* **IN THE HIGH COURT OF DELHI AT NEW DELHI**

% Judgment reserved on: 06.04.2026
Judgment delivered on: 06.07.2026

\+ C.A.(COMM.IPD-PAT) 24/2023

INTRA-CELLULAR THERAPIES, INC. .....Appellant

versus

THE CONTROLLER OF PATENTS .....Respondent

**Advocates who appeared in this case:**

For the Appellant : Mr. Ankush Verma, Mr. Debashish Banerjee, Ms. Vaishali Joshi, Mr. Pankaj Soni, Mr. Vineet Rohilla, Mr. Rohit Rangi, Ms. Gurneet Kaur and Mr. Tanveer Malhotra, Advocates.

For the Respondent : Mr. Arnav Kumar, Ms. Manya Gupta, Ms. Aishwarya Jain and Mr. Keshav Mittal, Advocates.

**CORAM:**
**HON'BLE MR. JUSTICE TUSHAR RAO GEDELA**

**J U D G M E N T**

**TUSHAR RAO GEDELA, J.**

1. The present appeal has been filed under Section 117A of the Patents Act, 1970 (hereinafter referred to as *"the Act"*) assailing the order dated 27.04.2023 (hereinafter referred to as *"impugned order"*) passed by the Controller of Patents and Designs (hereinafter referred to as *"learned Controller"*) whereby the Indian Patent Application bearing no.201817033732 (hereinafter referred to as *"subject application"*) was rejected on the grounds of lack of novelty under Section 2(1)(j), inventive step under Section 2(1)(ja) and non-patentability under Section 3(d) of the Act.

2. Briefly, the facts as stated in the appeal are as under:-

2.1 The appellant filed the subject application titled *"ORGANIC*

*COMPOUNDS",* before the Indian Patent Office, seeking grant of patent on 07.09.2018. It was numbered as Indian Patent Application no.201817033732. The First Examination Report (hereinafter referred to as *"FER"*) was issued on 31.10.2019. The appellant claims to have filed a detailed response to all the technical and formal objections taken in the said FER on 13.02.2020.

2.2 The respondent issued a notice of hearing on 04.02.2022 scheduling the hearing on 10.03.2022, which was attended to by the appellant. Thereafter, the appellant filed its written submissions alongwith amended claims on 22.03.2022.

2.3 Another hearing notice was issued by the respondent on 21.02.2023 scheduling the hearing on 14.03.2023, which was also attended to by the appellant. On 28.03.2023, the appellant requested for additional time to file its written submissions. On 26.04.2023, the appellant filed the written submissions alongwith a further set of amended claims.

2.4 Consequent thereto, *vide* the impugned order dated 27.04.2023, the subject application of the appellant was rejected. Aggrieved thereof, the present appeal has been preferred.

**CONTENTIONS OF THE APPELLANT:-**

3. Mr. Ankush Verma, learned counsel appearing for the appellant submitted that the subject patent application is in respect of a species patent arising from Markush Claims. He would submit that the patent relates to six specific compounds in three claims i.e. Claim 1, Claim 2 and Claim 3. While the first hearing notice dated 04.02.2022 did not raise any objection regarding lack of novelty, it raised objections of lack of inventive steps under Section 2(1)(ja) and non-patentability under Section 3(d) of the Act. The objection regarding lack of novelty under Section 2(1)(j) of the Act was raised only in the second hearing notice dated 21.02.2023.

4. Learned counsel contended that the respondent has committed an error in evaluating novelty by placing reliance on multiple prior arts as the closest prior art documents. Ordinarily, while determining novelty, it was submitted that a single document must be considered as the closest prior art.

5. That apart, he would submit that the objections under Section 2(1)(ja) regarding lack of inventive steps in the first hearing notice dated 04.02.2022 is the *verbatim* reproduction of the contents of European Search Opinion that has categorically acknowledged novelty and has opined that "*claims 1-16 appears to be novel within the meaning of Article 54(1) and (2) of the EPC as no prior art document discloses the specified deuterated compounds presently claimed*." He would contend that interestingly, the European examiner at the EPO in the corresponding European Patent Application cited the very same documents D1 to D7 to arrive at a conclusion that the criteria of novelty were met. Intriguingly, the Indian Patent Office while considering the very same prior art documents D1 to D7 has opined lack of novelty without any analysis or findings.

6. The evaluation of novelty by the respondent was challenged as erroneous. He states that the cited document D1 teaches, at Example 1.21, a compound wherein R1 and R6 are H, and X is NR5 where R5 is CD3 and R3 and R4 are D. However, it is stated that Formula 1.21 expressly modifies, in the alternative, any combination of the preceding 20 formulas. It is contended that in order to arrive at a compound alleged by the respondent, a person skilled in the art needs to first select that base compound i.e., the compound of Formula I and select R6 as H, and then must additionally select Formula 1.1 provided that R1 is H, and then Formula 1.21. Appellant would submit that in the hearing notice 04.02.2022 in fact, the respondent acknowledges with respect to cited document D1 that "multiple selections would be

necessary to arrive at the presently claimed compounds."

7. In continuation to the aforesaid, learned counsel would submit that while citing prior art D7, the respondent has only referred to the broadest embodiment of the compound of Formula 1. He would submit that multiple selections would be necessary to arrive at each of the compounds of Claims 1-3 from the disclosure of prior art D7. In the prior hearing notice, the respondent is stated to have pointed out that from Formula 1.4, on page 5 of D7, only further selection of R4 is H and R5 is H would be necessary while the appellant contends that the respondent has not shown how the skilled person would be motivated to make these selections.

8. It is also stated that the inventor's subsequent research has shown that the compounds at positions R4 and R5 in prior art D7 do not provide the expected benefits while the compound embraced by the amended claims do provide expected benefits. Learned counsel would submit that document D7 teaches deuteration at three positions of the molecule namely (a) on the methylene adjacent to the ketone, (b) on the methylene adjacent to the N-methylated piperazine nitrogen and (c) on the N-methyl group. Learned counsel relies upon the Clause 8 of the Manual of Patent Office Practice and Procedure to submit that a generic disclosure in the prior art may not necessarily take away the novelty of a specific disclosure.

9. Relying on paragraph 09.03.03.02 in Chapter 9 of the Indian Manual of Patent Office Practice and Procedure, learned counsel contended that the determination of inventive steps requires to consider the invention as a whole and not conclude that a claimed invention is obvious merely because individual parts of the claim taken separately are known or might be found to be obvious. According to the learned counsel, no reasoning whatsoever justifying the refusal on the ground of lack of inventive steps has at all been

provided by the respondent. He would submit that for this reason, the impugned order being contrary to the principles laid down in ***F. Hoffmann-La Roche Ltd. & Anr. vs. Cipla Ltd.: 2015:DHC:9674-DB*** and ***Agriboard International LLC vs. Deputy Controller of Patents and Designs: 2022:DHC:1206.***, ought to be set aside. According to the learned counsel, the judgments prescribed that it was the mandate of the Controller to analyse as to what is the existing knowledge and how a person skilled in the art would move from such existing knowledge to the subject invention which is captured in the application being considered by the Controller. In the absence of such analysis, the rejection of the patent application under Section 2(1)(ja) of the Act would be contrary to the provisions itself. Thus, according to him, there is nothing to justify as to how and why a skilled person would be motivated to modify the teachings of the prior art documents in order to arrive at the subject matter of the present invention.

10. So far as the decision on lack of inventive steps is concerned, there too, learned counsel contended that no reasoning at all has been provided. In order to elaborate, learned counsel referred to the penultimate paragraph of the impugned decision, which is extracted hereunder:-

> *"The office finds that, D4-D6 discloses, the "principle of using deuterated alternatives of known drugs"; and from the disclosure of any one among D4-D6, it is obvious for a person skilled in the art to bring a 'deuterated alternatives of known drugs' (as disclosed in D1 and/or D7). Therefore, the office concludes that, the subject matter of the present alleged invention, does not meet the requirements of section u/s 2(1)(ja) of The Patents Act 1970; and Inventive step for the claims 1-11 cannot be acknowledged in view of the disclosure of D1 and/or D7 in combination of the disclosure of any one among D4-D6."*

11. Referring to the aforequoted paragraph, the learned counsel would contend that there is no reference to any teaching or suggestion in any of the

cited documents D1 and/or D7 in combination with the document D4 - D6 which may render the claimed invention obvious. Merely relying generally on the teachings of the cited documents without connecting the dots and without ascertaining as to how the teachings would make the claimed invention obvious, renders the impugned decision of the respondent unsustainable in law.

12. Learned counsel would contend that the impugned order is cryptic and fails to discharge the burden of establishing that the prior art renders the claimed invention obvious. Thus, according to the learned counsel, the impugned order is rendered unsustainable and ought to be set aside.

13. Apart from the above, learned counsel strenuously emphasised that the impugned order ought to be set aside also for the reason that the respondent has completely disregarded and overlooked the affidavit of the co-inventor. He would contend that the reference to the affidavit of the co-inventor is conspicuous by its absence in the entire impugned order. It is contended by the appellant that the affidavit of the co-inventor was furnished on three different occasions. At the first instance, the declaration of the co-inventor namely, Dr. Peng Li, was submitted to the Patent Office alongwith response to the FER, second time with the written submissions filed subsequently to the first hearing and third time with the written submissions filed subsequently to the second hearing, yet, there is no reference at all to the said affidavit. Learned counsel would contend that the said action is squarely violative of the judgments passed by this Court in ***Milliken and Company vs. Controller of Patents and Designs & Anr.: 2025:DHC:1782*** and ***The Regents of the University of California vs. Union of India: 2019:DHC:2699.***

14. Learned counsel next argued that the respondent has incorrectly

concluded that the claims are proscribed by Section 3(d) of the Act. He would stoutly contend that for such proscription to sustain, the respondent is mandated to identify the "known" substance in the objections so raised, which is conspicuous by its absence in both the hearing notices. He would submit that in the first hearing notice, it was claimed that the claims 1 to 10 fall under Section 3(d) as the compounds are mere discovery of a new form of a known substance, while in the second hearing notice, it was merely stated that the subject matter as claimed in claim 1 to 11 is also not allowable under Section 3(d) of the Act. Thus, according to him, both the observations grossly lack in identifying the "known" substance and thus, the conclusion that the claims are barred under Section 3(d) of the Act is without any foundation.

15. That apart, he would contend that the aforesaid conclusion is contrary to and violative of the ratio laid down by this Court in ***D.S. Biopharma Limited vs. The Controller of Patents & Designs: 2022:DHC:3563*** and ***Taiho Pharmaceutical Co. Ltd. vs. The Controller of Patents: 2025:DHC:3777***. He relies on para 13 of the judgment in ***Taiho Pharmaceutical*** (*supra*), which is as under:-

> *"13. From the above extracted paragraphs, it can be inferred that in order to sustain an objection under Section 3(d) of the Act, the following factors have to be clearly identified by the Controller:*
> *i) the 'known substance' with 'known efficacy';*
> *ii) clear explanation as to how and why the claimed substance is a derivative or otherwise a new form of a 'known substance';*
> *iii) an objective comparison between the therapeutic efficacy of the claimed invention and that of the known substance."*

16. Mr. Verma, learned counsel also contended that the respondent has committed another serious infraction by conflating the criteria for novelty and inventive step and evaluating non-patentability under Section 3(d) of the Act on such parameters which is impermissible. He pointed out to the relevant portion of the impugned order which is extracted hereunder:-

> *"The office concludes (as explained earlier) that the compounds I-IV as claimed in claims 1-10 (and thus composition as claimed in claim 11) of present alleged invention, are same as disclosed in D1 & D7; the subject matter as claimed in claims 1-11 is not allowable under section 3(d) of The Patents Act 1970."*

17. Thus, according to learned counsel, an unsustainable conclusion was reached by the respondent by conflating two distinct and separate criteria required for evaluating novelty and inventive step on one hand and one required for evaluating non-patentability under Section 3(d) of the Act. He would stoutly contend that the criteria of evaluation for all three aspects are separate and distinct.

18. Learned counsel had also contended that the respondent failed to appreciate the experimental data provided with the complete specifications. Learned counsel specifically referred to Examples 5, 6 & 7 of the complete specifications to submit that in Example 5, the measurement of parent and metabolite levels in mice by *in vivo* tests were carried out by administering the compounds of Examples 1 to 3 and the compound of formula Q. It was stated that after a single dose of oral administration of the test compound, the plasma levels of parent compound and metabolite were measured at various durations. It is claimed that after normalizing for the extent of metabolism of the internal standard, it is found that the extent of amide formation for the compounds of Examples 1, 2 and 3 is significantly lower than for the non-deuterated compound Q. Using the formula, the relative amid formation was determined and the results were summarised in following table:-

| | Compound | Relative Amide Formation |
|---|---|---|
| Study 1 | Ex. 1 | 0.54 |
| Study 2 | Ex. 2 | 0.38 |
| Study 3 | Ex. 3 | 0.31 |
| Study 4 | Q | 0.79 |

19. Similarly, in Example 6, a comparison of pharmacokinetics between deuterated and non-deuterated compounds was tested on rats. In this procedure, the appellant conducted *in vivo* metabolites of the deuterated compound of Example 2 and compared that to its non-deuterated congener, the compound of Formula Q (tosylate salt). The pharmacokinetics of each compound was determined after oral and intravenous administration in cross-over studies in rats. The results were summarised as under:

| | Test Compound: | Formula Q | Example 2 (Formula I) |
|---|---|---|---|
| PO | Parent AUC | 56.0 | 58.5 |
| | Metabolite Q-1, AUC | 128.2 | 67.8 |
| IV | Parent AUC | 230.6 | 257.2 |
| | Metabolite Q-1, AUC | 6.7 | 3.7 |

20. It was stated that the results demonstrated a high degree of first-pass (hepatic) metabolism that proceeds predominantly by way of N-demythylation and alpha-N oxidation. Likewise, the learned counsel would submit that the comparison of pharmacokinetics between the deuterated and non-deuterated compounds in dogs was tested. The results are summarised hereunder:-

| | Test Compound: | Formula Q | Example 2 (Formula I) |
|---|---|---|---|
| SL | Parent AUC | 734 | 1262 |
| | Metabolite Q-1A, AUC | 23 | 103 |
| | Metabolite Q-1, AUC | N.Q. | N.D. |
| SC | Parent AUC | 813 | 785 |
| | Metabolite Q-1A, AUC | 20 | 49 |
| | Metabolite Q-1, AUC | N.D. | N.D. |

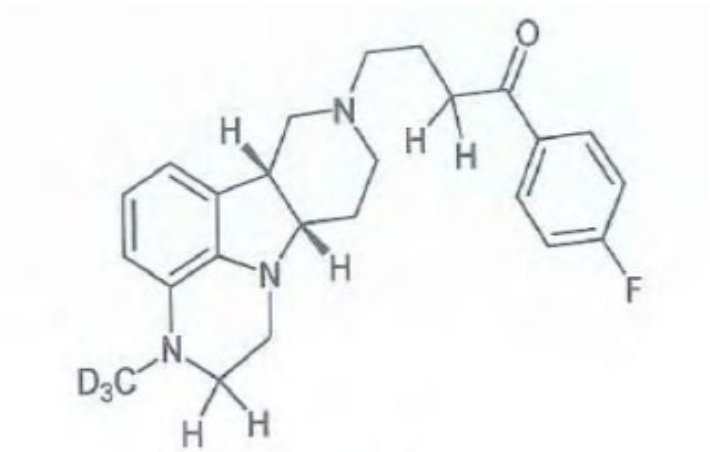
21. Learned counsel submits that the results displayed that the concentration of demethylated Q-1A metabolite was found to be higher for the deuterated compound compared to non-deuterated compound meaning thereby that deuteration is inhibiting the subsequent oxidation of the demythalated amine to its amide derivative.

22. Learned counsel vehemently contended that the tests which were conducted by way of Examples 5, 6 & 7 on mice, rats and dogs respectively and were compiled as a comparative data, were not even considered by the learned Registrar resulting in the impugned order.

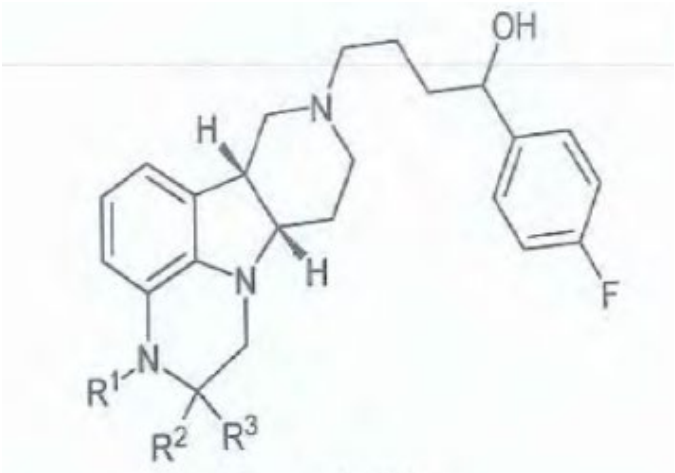
23. Predicated on the aforesaid submissions, learned counsel prays that the present be allowed and the impugned order dated 27.04.2023 passed by the respondent be set aside.

**CONTENTIONS OF THE RESPONDENT:-**

24. Mr. Arnav Kumar, learned counsel appearing for the respondent stoutly refuted the contentions made on behalf of the appellant. He would submit that the subject patent application consists of 11 claims which can be divided into two parts. Part 1 comprises claim 1-3 and 5-10 which ordinarily refer to the compound of Formula I. Part 2 comprises claims 4 and 5-7 which refer to the compound of Formula IV. The chemical formula of both parts is extracted hereunder:-




Formula I




Formula IV

25. He would submit that claim 11 pertains to the generic use of that drug as a composition and the allowability of claim 11 is entirely dependent on the allowability of claims 1 to 10.

26. So far as the objections of novelty under Section 2(1)(j) and the inventive step under Section 2(1)(ja) of the Act are concerned, it was submitted that the respondent had correctly concluded and refused the patent application as the claims do not meet the requirement under those provisions. In order to support the analysis and conclusion reached by the respondent, learned counsel referred to the prior art documents in the FER/hearing notice

to demonstrate that contrary to the assertions of the appellant, there is neither any inventive step nor any novelty so far as the claimed invention is concerned. He would refer to the following prior art documents:

(i) D1: WO 2015/154030 A1

(ii) D2: WO 2018/106916 A1

(iii) D3: WO 2017/117514 A1

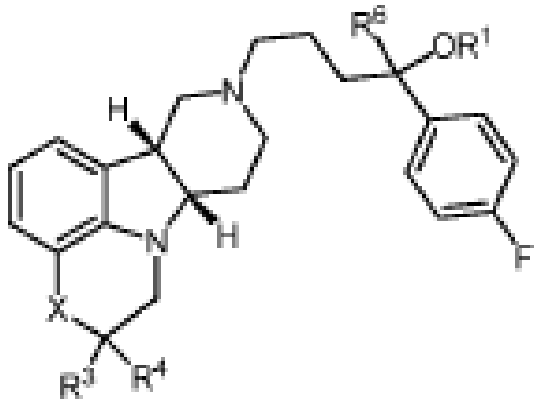
(iv) D4: WO 2014 110322 A2

(v) D5: Robert H. Howland: "Deuterated Drugs". Journal of Psychological Nursing and Mental Health Services, vol. 53, no.9, 1 September 2015

(vi) D6: Graham S Timmins: "Deuterated Drugs: where are we now?", Expert Opinion on Therapeutic Patents, 29 July 2014.

(vii) D7: WO 2015/154025 A1

27. Learned counsel emphasized that the prior arts D1 and D7 clearly disclose the compound which follows the same formula as used in the present claimed invention. In support of his submission, the following formula I of D-1 is extracted hereunder:-

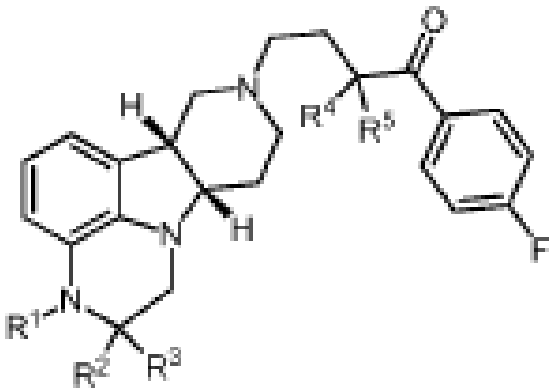



Formula I

28. He would submit that Example 1.21 of document D1 reveals that R1 and R6 are -H, X is -N(R5) wherein R5 is -CD3 and both R3 and R4 are -D. Based on the aforesaid disclosure in prior art D1, he would contend that when

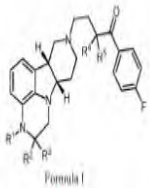
R1 and R6 are -H, X is -N(R5) wherein R5 is -CD3 and both R3 and R-4 are -D, it results in the compounds of Formula IV which is claimed in the present claims 4 and 5-7. Thus, according to him, the subject matter claimed in claims 4 and 5-7 do not meet the requirement of Section 2(1)(j) of the Act i.e., novelty.

29. He would contend that the next closest prior art declared by the respondent is D7. He would submit that D7 discloses the compound of the following formula for the same use as that of the present claimed invention, which is reproduced hereunder:-




Formula I

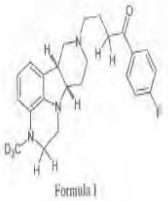
30. Learned counsel would submit that from the disclosures of D7, it can be easily perceived that when R1 is CH3 or CD3, R2 and R3 are each independently H or D, R4 and R5 are each independently H or D provided that R2, R3, R4 and R5 are not all H when R1 is CH3 (claim 1 of D7), it results in the compounds of Formula I-III. He would submit that these formulas are the same as claimed in the present claims 1-3 and 5-10. Predicated on the above, he would strenuously contend that therefore, the subject matter as claimed in claims 1-3 and 5-10 do not meet the requirements of Section 2(1)(j) of the Act. Just to substantiate the aforesaid arguments, the structural presentation is described hereunder:-



of D7

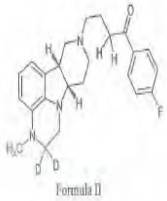
WHEN
R4 and R5 are each independently H
R1 is CD3
R2 and R3 are each independently H

RESULTS
Compound of Formula-I (as that of present alleged Invention)



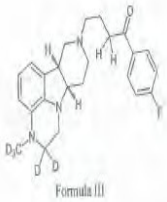
WHEN
R4 and R5 are each independently H
R1 is CH3
R2 and R3 are each independently D

RESULTS
Compound of Formula-II(as that of present alleged Invention)



WHEN
R4 and R5 are each independently H
R1 is CD3
R2 and R3 are each independently D

RESULTS
Compound of Formula-III (as that of present alleged Invention)



31. Learned counsel further contended that the claimed invention in the subject patent application is nothing other than the generic compound of Formula I-III and therefore, the conclusion reached by the respondent that the claimed subject matter of the present invention having been disclosed in the prior arts D1 and D7, the claims 1 to 10 are not novel within the meaning of Section 2(1)(j) of the Act cannot be doubted or distinguished.

32. So far as the composition claim 11 is concerned, learned counsel would contend that as the product claimed in claims 1 to 10 have been found to lack novelty, the said composition claim comprising the compounds claimed in the aforesaid claims 1 to 10, claim 11 would also lack novelty and is not allowable under Section 2(1)(j) of the Act.

33. As an upshot of the aforesaid arguments and analysis, learned counsel would contend that the conclusion reached by the respondent that the compound formula I-IV as claimed in claims 1 to 10 and composition claim 11 of the subject invention are already disclosed in prior arts D1 and D7, the objection regarding lack of novelty cannot be set aside. Mr. Kumar submitted

that the claimed compounds are expressly disclosed and claimed in the prior arts.

34. Predicated entirely on the claims 1 to 10 lacking novelty, the requirements under Section 2(1)(ja) regarding inventive steps, according to the learned counsel, are also not met. He would contend that the respondent clearly found that the prior arts D4 to D6 disclose the principle of using deuterated alternatives of known drugs. The disclosure from any of the prior arts D4 to D6, being in the same field, would make it obvious for a person skilled in the art to bring a deuterated alternative of a known drug. Thus, the conclusion of the respondent that the claimed invention is an obvious deuterated alternative of known drugs as disclosed in D1 and D7 when combined with the disclosure among D4 to D6, is perfectly sustainable. He would contend that in view of the aforesaid disclosures, it is obvious and rightly concluded that the present claimed invention does not meet with the requirements of either Section 2(1)(j) or Section 2(1)(ja) of the Act.

35. Learned counsel further submitted that it is settled law that serial parenting in order to evergreen a particular monopoly is not permissible. It is stated that in the present case, the inventor of the prior arts and claimed invention is the same i.e. the appellant. While relying upon the judgement of this Court in ***AstraZeneca Ab vs. Intas Pharmaceuticals Ltd.: 2021 SCC OnLine Del 3746***, learned counsel stated that in the circumstances of the present case, the test of anticipation of publication cannot be in the context of a 'person ordinarily skilled in art' but have to be the 'person in the know'.

36. So far as the objection under Section 3(d) of the Act is concerned, learned counsel would forcefully contend that such objections have not at all been met with by the subject invention. He would contend that the compound formula I-IV as claimed in claims 1 to 10 are the same as disclosed in the

prior arts D1 and D7, and the same is merely a discovery of a new form of a known substance. Since the compounds in the present invention are not considered as a new product, the claimed compound would be non-patentable under Section 3(d) of the Act. Moreover, learned counsel would contend that, even if the appellant is able to demonstrate novelty under Section 2(1)(j) of the Act, the claimed compound would still not be patentable as the appellant has failed to establish technical advancement in terms of 'therapeutic effect'. In support of the aforesaid contention, he relied upon the judgment of the Supreme Court in ***Novartis AG vs. Union of India & Ors.: (2013) 6 SCC 1***.

37. To the *in-vivo* studies claimed to have been conducted by the appellant with mice and rats to determine the extent that each of the claimed compounds in comparison to the compound of Formula Q (non-deuterated analogue) having converted to the major amide metabolite X and the comparative data submitted, learned counsel would contend that the same was considered and found to be insufficient to prove a significant increase in the therapeutic efficacy of the claimed compound. According to the learned counsel, the data in respect of the study conducted on the mice and the one conducted on rats is concerned, he would contend that the results only show better performance of the drug in comparison to the original version of Formula Q, however, did not disclose a significant increase in the therapeutic efficacy and thus, were insufficient to overcome the proscription under Section 3(d) of the Act.

38. Thus, the appellant having failed to show a remarkable therapeutic effect of the claimed compound in comparison to the compounds available in the prior art documents D1 and D7, learned counsel would contend that the claimed invention does not meet with the requirement of Section 3(d) of the Act.

39. According to the learned counsel, the reliance placed by the appellant on their international patents granted is misplaced. He would submit that it is trite that patent rights are territorial rights and would be governed purely by the provisions of the Patents Act, 1970, in India and there is no provision under the Act or Rules that warrants the respondent to follow or rely upon any grant of patent in foreign jurisdictions. In other words, learned counsel would contend that the patentee is obliged to satisfy the objections raised by the Indian Patent Office in terms of the provisions contained in the Act, failing which the patents granted by foreign jurisdictions, would not come to its rescue. To buttress his arguments, he relied upon the judgement of this Court in ***Communication Components Antenna Inc. vs. Ace Technologies Corp.: 2019 SCC OnLine Del 9123***.

**ANALYSIS AND CONCLUSIONS:-**

40. Heard learned counsel for the parties and perused the records of the case.

***THE INVENTION:***

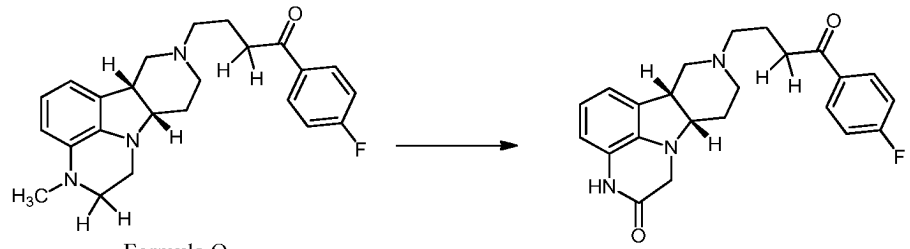
41. The present invention under the subject application is titled *"ORGANIC COMPOUNDS"* and pertains to particular deuterated heterocycle-fused gamma-carbolines, in the form of free, pharmaceutically acceptable salt and/or substantially pure form. The pharmaceutical composition and method of use under the present invention is for the treatment of diseases involving 5-HT2A receptor, serotonin transporter (SERT) and/or pathways involving dopamine D1/D2 receptor signalling systems. The claimed invention also has application in the treatment of diseases/disorders like anxiety, psychosis, schizophrenia, sleep disorders, sexual disorders, migraine, etc. For clarity, the field of invention of the Complete Specification (hereinafter referred to as *"CS"*) of the subject

application is reproduced as follows:

FIELD OF THE INVENTION

**[0002]** The invention relates to particular deuterated heterocycle fused gamma-carbolines, in free, pharmaceutically acceptable salt and/or substantially pure form as described herein, pharmaceutical compositions thereof, and methods of use in the treatment of diseases involving 5-$HT_{2A}$ receptor, serotonin transporter (SERT) and/or pathways involving dopamine $D_1/D_2$ receptor signaling systems, e.g., diseases or disorders such as anxiety, psychosis, schizophrenia, sleep disorders, sexual disorders, migraine, conditions associated with cephalic pain, social phobias, gastrointestinal disorders such as dysfunction of the gastrointestinal tract motility and obesity; depression and mood disorders associated with psychosis or Parkinson's disease; psychosis such as schizophrenia associated with depression; bipolar disorder; and other psychiatric and neurological conditions, as well as to combinations with other agents.

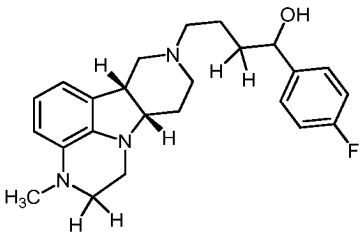
42. As per the CS, the inventor of the subject application has discovered that the major routes of metabolism of fused heterocycle gamma carboline of Formula Q are by way of N-dealkylation and alpha-oxidation at the piperazine ring as well as by reduction of the carbonyl resulting into the compounds of Formula Q-1, Q-2 and Q-3. As per the CS, it was also found that the alcohol metabolite of Formula Q-2 retains significant pharmacological activity. Formula Q-1, Q-2 and Q-3 shown below:-



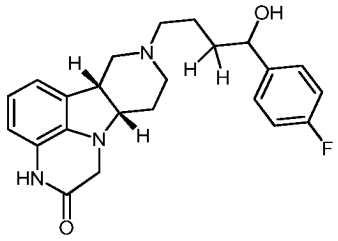
Formula Q



Formula Q-1



Formula Q-2



Formula Q-3

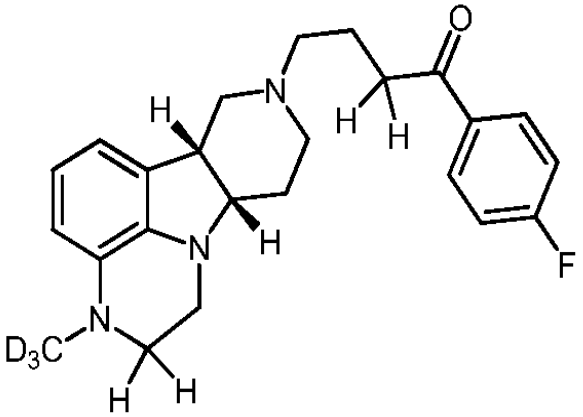
43. The CS of the subject application under para [00014], states that the present invention provides compounds which specifically limit and/or prevent metabolism occurring by the said pathways. As the deuterium (2H) atoms and normal hydrogen atoms (1H) have similar properties, drug compounds in which deuterium is substituted for hydrogen are believed to generally have similar biological activity to the non-deuterated analog, but potentially with improved pharmacokinetic properties. The extent to which such a substitution will result in an improvement of pharmacokinetic properties without a too severe loss in pharmacologic activity is variable. Therefore, as per the CS, in some circumstances, the produced deuterated compound may have moderate increase in pharmacokinetic stability, while in other circumstances, it may have significantly improved stability.

44. In conclusion, as per the said CS, it may be difficult to predict the effects of simultaneous deuterium substitutions with certainty and this may or may not result in additive (synergistic) improvement in metabolic stability.

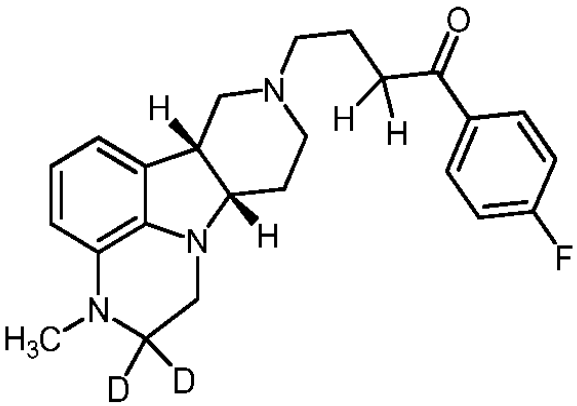
45. The CS of the subject application under para [00015], specifies that the

claimed invention under the subject application provides compounds containing a trideuterated N-methyl, and/or a di-deuterated methylene adjacent to the N-methyl and these compounds antagonize 5-HT2A receptors, inhibit the serotonin re-uptake transporter, and modulate dopaminergic protein phosphorylation, in a manner similar to their natural hydrogen analogs. However, these compounds display an unexpectedly improved metabolic stability.

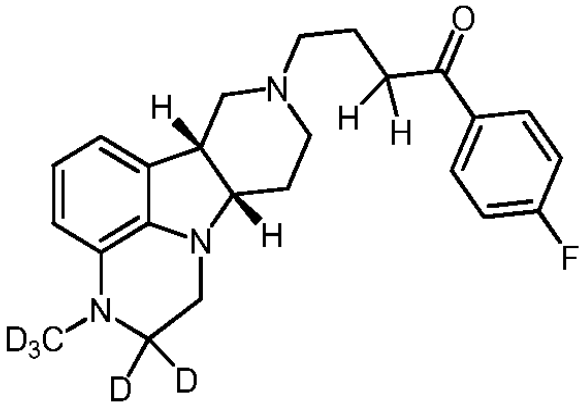
46. In the different embodiment, the invention provides a compound of Formula I, II and III which are reproduced as follows:-



Formula I

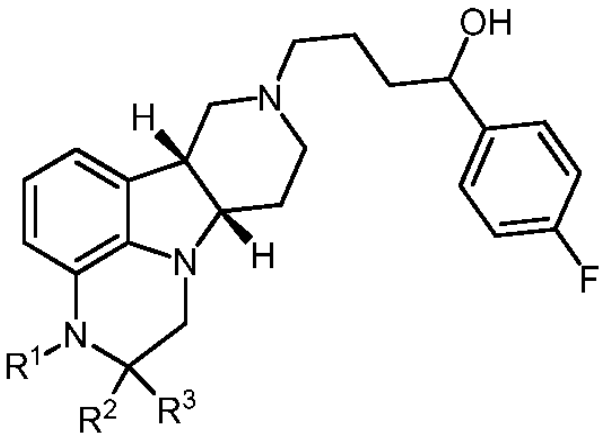


Formula II




Formula III

47. In another embodiment, the invention provides a compound of Formula IV, in which R1 is CH3 or CD3; R2 and R3 are either both H or both D, provided that when R1 is CH3, R2 and R3 are both D. The compound of Formula IV is reproduced as follows:-

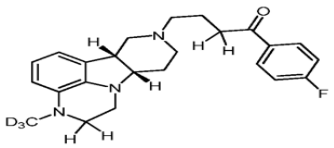



Formula IV

48. Claim 1 and 11 of the subject application as filed with written submission dated 26.04.2023 is reproduced as follows:-

Claims:

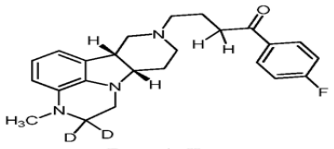
1. A compound of formula I,



Formula I

in free or salt form.

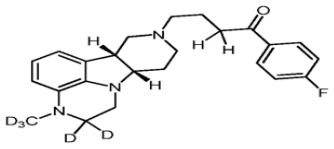
2. A compound of formula II,



Formula II

in free or salt form.

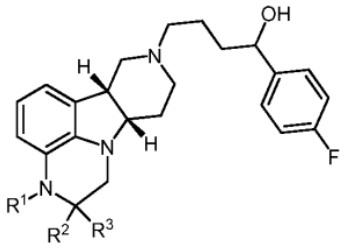
3. A compound of formula III,



Formula III

in free or salt form.

4. A compound of formula IV,



Formula IV

wherein:

$R^1$ is $CH_3$ or $CD_3$;

$R^2$ and $R^3$ are either both H or both D;

provided that when $R^1$ is $CH_3$ $R^2$ and $R^3$ are both D;

free or salt form.

Formula IV

wherein:

$R^1$ is $CH_3$ and $R^2$ and $R^3$ are either both D; or

$R^1$ is $CD_3$ and $R^2$ and $R^3$ are either both H; or

$R^1$ is $CD_3$ and $R^2$ and $R^3$ are both D;

free or salt form.

11. A pharmaceutical composition comprising a compound as claimed in any one of claims 1-10, in free or pharmaceutically acceptable salt form, in combination or association with a pharmaceutically acceptable diluent or carrier, wherein the composition is formulated for oral administration and comprises from 2.5 to 50 mg of the compound.

49. Therefore, as per para [00015], the claimed compounds, i.e., Formulas I, II, III antagonize 5-$HT_{2A}$ receptor, inhibit the serotonin re-uptake transporter, and modulate dopaminergic protein phosphorylation in the like manner as to their natural hydrogen analog. Additionally, as per the CS, these compounds display an unexpectedly improved metabolic stability.

50. Now this Court will proceed to examine the objections raised in the impugned order.

***OBJECTION ON THE GROUND OF NOVELTY UNDER SECTION 2(1)(j) OF THE ACT:***

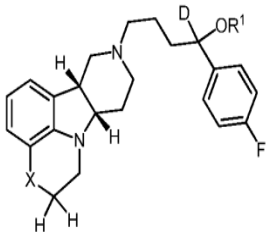
**PRIOR ART D1** (WO 2015/154030 Al)

51. The invention under prior art D1 relates to substituted heterocycle fused gamma-carbolines, their prodrugs, in free, solid, pharmaceutically acceptable salt and/or substantially pure form. The pharmaceutical compositions have use in the treatment of diseases involving 5-$HT_{2A}$ receptor, serotonin transporter (SERT) and/or pathways involving dopamine Dl/D2

receptor signalling systems, and/or the treatment of residual symptoms.

52. Under Example 1.21, at page 6, D1 discloses that R1 & R6 is -H, X is -N(R5) wherein R5 is -CD3 and both R3 & R4 are -D. The relevant para is reproduced as follows:-

**[0014]** In a second aspect, the invention provides the Compound of Formula I-B:




Formula I-B

wherein:

X is N(H), N($R^5$) or O;

$R^5$ is $C_{1-6}$ alkyl;

$R^1$ is H, or

$C_{1-6}$ alkyl, or

a pharmaceutically acceptable and physiologically labile moiety, e.g. a pharmaceutically acceptable and physiologically labile acyl moiety, for example, wherein the labile moiety is -C(O)-$R^2$, and $R^2$ is a $C_{1-21}$ alkyl, e.g., a linear $C_{1-21}$ alkyl,

and wherein D is deuterium;

**[0015]** In a further embodiment, the invention provides the Compound of Formula I or I-B, as described in the following formulae:

1.1 the compound of Formula I or I-B, wherein $R^1$ is H;

1.2 the compound of Formula I or I-B, wherein $R^1$ is $C_{1-6}$alkyl (e.g., methyl);

1.3 the compound of Formula I or I-B, wherein $R^1$ is $C_{1-6}$ alkyl optionally substituted with D;

1.4 the compound of Formula I or I-B, wherein $R^1$ is $CH_3$;

1.5 the compound of Formula I or I-B wherein $R^1$ is $CD_3$;

1.6 the compound of Formula I or I-B, wherein $R^1$ is a pharmaceutically acceptable and physiologically labile moiety, e.g. a pharmaceutically acceptable and physiologically labile acyl moiety;

1.7 the compound of Formula I or I-B, wherein R1 is -C(O)-$R^2$, and wherein $R^2$ is $C_{1-21}$ alkyl;

1.8 the compound of Formula I or I-B, wherein R1 is -C(O)-$R^2$, and wherein $R^2$ is $C_{1-15}$ alkyl;

1.9 the compound of Formula I or I-B, wherein R1 is -C(O)-$R^2$, and wherein $R^2$ is $C_{1-9}$ alkyl;

1.10 the compound of Formula I or I-B, wherein R1 is -C(O)-$R^2$, and wherein $R^2$ is methyl, ethyl or propyl;

1.11 the compound of Formula I or I-B, wherein R1 is -C(O)-$R^2$, and wherein $R^2$ is methyl;

1.12 the compound of Formula I or I-B or any of formulae 1.1-1.11 wherein X is N(H), N($R^5$) or O;

1.13 the compound of Formula I or I-B or any of formulae 1.1-1.11, wherein X is O;

1.14 the compound of Formula I or I-B or any of formulae 1.1-1.11, wherein X is N(H);

1.15 the compound of Formula I or I-B or any of formulae 1.1-1.11, wherein X is N($R^5$), and wherein $R^5$ is $C_{1-4}$ alkyl;

1.16 the compound of Formula I or I-B or any of formulae 1.1-1.11, wherein X is N($R^5$), and wherein $R^5$ is $CH_3$;

1.17 the compound of Formula I or I-B or any of formulae 1.1-1.11, wherein X is N($R^5$), and wherein $R^5$ is $CD_3$;

1.18 the compound of Formula I or I-B or any of formula 1.1-1.17, wherein $R^3$ is D;

1.19 the compound of Formula I or I-B or any of formula 1.1-1.17, wherein $R^4$ is D;

1.20 the compound of Formula I or I-B or any of formula 1.1-1.17, wherein $R^3$ and $R^4$ are D;

1.21 the compound of Formula I or I-B or any of formula 1.1-1.20, wherein X is N($R^5$), and $R^5$ is $CD_3$ and $R^3$ and $R^4$ are both D;

1.22 the Compound of Formula I or I-B or any of formulae 1.1-1.21, wherein the Compound is:

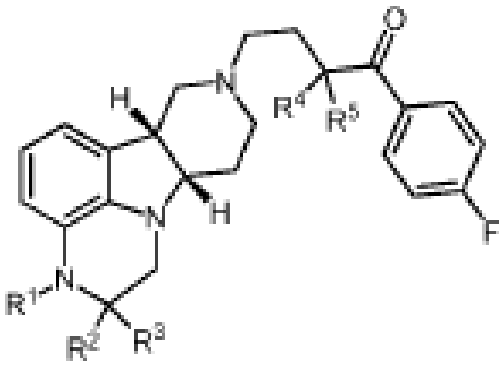
53. Considering the abovementioned disclosure of D1, when R1 and R6 is -

H and X is -N(R5) wherein R5 is -CD3 and both R3 and R4 are -D as given under Example 1.21 of prior art D1, it results in the compounds of Formula-IV (which is claimed in claims 4 & 5 to 7 of the subject application.

**PRIOR ART D7** (WO 2015/154025 A1)

54. Prior art D7 is titled as "ORGANIC COMPOUNDS" and pertains to specific substituted heterocycle fused gamma-carbolines, their prodrugs, in free, solid and pharmaceutically acceptable salt and/or substantially in pure form. The invention under D7 is pharmaceutical compositions and methods of use are in the treatment of diseases involving 5-HT2A receptor, serotonin transporter (SERT) and/or pathways involving dopamine D1/D2 receptor signalling systems, and/or the treatment of residual symptoms.

55. As per para [00012] of D7, it discloses the following compound:-



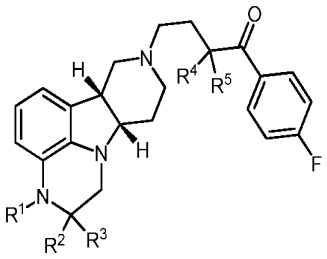

" Formula I

*Where*
*R1 is CH3 or CD3;*
*R2 and R3 are each independently H or D;*
*R4 and R5 are each independently H or D;*
*provided that R2, R3, R4, and R5 are not all H when R1 is CH3;*
*and wherein D is deuterium;"*

56. Additionally, Claim 1 of D7 is reproduced as follows:-

Claims:

1. A compound of formula I:



Formula I

wherein:

$R^1$ is $CH_3$ or $CD_3$;

$R^2$ and $R^3$ are each independently H or D;

$R^4$ and $R^5$ are each independently H or D;

provided that $R^2$, $R^3$, $R^4$, and $R^5$ are not all H when $R^1$ is $CH_3$,

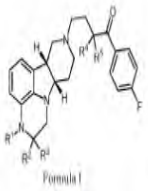
and wherein D is deuterium;

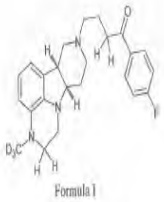
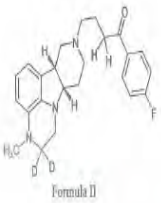
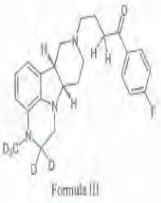
in free or salt form.

57. Claim 7 of cited document D7 is a dependent claim of independent Claim 1. Under Claim 7, D7 claims all R2, R3 and R5 as D. Claim 7 of D7 reads as *"The compound according to claim 1, wherein R2 and R3 and R4 and R5 are all D*".

58. As per the abovementioned disclosure under D7, when R1 is CH3 or CD3, R2 and R3 are each independently H or D and R4 and R5 are each H and considering that R2, R3, R4, and R5 are not all H when R1 is CH3, it results into the compounds of Formula-I to III as claimed in claims 1 to 3 and 5 to 10 of the subject application.

59. For better understanding, illustration provided under the impugned order is reproduced as follows:-


of D7

| | | |
|---|---|---|
| WHEN<br>R4 and R5 are each independently H<br>R1 is CD3<br>R2 and R3 are each independently H | RESULTS<br>Compound of Formula-I (as that of present alleged Invention) |  |
| WHEN<br>R4 and R5 are each independently H<br>R1 is CH3<br>R2 and R3 are each independently D | RESULTS<br>Compound of Formula-II(as that of present alleged Invention) |  |
| WHEN<br>R4 and R5 are each independently H<br>R1 is CD3<br>R2 and R3 are each independently D | RESULTS<br>Compound of Formula-III (as that of present alleged Invention) |  |

60. From the above, it follows that the prior art D7 discloses the compounds of Formula I to III as claimed in claims 1 to 3 and 5 to 10 of the subject application. Therefore, the subject matter as claimed in claims 1-3 & 5-10 is not allowable under Section 2(1)(j) of the Act, as the claimed compound is not novel.

61. Similarly, as per the abovementioned disclosure under prior art D1, the compounds of Formula-IV, which is claimed in claims 4 & 5 to 7 of the subject application, are disclosed and therefore, not novel and are barred under Section 2(1)(j) of the Act for lack of novelty.

62. The appellant argued that considering the disclosure in D1, multiple selections have to be considered to arrive at the presently claimed compounds under the subject application. For better understanding, the submissions of the appellant are reproduced as follows:-

> *"The Appellant submits that in the hearing notice dated February 4, 2022, the Respondent has acknowledged with respect to cited document D1 that "multiple selections would be necessary to arrive at the presently claimed compounds."*

*While citing prior art D7, the Respondent has only referred to the broadest embodiment of the Compound of Formula I, as disclosed on page 4 of D7. It is submitted that multiple selections would be necessary to arrive at each of the compounds of claims 1-3 from this disclosure of D7. Furthermore, the Appellant submits that in the prior hearing notice, the Respondent particularly pointed that from Formula 1.4, in paragraph [0013], on page 5 of D7, only the further selection of R4 is H and R5 is H would be necessary. The Appellant humbly submits that the Respondent has not shown as to how the skilled person would be motivated to make these selections.*

*Moreover, to the extent that D7 discloses compounds deuterated at positions R4 and R5 thereof, the inventor's subsequent research has shown that these compounds do not provide the expected benefits, whereas the compound embraced by the amended claims do. D7 generally teaches deuteration at three positions of the molecule, or any combination thereof. The three positions are (a) on the methylene adjacent to the ketone (R4 and R5 of D1's Formula I), (b) on the methylene adjacent to the N-methylated piperazine nitrogen (R2 and R3 of D1's Formula I), and (c) on the N-methyl group (R1 of D1's Formula I)."*

63. However, it is a settled position that where a compound is disclosed under the genus patent (i.e. prior art D1 and D7 in this case), specific disclosure is immaterial. Therefore, the submissions of the appellant that, under prior art D1, it needs to consider the multiple selections to arrive at the presently claimed compounds under the subject application, is not acceptable. This Court in ***AstraZeneca AB (DB)*** *(supra)* emphasised that if a product is specifically "covered" in the claims of a patent in question, whether specific disclosure of that product (compound in this case) concerning the same has been made or not is immaterial. For clarity, para 90 of ***Boehringer Ingelheim Pharma GMBH & Co. KG vs. Vee Excel Drugs and Pharmaceuticals Private Ltd. & Ors.: 2023 SCC OnLine Del 1889*** held as follows:-

*"90. In the present case also, the plaintiffs are trying to make a distinction between the words, "claimed", "covered", "encompassed" and "disclosed". **The words, "covered" and "encompassed" essentially mean the same thing and the plaintiffs are only relying on semantics to make an artificial distinction, which does not exist. When the product is specifically "covered" in the claims of a patent, whether specific disclosure with regard to the same has been made or not is immaterial.** In fact, if the submissions of the plaintiffs that Linagliptin has not been disclosed in the*

*suit patent is to be accepted, it would result in violation of the requirement of Section 10(4) of the Patents Act that every complete specification of a patent must satisfy."*

[emphasis supplied]

64. Further, the Supreme Court in the case of ***Novartis AG*** *(supra)* had on an earlier occasion held as follows:-

***"139. The dichotomy that is sought to be drawn between coverage or claim on the one hand and disclosure or enablement or teaching in a patent on the other hand, seems to strike at the very root of the rationale of the law of patent. Under the scheme of patent, a monopoly is granted to a private individual in exchange of the invention being made public so that, at the end of the patent term, the invention may belong to the people at large who may be benefited by it. To say that the coverage in a patent might go much beyond the disclosure thus seem to negate the fundamental rule underlying the grant of patents.***

*156. However, before leaving Hogan [Hogan, In re, 559 F 2d 595 (CCPA 1977)] and proceeding further, we would like to say that in this country the law of patent, after the introduction of product patent for all kinds of substances in the patent regime, is in its infancy.* ***We certainly do not wish the law of patent in this country to develop on lines where there may be a vast gap between the coverage and the disclosure under the patent ;*** *where the scope of the patent is determined not on the intrinsic worth of the invention but by the artful drafting of its claims by skilful lawyers, and where patents are traded as a commodity not for production and marketing of the patented products but to search for someone who may be sued for infringement of the patent."*

[emphasis supplied]

65. Therefore, in light of the above discussion, the submissions of the appellant that in order to arrive at the present invention under the subject application, multiple selections have to be considered in the prior art D1, cannot be accepted.

***OBJECTION ON THE GROUND OF NON-PATENTABILITY UNDER SECTION 3(d) OF THE ACT:***

66. Before adverting to the facts, it would be apposite to examine the law surrounding interpretation of Section 3(d) of the Act, which is reproduced as under:-

*"Section 3. What are not inventions: The following are not inventions within*

*the meaning of this Act —*

*xxx xxx xxx*

*(d) the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new property or new use for a known substance or of the mere use of a known process, the machine or apparatus unless such known process results in a new product or employs at least one new reactant.*

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

67. It is important to note that Section 3(d) of the Act was interpreted by the Supreme Court in ***Novartis AG (supra).*** After a detailed examination of law and facts, and having regard to the goods being manufactured under Class 5, i.e., medicinal preparations, the Supreme Court held that a mere new form of a known substance is unpatentable ***unless it differs significantly in properties concerning efficacy***. The Court held that "*efficacy*" in the pharmaceutical context means **therapeutic efficacy**, not any beneficial physicochemical property. Thus, unless the compounds demonstrate enhanced "efficacy" (therapeutic), they would be non-patentable and proscribed under the provisions of Section 3(d) of the Act.

68. In the present case, it would be relevant to note that the compound Q, which is admittedly a known compound, is in fact, disclosed in the cited document D1 and D7 under paras [0096] and [0094] respectively.

69. However, the appellant had argued that Example 7 shows the therapeutic efficacy and therefore, the invention is not barred under Section 3(d) of the Act. Example 7 is reproduced as follows:-

*"EXAMPLE 7: Comparison of Pharmacokinetics between Deuterated and Non- Deuterated Compounds in Dogs*

*[000119] In vivo metabolism (demethylation and alpha-oxidation) of the deuterated Compound of Example 2 (the Compound of Formula I, tosylate*

*salt) is compared to that of its non-deuterated congener, the Compound of Formula Q (tosylate salt). The pharmacokinetics of each compound is determined after both sublingual (SL) and subcutaneous (SC) administration in non-cross over sequential studies in dogs.*

*[000120] SC Administration: Six male beagle dogs between 2 and 5 years of age are randomized in two groups of three dogs each. Dogs in group 1 are administered the compound of Formula Q at a dose of 1 mg/kg (free base equivalent) in a 0.5% methylcellulose/distilled water vehicle. Dogs in group 2 are administered the compound of Example 2 at a dose of 1 mg/kg (free base equivalent) in a 0.5% methylcellulose/distilled water vehicle. Administration is subcutaneous in the intrascapular region via a 22 or 23 gauge needle. Whole blood samples are collected via the dog's cephalic vein pre-dose, and at postdose time-points 5, 15 and 30 minutes, 1, 2, 4, 6, 8 and 24 hours. Following a minimum 7- day washout period, the dogs are transferred to the sublingual portion of the study.*

*[000121] SL Administration: The dogs of group 1 are administered the compound of Formula Q at a dose of 1 mg/kg (free base equivalent) in a 0.5% methylcellulose/distilled water vehicle. Dogs in group 2 are administered the compound of Example 2 at a dose of 1 mg/kg (free base equivalent) in a 0.5% methylcellulose/distilled water vehicle. The animals are anesthetized prior to administration of the dose using propofol (6 mg/kg) and anesthesia is maintained for 30 minutes using 3-4.5% isoflurane. Administration is sublingual and the dosage is applied for 30 minutes, then wiped off using unwoven gauze. Whole blood samples are collected via the dog's cephalic vein pre-dose, and at post-dose time-points 5, 15 and 30 minutes, 1, 2, 4, 6, 8, 24, 36 and 48 hours.*

*[000122] All blood samples are processed to plasma and analyzed for parent and metabolite concentrations using liquid chromatography-tandem mass spectrometry (LCMS/ MS). The metabolites analyzed include the N-demethylated compound Q-lA (shown below), and the N-demethylated/alpha-oxidized amide compound Q-1 (discussed supra). Area under the curve (AUC) of parent and metabolites based on plasma versus time data are calculated using Prism 5.04 software (GraphPad Software, Inc.).*

*[000123] The results are summarized in Table 2 below (AUC is shown for 0-24 hours, measured in ng-hr/ml.):*

| | Test Compound: | Formula Q | Example 2 (Formula I) |
|---|---|---|---|
| SL | Parent AUC | 734 | 1262 |
| | Metabolite Q-1A, AUC | 23 | 103 |
| | Metabolite Q-1, AUC | N.Q. | N.D. |
| SC | Parent AUC | 813 | 785 |
| | Metabolite Q-1A, AUC | 20 | 49 |
| | Metabolite Q-1, AUC | N.D. | N.D. |

*[000124] It is found that SL dosing of the compound of Example 2 results in about 72% higher parent AUC compared to dosing of the compound of Formula Q. AUC of the desmethyl metabolite Q-lA is about 3% of parent for the compound of Formula Q, and about 8% of that of the parent for the compound of Example 2. The concentration of the amide metabolite Q-1 is detectable at less than 1 ng/mL at each time point for SL administration of the compound of Formula Q (AUC not quantified), but is undetectable for SL administration of the compound of Example 2 ( < 0.1 ng/mL).*

*[000125] In contrast, SC dosing resulted in more comparable results between the two compounds. For the compound of Formula Q, the Q-lA metabolite AUC is about 3% of parent, while for the of the compound of Example 2, the Q-lA metabolite AUC is about 6% of parent. For SC dosing, the metabolite Q-1 was undetectable (< 0.1 ng/mL) for both compounds. The AUC of parent is found to be comparable between the deuterated and nondeuterated compounds.*

*[000126] Comparing the SC to SL results, for the compound of Formula Q, SL administration resulted in 10% less net AUC of parent compound compared to SC administration. In contrast, dosing the deuterated compound of Example 2 leads to 61 % higher parent AUC for SL compared to SC. Without being bound by theory, it is believed that this difference is related to differences in the rate of absorption from the subcutaneous space between the deuterated and non-deuterated species.*

*[000127] Taken together, these results show that deuteration of the methylene group adjacent to the piperazine nitrogen reduced metabolism of the compound of the invention compared to its non-deuterated analog, resulting in higher and more prolonged plasma concentrations of the parent drug. Since the concentration of the de-methylated Q-lA metabolite is found to be higher for the deuterated compound, compared to the non-deuterated compound, the results suggest, as seen in rats, that deuteration is inhibiting the subsequent oxidation of the de-methylated amine to its amide derivative (Q-1).”*

70. In contradistinction, the impugned order states that there is no data provided by the appellant to show the therapeutic efficacy of the present

invention. Therefore, it is important to know whether Example 7 shows the therapeutic efficacy of the present invention.

71. Let's understand Example 7, which was relied upon by the appellant.

72. The compounds considered under the example are Compound Q (tosylate salt) and deuterated Compound of Example 2 (the Compound of Formula I, tosylate salt). *In vivo* metabolism (demethylation and alpha-oxidation) of the deuterated Compound of Example 2 is compared to that of its non-deuterated congener, the Compound of Formula Q (tosylate salt). Thereafter, the pharmacokinetics of each compound is determined after experiments are done by two types of administration which are sublingual (SL) and subcutaneous (SC) in non-cross over sequential studies in dogs.

73. The blood samples are processed to plasma and analysed for parent and metabolite concentrations by using liquid chromatography-tandem mass spectrometry (LCMS/ MS). The metabolites analysed include the N-demethylated compound Q-lA, and the N-demethylated/alpha-oxidized amide compound Q-1. Area under the curve (AUC) of parent as well as the metabolites, based on plasma versus time data was calculated by using Prism 5.04 software.

74. The results are provided in Table 2 under para 123 of the CS. The following can be determined from Table 2:-

<u>Sublingual (SL) dosing:</u>

- The deuterated compound gave about 72% higher parent-drug AUC than Q.
- The desmethyl metabolite Q-1A was about 3% of the parent for Q, but about 8% of the parent.
- The amide Q-1 was a trace for Q and undetectable for compound compound of example 2.

Subcutaneous (SC) dosing:

- Q-1A was 3% of the parent for Q vs and 6% for compound of example 2.
- Q-1 was undetectable for both.
- Parent AUC was comparable.

75. As a result, it can be asserted that the deuterated compound leaves more intact parent drug in the blood, which is about 72% higher parent exposure. The Appellant's claim that in the study conducted with mice, all versions of deuterated compound (Formula.I) produced less of Metabolite X compared to the original version of Formula Q.

76. Now, the question arises whether this result is sufficient to overcome the requirement of Section 3(d) of the Act. In other words, this Court now needs to determine whether the claimed invention has any "efficacy" in terms of Section 3(d) of the Act.

77. The word "efficacy" came to be defined and interpreted by the Supreme Court in ***Novartis AG*** *(supra).* The relevant part is reproduced hereunder:-

> *"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".** The question then arises, what would be the parameter of therapeutic efficacy and what are the advantages and benefits that may be taken into account for determining the enhancement of therapeutic efficacy? With regard to the genesis of section 3(d), and more particularly the circumstances in which section 3(d) was amended to make it even more constrictive than before, we have no doubt that the "therapeutic efficacy" of a medicine must be judged strictly and narrowly. **Our inference that the test of enhanced efficacy in case of chemical substances, especially medicine, should receive a narrow and strict interpretation is based not only on external factors but there are sufficient internal evidence that leads to the**

> ***same view.*** *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 to "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."***
>
> [emphasis supplied]

78. In the present case, under Example 7, the deuterated Example 2 can be considered as a "derivative" of the known Formula Q.

79. The Court notes that enhanced bioavailability does not, by itself, lead to enhanced therapeutic efficacy, and the appellant has to show, with research data, that the improved bioavailability actually translates into a therapeutic benefit.

80. Further, in ***Natco Pharma vs. Novartis AG & Anr.,*** FAO(OS) (COMM) 178/2021, decision dated 24.04.2024, the learned Division Bench of this Court has reiterated the same as follows:-

> *"74. After noting the submissions on behalf of the Objectors [as recorded in Paragraphs 161 to 163 in Novartis v. UoI1], the Supreme Court clarified that it did not propose to make pronouncement on the issues raised as the matter could be decided without adverting to those contentions. It is also apparent that the Supreme Court did not accept that a demonstration of increase in bioavailability was a demonstration of increase in enhanced efficacy. This is evident from the observations made by the Supreme Court that "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".*
>
> **** **** ****
>
> *84. We are unable to concur with the said view as the data clearly discloses that it sets out the comparison between the bioavailability data of milled ELT free acid and milled Ethanolamine Salt. Bioavailability is one of the pharmacokinetic parameters and not a direct measure of therapeutic efficacy.*
>
> **** **** ****
>
> *86. Enhanced bioavailability is not synonymous with higher therapeutic efficacy. As noted above, in Novartis v. UoI 1, the Supreme Court had – without going into the question whether increased bioavailability by itself would lead to an enhancement of therapeutic efficacy, expressly held that, if such a claim is made, the same would require to be established by research and data.*

*87. The assumption that enhanced bioavailability necessarily leads to higher therapeutic efficacy is too broad an assumption. It is desirable to have optimal pharmacokinetic parameters. In cases where a formulation has side effects, a lower bioavailability may be more beneficial."*

81. Further, it is important to note that the appellant has also submitted data through the affidavit dated 12.02.2020 along with the written submissions dated 22.03.2022, before the Patent Office. Since the respondent failed to consider the submitted data, this Court would examine the same.

82. The data submitted in the said affidavit is reproduced as follows:-

17. Moreover, the results unexpectedly showed that while all three of the deuterated compounds tested (compound of Formula I, II and III, as claimed in the instant claims) had reduced metabolism to the compound of formula X, the compound of Formulas II and III reduced metabolism to the compound of Formula X significantly more than did the compound of Formula I. The results are shown in this table:

| Compound | Relative Amide Formation |
|---|---|
| I | 0.54 |
| II | 0.38 |
| III | 0.31 |
| Q | 0.79 |

18. Another *in vivo* study was conducted in rats to compare the levels of circulating plasma drug compound between administration of the Compound of Formula Q (all H) and the administration of the Compound of Formula II. The results of the study showed that the circulating plasma concentration of the major metabolite, X, was reduced by 40-50% due to deuteration of the piperazine ring after both intravenous (IV) and oral (PO) administration. The data is shown in the table below:

| | Compound Administered | | | |
|---|---|---|---|---|
| | II (IV) 1 mg/kg | Q (IV) 1 mg/kg | II (PO) 10 mg/kg | Q (PO) 10 mg/kg |

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| | | | | |
|---|---|---|---|---|
| Plasma AUC of Metabolite X, ng-hr/ml | 3.7 | 6.7 | 67.8 | 128.2 |

19. In addition, a side-by side receptor binding study confirmed that these two compounds have substantially similar pharmacological activity:

| | $IC_{50}$, nM | | | |
|---|---|---|---|---|
| | 5-$HT_{2A}$ | SERT | D1 | D2 |
| Compound Q | 0.63 | 15 | 56 | 140 |
| Compound II | 0.61 | 20 | 67 | 130 |

20. Because the claimed Compounds of Formula IV are also subject to the same metabolism at the piperazine ring as the Compound of Formula I-III, there is a reasonable basis to expect that the deuteration in the claimed Compounds of Formula IV would similarly result in pharmacokinetic improvements.

83. The table under para 17 shows that the amide formation in compounds I, II and III is roughly 30%, 50% and 60% less as compared to amide

formation in compound Q. Similarly, the *in vivo* study given under para 18 of the declaration showed that the circulating plasma concentration of the major metabolite, X is reduced by 40-50%, concluding that the metabolite X plasma concentration was cut by roughly 40 to 50% due to deuteration of the piperazine ring by both routes.

84. The data under paras 17 and 18 result in the same outcome as data given under Example 7. Therefore, as discussed above, such data is not sufficient to establish the therapeutic efficacy.

85. The data submitted under the para 19 of the said affidavit, in the table lists four targets in the body. The numbers underneath $IC_{50}$, nM indicates the strength of the drug to grab on the given targets.

86. Based on the data under para 19, the affidavit states that the side-by-side receptor binding study confirmed that these two compounds have substantially similar pharmacological activity. In other words, it can be said that the result of the para 19 data of the affidavit indicates that the drug still behaves the same way pharmacologically. However, the statement that the pharmacological activity of compound II is similar to compound Q, is not the same as proving that it treats the disease better, or results in therapeutic efficacy. The appellant has to show how the improved bioavailability, as shown by the data cited above, leads to enhancement of therapeutic efficacy in any given case, and the same must be specifically claimed and established by research data. In this regard, it would be relevant to refer to the findings in ***Novartis*** *(supra)* in the following para:-

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

**** **** ****

*189. Thus, even if Mr. Grover's submission is not taken into consideration on the question of bioavailability, the position that emerges is that just increased bioavailability alone may not necessarily lead to an enhancement of therapeutic efficacy.* ***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****. In this case, there is absolutely nothing on this score apart from the adroit submissions 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."*

[emphasis supplied]

87. Therefore, the data submitted by way of the affidavit of the co-inventor does not overcome the requirement of Section 3(d) of the Act.

88. As this Court has considered the contents of the affidavit and rendered an opinion on merits, the judgements relied upon by the appellant to support its contentions in this regard need not be looked into.

89. As a result, the appellant has been unable to meet with the requirement of proscription under Section 3(d) of the Act. This Court is not persuaded by the submissions of the appellant on this score.

90. Further, since the objection on the ground of novelty under Section 2(1)(j) of the Act and non-patentability under Section 3(d) of the Act is upheld, this Court does not feel the requirement to address the objection on the ground of lack of inventive step.

91. *Ergo,* having regard to the aforesaid analysis and observations, the impugned order dated 27.04.2023 passed by the respondent, is upheld and the present appeal stands dismissed. No order as to costs.

**TUSHAR RAO GEDELA**
**(JUDGE)**

**JULY 06, 2026**/*rl*