the opponent has pleaded his case on the various documents relied upon by them in their written statement (at page 6 of the opponents written arguments). Whether these documents relied upon by the opponent in combination with the common general knowledge will be adequate to establish their challenge on the ground of obviousness will be dealt with by me hereinafter.

Inventive Step (Section 25(2) (e)

Section 25(2)(e) Claims obvious and lacking in inventive step:

The patentee has stated that the opponent is incorrect in stating that the inventive step of the present invention lies in the particle size of the active and it is respectfully submitted that the problem underlying the invention is not to determine the effective particle size range but lies in identifying and finding a novel pharmaceutical substance that can be converted into the particle size range which is effective in entering the lungs when administered by inhalation. From the patentees' statement, it is clear that there is a need to identify a pharmaceutical substance which will possess a specific property suitable for inhalation and entering the lungs.

Now, I will consider the teachings of the documents relied upon by the opponent and their respective rebuttal by the patentee.

Opponent's position:

i. Tiotropium bromide is an effective anti-cholinergic agent thereby capable of providing therapeutic benefit in the treatment of COPD D3;

ii. Polymorphs have different stabilities and may spontaneously convert from a metastable form (unstable form) to the stable form D4;

iii. Particle size of active in the range of 0.01 10 micron for effective lung penetration for drugs which are administered by the inhalation route D5;

iv. Crystalline monohydrate been stable to micronization and grinding.

Patentee's position:

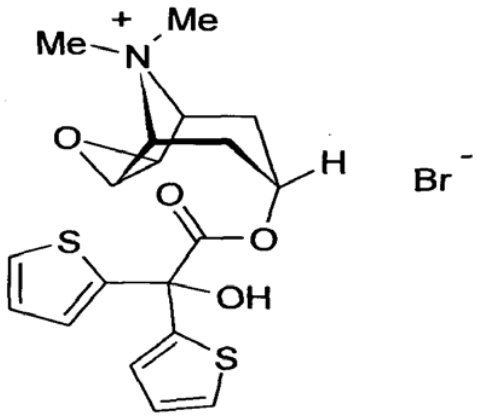
i. There is no teaching or motivation in D3 to arrive at a tiotropium bromide monohydrate form;

ii. D4 is therefore nothing more than a conscious pick and choose exercise by the opponent, to find documents related to monohydrate in hindsight;

iii. Document D5 (US3634582) is a document of 1972. This document generally relates to pharmaceutical composition with an effective particle size of 0.01 to 10 microns. There is no mention of tiotropium bromide in the said document, let alone a monohydrate form of tiotropium bromide;

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

It is evident from the description and claims of the present patent that this patent relates to a crystalline monohydrate of (1α, 2β, 4β, 5α, 7β)-7-[(hydroxydi-2-thienylacetyl) oxy]-9, 9- dimethyl-3-oxa-9-azoniatricyclo [3.3.1.0] nonane bromide, processes for the preparation thereof and having an anticholinergic activity. Tiotropium bromide is known from European Patent EP 418716 or US 5610163 (mentioned in the background section of the specification of the instant application, and relied upon by the Opponent herein as D3) and has the following chemical structure:



Tiotropium bromide is a highly effective anticholinergic and can therefore provide therapeutic benefit in the treatment of asthma or chronic obstructive pulmonary disease (COPD). Tiotropium bromide is preferably administered by inhalation.

After careful consideration of the arguments of both the parties on the documents cited it is clear, that document D1 relates to mechanistical consideration and clinical profile in obstructive lung disease discloses tiotropium as a specific highly potent antimuscarinic demonstrating very slow dissociation from muscarinic receptor. The dose of tiotropium taught in D1 is 18µg. D1 in general discloses tiotropium bromide, whereas D2 relates to long-acting bronchodilation with Tiotropium bromide in suitable COPD. Neither D1 nor D2 disclose the crystalline mono hydrate form of Tiotropium bromide as claimed in the impugned patent. Document D3 (i.e. EP 418716 while it's US corresponding is US 5610163), which is an acknowledged prior art by the patentee in its complete specification. D3 essentially teaches Tiotropium Bromide. The abstract of D3 expressly discloses that Tiotropium Bromide is used as anticholinergic and suggests its administration through inhalation, useful for

the treatment of chronic obstructive bronchitis, asthma etc. D3 further suggests that the drug may be administered through the intravenous or oral routes as well. Claim 4 and Claim 5 of document D3 discloses the molecule Tiotropium bromide. Document D3 does not disclose the crystalline monohydrate form of Tiotropium bromide as claimed in the impugned patent.

Document D4 which has a publication date prior to the priority date of the Patentee's specification addresses the technical problem of providing physical and chemical stability faced by a person skilled in art, difficulties in prior art like moisture absorption tendency of a drug, stability problems of an active ingredient due to polymorphic modifications, variation in crystal lattice during milling (Column 1 and Column 2). Document D4 on column 4, discusses the specific advantages of monohydrate crystalline forms in pharmaceutical preparations with regard to hygroscopicity, physical and chemical stability during manufacturing process and during storage in form of pharmaceutical preparations.

The teaching that flows form D4 is that the monohydrate forms show better stability than the anhydrous from of the prior art compound. It also reveals the tolerance of a particular polymorphic form to micronization stress.

Certainly for a skilled person in the art, it is clear cut motivation to prepare the crystalline hydrate form of Tiotropium bromide as claimed in the impugned patent with enhanced properties with reasonable success by combining the above teachings of any of the references D1 to D3 combined with D4.

To clear the test of inventiveness, the patentee has to show some surprising effect in comparison to closest prior art D3 but patentee has failed to show such surprising effect over D3. Therefore, the claims of present patent are considered obvious to a person skilled in the art and do not involve any inventive step.

D5 the counterpart of the patent DE-1792207 acknowledged in the specification of the impugned patent in particular teaches a pharmaceutical powder composition for inhalation comprising a mixture of a solid finely divided medicament having an effective particle size in the range 0.01 to 10 microns and a solid pharmaceutically acceptable water-soluble carrier having an effective particle size in the range 30-80 microns.

The teaching that flows from D5 is that particles in the size range of 0.01 to 10 microns alone are effective, for penetration into the lungs and that the composition should contain a coarser solid diluents or carrier for ready fluidization in other words ease of inhalation of the composition. Thus for powdered inhalable preparations in order to achieve maximum penetration into the lungs, it should be prepared of a controlled particle size i.e. a suitable particle size range being 0.01 to 10, usually 1-10, microns.

D6 relates to powder for inhalation and is specifically directed to inhalation powders and the desired particle size. It is observed from the disclosure of D5 and D6 reveals that the alleged invention is merely a combination of known features from the prior art and is a product of mere trial and error and does not involve any inventive skill.

D7 provides crystalline Tiagabine hydrochloride monohydrate, process for its preparation, composition containing the same and its use as a therapeutic anti-epileptic agent.

However the example 2 of D7 teaches the same process parameters and discloses that the water can be used as a crystallizing solvent for this compound giving very reproducible results of a monohydrate crystal form. Claim 4 and 5 of the present patent differs from the D7only in that the patentee has used activated charcoal for decolourising step which is a common process step for preparing crystalline forms. In view of D7, the process as claimed in claim 4 and 5 does not involve inventive step.

In order to establish the ground of Inventive step as mandated under section 2(1)(j) of the Patent Act, the Patentee had asserted that the claimed crystalline had an unexpected surprising advantageous technical effect in meeting the stringent requirements imposed on pharmaceutically active substances to be used for inhalation. However it is crystal clear that the applicant has failed miserably to disclose any surprising advantageous technical effect in the description and in the evidences and therefore cannot be relied upon for assessing inventiveness. As such there is no evidence, sufficient enough in the description to make it specious that unexpected surprising advantageous technical effect is achieved by the claimed crystalline Tiotropium bromide monohydrate compound as claimed by the Patentee in his admission, the purity and stability (among the unexpected effects) could not be predicted by one person skilled in the art over the cited document D3-D6. Thus

for skilled artisan it would be easily possible to arrive at the invention based on the above teachings & disclosure made in documents D3-D6,thus the claims are obvious. After complete reading of the specification, it is clear that the applicants had failed to provide sufficient comparative data for any unexpected surprising advantageous technical effects verified in the description over the closest prior.

After considering the arguments of the both the parties meticulously relating to inventive step, it is very obvious for a skilled artisan to combine the teaching of the two documents D3 and D4 (both documents being of patentee) with the proposed stability of the Tiotropium bromide monohydrate. Document D4 addresses the problems of physical and chemical stability, difficulties in prior art like moisture absorption tendency of a drug, stability problems of an active ingredient due to polymorphic modifications, variation in crystal lattice during milling.

The teaching that flows from the document D4 clearly enlightens the fact that when there is a problem with a particular form of a drug substance, it can simply be converted to another polymorphic form that exhibit stability while processing i.e. during the milling process and show uniform content in the final dosage form and demonstrates the effect of milling studies and the uniformity content in the monohydrate forms.

An important point to be noted is that the results of both the tests i.e. the accelerated stability tests and normal stability tests, revealed the fact that the monohydrate forms have far better stability than the anhydrous forms of the prior art.

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

Also the position itself is clear in the landmark judgment which has been aptly applied by the opposition board for judging Inventive step. I do rely on the landmark judgment, which goes as

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

"*It is important that in order to be patentable an improvement on something known before or a combination of different matters already known, should be something more than a mere workshop improvement; and must independently satisfy the test of invention or an 'inventive step'. To be patentable the improvement or the combination must produce a new result, or a new article or a better or cheaper article than before. The combination of old known integers may be so combined that by their working interrelation they produce a new process or improved result. Mere collection of more than one integers or things, not involving the exercise of any inventive faculty, does not qualify for the grant of a patent.*"

From the aforesaid, I am of the opinion that the compound tiotropium bromide is known in the art. The requirement of

administering a specific particle size for entering the lungs as shown by the patentee at page 18 of their written arguments is a fact known in the art and there is no inventive contribution of the patentee atleast in this arena. Now, taking up the question of whether identifying the suitable pharmaceutical substance that can be converted to a particular particle size for administration, I see from the various documents that there is a disclosure of the crystalline monohydrate forms of other actives been micronized and yet retaining stability. Now, while judging obviousness any factor that will lead to reasonable expectation of success is relevant and a person skilled in the art has a sound knowledge in this field and not completely ignorant. This being the opinion of the Hon'ble IPAB, I am convinced that having known the therapeutic activity of tiotropium, the requirement of a specific particle size, identifying the suitable form which will exhibit these characteristics will be routine experimentation and cannot be considered as inventive. The position of the patentee that non-analogous prior art is irrelevant while judging obviousness is incorrect since all knowledge before the priority date of the patent which is not specific to this field will be held to constitute common general knowledge. Grant of a patent in other countries cannot be cited as a proof of inventiveness (the fact as clear from the Chinese prosecution, where the Supreme People's Court of People's Republic of China upheld the invalidity of Boehringer's crystalline tiotropium bromide monohydrate patent application reasoning that it lacked 'unexpected technical effects' and hence was not 'creative'.) I therefore hold that the product claims are

obvious.

Regarding, claims 4 and 5, the process of forming the monohydrate of any compound is disclosed in D7 and the patentees argument that this document relates to the active tiagabine which is a hydrochloride salt, is used as an anti-epileptic agent and used for oral administration cannot be taken as a defence for obviousness. I am of the view that this document gives a clear direction for the preparation of a crystalline monohydrate in general. I therefore hold that claims 4 and 5 are obvious on the face of the prior art.

I therefore conclude that the invention as claimed in the claim 1 & its dependent claims lack inventive step & is obvious to a person skilled in the art & the opponents ground of opposition is validly established.

Section 25(2)(f) Claims not patentable under Section 3(d)

The opponent has argued that the subject-matter of IN 254813 being a new form of known substance, can be granted patent only and only, if the patentee establishes by way of comparative data, that the new form has resulted in enhancement of therapeutic efficacy over the known substance. The opponent submits that the new form does not elicit any enhancement in the therapeutic efficacy of the drug and the so called physical stability under milling stress cannot be considered sufficient to fulfill the requirement of therapeutic efficacy as mandated by section 3(d) of the Patents Act.

The Patentee has stated that the invention claimed in IN254813 is not mere discovery and therefore, Section 3(d) would not

apply. Even if Section 3(d) is applied, the patentee has shown increase in pharmaceutical properties and therapeutic efficacy of claimed form *vis- a -vis* a closest known compound tiotropium bromide disclosed in D3. The efficacy for inhalative formulation requires that the active ingredient reaches the target side in the lung. In order to achieve the objective, it required that the active is of a specific particle size and remains stable in that particle size. The stability of the active therefore has a bearing on the efficacy of the claimed compound as also affirmed by the experts Dr. Markus Weymann and Dr. Michael Trunk (Para 16 onward of Dr. Weymann's evidence and Para 10.19 of Dr. Trunks evidence).

After going to the arguments of both the parties, I am of the opinion that for a polymorph to qualify for an invention under section 3(d) of the of the Indian Patents Act, has to show significant improvement of therapeutic efficacy as compared to known form. The impugned patent relates to the crystalline tiotropium bromide monohydrate which is a polymorph of tiotropium bromide, however there is no disclosure in the specification as to enhancement in the therapeutic efficacy as compared to its structurally similar compounds i.e. tiotropium bromide as cited in document D3.

All the evidences as filed by the patentee do not provide any specific data establish the ground of inventive step and u/s 3(d) in the impugned patent, rather the evidence filed by Dr. Ganga Srinivasan supports the fact that efficacy is not related to 1) particle size, 2) Stability of the polymorphic form of the drug substance during or after micronization or grinding 3) Stability

of the polymorphic form during formulation of the inhalable product 4) Drug product to reach the targeted size to treat the disease. Since these factors will have influence on the bioavailability of the drug rather than the therapeutic efficacy of the drug. The physical stability of the compound during formulation cannot be considered as a sole factor for improvement of therapeutic efficacy of the drug under as required under section 3 (d) of the Indian Patent Act, almost the same view was expressed in the landmark decision issued by Hon'ble Supreme court in Novartis case (referring to paragraphs 180-192).

Also the claim of applicant that the efficacy is to be interpreted on a case to case basis specifically in terms of respiratory diseases the efficacy of the drug is measured in terms of FEVI or forced expiratory volume of the lungs within one second which depends on the drug reaching desired locations in the lungs and as claimed crystalline form of the tiotropium bromide reaches the desired locations of the lungs, it results in improved FEVI and therefore enhances therapeutic efficacy. The claim of the applicant even if taken into consideration, does not have a legal standing in view of absence of any clinical trials or any research data demonstrating the fact that the newly formed crystalline tiotropium bromide monohydrate is more efficacious than tiotropium bromide in terms of therapeutic effects. The submissions made in the affidavits are not based on any actual facts or trails, therefore cannot be called improvements.

Here, I see that all the data furnished by the Patentee which

had been considered by the Ld. Controller Mr. S.K.Roy in a pre-grant opposition. Such data pertains to lower crystalline growth tendency and as compared to D3 such growth has been significantly lowered. By achieving this, the patentee although has tried to demonstrate that the percentage and amount of particle reaching the lungs is higher, the requirement of showing enhanced therapeutic efficacy still remains unaddressed.

The Hon'ble Supreme court has held in the Novartis case that para *173. The aforesaid properties, (physical attributes according to Manley), would give the subject product improved processability and better and longer storability but, as we shall see presently, on the basis of those properties alone, the beta crystalline form of Imatinib Mesylate certainly cannot be said to possess enhanced efficacy over Imatinib Mesylate, the known substance immediately preceding it, within the meaning of section 3(d) of the Act.*

In the present case, I would say that the Patentee achieved lowering of crystal growth of the active during the micronization process and such reduced particle size is effective to penetrate the lungs. But this cannot be considered to translate or exhibit enhanced therapeutic activity over the known substance i.e. D3.The data relating Patentee arguments that crystal of Example 4 (prior art) in D3 are different from crystalline form presently claimed and the stability tests provided in the reply statement clearly prove the superior properties of the Monohydrate form in comparison with the prior art form (Example 4 of D3) does not appear convincing as the data

relating to stability does not have any relation with the therapeutic efficacy. The data as submitted by the applicant relating to stability test provided in the reply statement fails to prove clearly the superior properties of the Monohydrate form in comparison with the prior art form (Example 4 of D3), as stability does not have any relation with the therapeutic efficacy.

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

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

4) Referring to the ground of opposition U/s 25(2) (h), the failure to disclose details of corresponding foreign applications; applicant to provide information and undertaking relating to foreign filings within the prescribed period. Section 8(2) also casts a duty on the applicant to provide information to the controller as and when required relating to the processing of the application

Section 8(1) mandates the in a country outside India. Thus it is clear in the present case that nothing specific in writing was required by the controller, therefore as such applicant was not bound to provide any doc. u/s 8(2). Moreover the applicant has rightly filed petition for delay in providing information to condone the irregularity in filing the details of foreign countries. The then controller has also allowed the petition, thereby by regularizing it. Thus the patentee has met the all the requirements as per section 8 of Patent Act. The opponent has not brought to the

notice of controller their findings in respect of which the patentee has not provided the details corresponding foreign applications.
I conclude that such a ground of opposition is not validly established by the opponent.

Considering the post-grant opposition & recommendations of the Opposition Board, pleadings of both the parties & in view of my above findings, I hereby order to revoke the Patent IN 254813 granted on the Patent Application no.558/DELNP/2003.There is no order as to costs.

Dated this 04th March, 2015

(Dr.Ajay S.Thakur)
Assistant Controller of Patents and Designs.

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