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

\+ C.A.(COMM.IPD-PAT) 93/2024

CALICO LIFE SCIENCES LLC AND ANR .....Appellants

Through: Ms. Vindhya S. Mani and Ms. Ardra Goodwin, Advocates.

versus

THE JOINT CONTROLLER OF PATENTS AND DESIGNS .....Respondent

Through: Ms. Shiva Lakshmi, SPC with Ms. Pankhuri Tiwari, Advocate.

CORAM:
HON'BLE MS. JUSTICE JYOTI SINGH

O R D E R

% 13.07.2026

1. This appeal is filed on behalf of the Appellants under Section 117A of the Patents Act, 1970 ('1970 Act') laying a challenge to impugned order dated 11.07.2024, whereby Patent Application No. 202117021158 filed by the Appellant has been refused. Direction is sought to the Respondent to grant patent for currently pending claims 1-4 and in the alternative proposed set of claims 1-3 set out in the appeal.

2. To the extent necessary the facts as pleaded in the appeal are that Appellants filed a PCT application no. PCT/US2019/055850 on 11.10.2019 with 1 to 61 claims originally, claiming benefit of priority from US application no. 62/744,293 filed on 11.10.2018. Appellants filed the present application with Indian Patent No. 202117021158 on 10.05.2021 with 1-61 claims originally and the application was published in the Patents Journal on 29.10.2021. Appellants filed a request for examination before the Controller

of Patents *via* Form-18 on 07.10.2022. The First Examination Report (FER) was issued on 07.12.2022 to which reply was filed by the Appellants on 07.09.2023 along with amended claims 1-40. Hearing notice was issued on 21.02.2024 under Section 14 of 1970 Act scheduling the hearing on 11.03.2024, which was postponed and finally, the application was heard on 30.04.2024, followed by filing of written submissions by the Appellants along with amended claims 1 to 4. Respondent passed the impugned order on 11.07.2024 and rejected the application for grant of patent.

3. It is stated in the appeal that the Appellants jointly filed the present application titled *'PRODRUG MODULATORS OF THE INTEGRATED STRESS PATHWAY'* with 1 to 61 claims in original. In the FER, the Respondent raised an objection of lack of inventive step under Section 2(1)(ja) of 1970 Act citing two prior art documents WO2017193034A1 and US20140323748A1. Claims 38-61 were objected under Section 3(i) of 1970 Act as relating to method of medical treatment of humans and claims 36-37 were objected to under Section 3(e) on the ground that the claimed composition appears to have been obtained by a mere combination of one or more components, resulting only in an aggregation of the properties of the components without any synergistic effect. Objection was raised *qua* claims 1-35 under Section 3(d) and claims 1-2, 6, 46, 58 were found to be vague and unclear as not meeting the requirement of Section 10(4)(c) of 1970 Act, amongst other objections. Some objections were raised in the hearing notice also, however, in order to overcome the objections Appellants filed written submissions on 14.06.2024 along with amended claims 1-4 only.

4. Learned counsel for the Appellants submits that the impugned order suffers from multiple errors. 'Inventive step' is defined in Section 2(1)(ja) to

mean a feature of an invention that involves technical advance as compared to existing knowledge or has economic significance or both which makes the invention not obvious to a person skilled in the art and therefore, the first step required to be undertaken by the Respondent was to identify an ordinary person skilled in the art, which has not been done in the instant case, contrary to the judgement of this Court in ***F. Hoffmann-La Roche Ltd. & Anr. v. Cipla Ltd., 2015 SCC OnLine Del 13619,*** where the Division Bench laid down a five-step test to determine obviousness/lack of inventive step as follows:-

> *"Step No. 1 To identify an ordinary person skilled in the art,*
>
> *Step No. 2 To identify the inventive concept embodied in the patent,*
>
> *Step No. 3 To impute to a normal skilled but unimaginative ordinary person skilled in the art what was common general knowledge in the art at the priority date.*
>
> *Step No. 4 To identify the differences, if any, between the matter cited and the alleged invention and ascertain whether the differences are ordinary application of law or involve various different steps requiring multiple, theoretical and practical applications,*
>
> *Step No. 5 To decide whether those differences, viewed in the knowledge of alleged invention, constituted steps which would have been obvious to the ordinary person skilled in the art and rule out a hideside approach."*

5. Additionally, the order does not reflect how the Respondent came to the erroneous conclusion that the cited prior arts would teach and motivate a person skilled in the art to arrive at the claimed invention, without any research and development and/or experimentation. Pertinently, this Court in ***Agriboard International LLC v. Deputy Controller of Patents and Designs, 2022 SCC OnLine Del 940,*** has held that while determining whether the claimed invention lacks inventive step, discussion on prior art(s), subject invention and the manner in which the invention will be obvious to a person skilled in the art, is mandatory. This exercise is lacking in the instant case

and in fact, Respondent has carried out a hindsight reconstruction by using the instant application as a guide through the maze of prior art references, which has been held to be illegal by this Court in ***Bristol-Myers Squibb Holdings Ireland Unlimited Company and Others v. BDR Pharmaceuticals International Pvt. Ltd. and Another, 2020 SCC OnLine Del 1700.***

6. It is argued that the Respondent failed to appreciate that prior art D1 relied upon in the impugned order was cited in the International Search Report (ISR) of International Application PCT/US2019/055850. It is well known that ISR is used as a benchmark while establishing the novelty and inventive step of the National Phase Application throughout the various jurisdictions of the world. Despite D1 being cited in the ISR and patents with similar claims having been granted to the Appellants in several other jurisdictions such as Brazil, Chile, Taiwan and USA, the present application has been refused for grant of patent. Grant of corresponding applications in other jurisdictions may not be binding on the Respondent, however, it is persuasive as the grant indicates inventive merit, patentability, commercial interest and industrial applicability of the claimed invention.

7. Without prejudice, it is argued that the disclosures in the prior arts do not in any manner teach, suggest or motivate a person skilled in the art to arrive at the invention. The instant application posits both technical and/or economic significance over the cited prior arts. Respondent acknowledged that the claimed compounds are different from those of D1 in terms of substituent R^1 and moreover, currently pending claims 1-4 for specific compounds are not disclosed in D1. The technical problem that the claimed inventions seeks to solve is to identify and improve ISR modulators for

therapeutic uses in patients and through extensive research, inventors have identified a particular compound of D1 i.e., compound 297 of D1 and compound of Formula (II) as the scaffold and modified the said compound at the position corresponding to R1 of Formula (I) (PAGE 57 OF PDF) to achieve prodrugs with enhanced solubility and PK profiles as therapeutic agents suitable for being administered to patients. A person of ordinary skill in the art will appreciate that the exact properties such as solubility and PK of the claimed compounds are based and dependent on overall constituents selected but D1 does not teach or suggest how to select or which compound disclosed therein could be modified to be in the prodrug form for therapeutic use and D1 also does not teach or suggest how to modify i.e., at what position any compound will result in prodrugs with improved solubility and PK. Even assuming that person skilled in the art was to select compound 297 of D1 for modification, it will have no guidance how to modify for improved solubility and PK.

8. It is urged that the claimed compounds have unexpected technical effects and superior properties compared to the parent compound. Illustratively, Example 43 describes a solubility assay and demonstrates that compounds of instant application may have greater solubility than parent compound and Example 44 describes a pharmacokinetic assay and shows that the claimed compounds have greater C_{max} and AUC values than the parent compound (P), where C_{max} is the maximum plasma concentration of the drug and AUC is the measurement of extent of drug bioavailability.

9. It is argued that prior art D2 is cited for disclosing prodrug of ursodeoxycholic acid for intravenous administration and does not contain any disclosure related to integrated stress pathway modulators or their

modifications e.g. to improve PK properties and thus, a person skilled in the art while reading D2 will not be able to use the prior art to extend the teachings of D1. Hence, the claimed invention does not lack inventive step and the impugned order is perverse and arbitrary.

10. It is further argued that the rejection of the application on ground of non-patentability under Section 3(d) is also erroneous. As per the said provision, the mere discovery of a new form of a known substance which does not result in enhancement of known efficacy of that substance is not an invention. Neither in the FER nor the hearing notice, there is any information regarding the 'known substance' or 'known efficacy' of the 'known substance' and in the absence of this information, it was not open to the Respondent to assert that the claimed compounds were new forms of such 'known substance'. In fact, Appellants have been deprived of an opportunity to even correctly respond to this objection and importantly, in the hearing notices, Respondent had himself noted that '*Compounds as claimed in the instant application differ from compound of document D1 with respect to R1 only*'. The 'known substance' was identified for the first time in the impugned order as the compound of Formula (II) and this vitiates the impugned order.

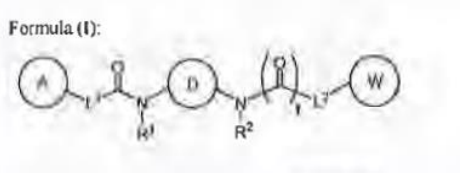
11. Learned counsel also argued that Respondent's interpretation of the judgment in ***Novartis AG v. Union of India and Others, (2013) 6 SCC 1,*** is completely flawed and basis this erroneous interpretation, Respondent concluded that notwithstanding the fact, that no comparative data is submitted, the bioavailability also cannot be considered as a factor towards establishing any superior therapeutic efficacy. Reading of the judgment shows that the Supreme Court has held that increase in bioavailability may

lead to enhancement of therapeutic efficacy, if established by research data. Reliance is placed on articles on the subject by Gary Price and Deven A. Patel as also by Michele Philip in this regard to highlight that bioavailability refers to the extent and the rate at which the API in a formulation reaches the intended site of action in the body. One of the factors impacting the bioavailability is the mode of administration and the measurement is done on different benchmarks, the most effective being to determine the blood plasma concentration of the API over time i.e., AUC and the other being the C_{max}, which a drug achieves in a specified area of the body.

12. Respondent, it is urged, has observed that bioavailability cannot be considered as a factor towards establishing superior therapeutic efficacy, which is an erroneous observation inasmuch as bioavailability is a pharmacokinetic property and not a pharmacodynamic property and thus it is not possible theoretically to establish that increased bioavailability enhances intrinsic pharmacological activity and as a corollary, a monopoly claimed for increased therapeutic efficacy owing to increased bioavailability will be untenable. Had the Respondent communicated the objection at the right time and in a precise manner instead of a passing reference in the impugned order, Appellants would have succeeded in overcoming the said objection. Appellant has been deprived of contesting the objection at the appropriate stage and this violates principles of natural justice.

13. Ms. Shiva Lakshmi, learned SPC appearing for the Respondent defends the impugned order and submits that the instant application has been rightly refused. Objections were raised under Sections 2(1)(ja), 3(d) and 3(e) of 1970 Act in the FER and after granting opportunity of hearing and deliberating on the response, the application was refused. Appellants filed

amended set of claims 1 to 4 along with the written submissions and also deleted the term 'Heteroaryl'. Respondent found that the application featured compounds, compositions and methods comprising a compound of Formula (I) or a pharmaceutically acceptable salt, co-crystal, solvate, hydrate, tautomer, ester, N-oxide or stereoisomer thereof for use e.g. in the modulation of elF2β and the attenuation of the ISR signalling pathways. In some embodiments, compound of Formula (I) is a prodrug of a biologically active compound that modulates elF2β, elF2α or component of the elF2 or ISR pathways. In some embodiments, a compound of Formula (I) is a prodrug of the compound of Formula (II). The term 'prodrug' may be used to describe compounds of the present invention that readily undergo chemical changes under physiological conditions to provide a biologically active compound that modulates elF2β, elF2α or a component of eIF2 or ISR pathways. Additionally, the prodrug compounds of the present invention can be converted to a biologically active compound that modulates elF2β, elF2α or a component of the eIF2 or ISR pathways by chemical or biochemical methods in an ex-vivo environment. For example, the prodrug compounds of the present invention may be slowly converted to a biologically active compound that modulates elF2β, elF2α, or a component of eIF2 or ISR pathways when placed in a transdermal patch reservoir with a suitable enzyme or chemical agent. DI relates to a compound of



or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof and the compounds, compositions and methods are useful for modulating the ISR and for treating

related diseases; disorders and conditions. Compounds of the instant application, therefore differ from D1 with respect to R^1 only and do not exhibit any advance technical effect and hence, the claimed invention lacks inventive step and proposed amended claims 1-39 were rightly not allowed under Section 2(1)(ja).

14. It was further argued that Respondent has rightly refused the application on ground of non-patentability under Section 3(d). Respondent has correctly analysed the invention vis-à-vis the provision in light of the judgment of the Supreme Court in ***Novartis (supra).*** Appellant relied on Example 43 to urge that compounds of the instant application may have a greater solubility than the parent compound and also relied on Example 44 describing a pharmacokinetic assay to assert that the claimed compound describes the feature and has greater C_{max} and AUC value as compared to the parent compound (P). However, these assertions are misconceived since a prodrug will obviously have a difference with the main pharmaceutical drug as the prodrug converts itself *in vivo* into actual pharmaceutical drug being metabolized either chemically or enzymatically in a regulated manner. Moreover, increase in solubility does not guarantee higher therapeutic efficacy and cannot be considered as a factor of therapeutic efficacy. Again, AUC is dependent on bioavailability and clearance of the drug from the body and higher the bioavailability, the higher will be the AUC and vice versa. In the instant application, there is no data to exhibit the results of the efficacy in case the corresponding active pharmaceutical substance of the prodrug is available in the body and Appellants have only provided the C_{max} and AUC value for the prodrugs itself which at best indicate the bioavailability. There is no data to substantiate the fact that the prodrug as

contemplated in the instant application will lead to the active compound in such a way that the results in a patient will be better as compared to a case where the actual drug molecule is directly used as a dosage and acts itself without conversion *in vivo.* Even otherwise, the bioavailability is not a factor to establish any superior therapeutic efficacy and hence, the grant of patent is proscribed by provisions of Section 3(d).

15. Heard learned counsels for the parties and examined their rival submissions.

16. Instant application relates to claimed invention titled *'PRODRUG MODULATORS OF THE INTEGRATED STRESS PATHWAY'* and was filed on 10.05.2021. Originally claims 1-61 were filed and objections were raised in the FER under Sections 2(1)(ja), 3(d), 3(e), 3(i) and 10(4)(c) of 1970 Act. Response to the FER was filed on 07.09.2023 with amended set of claims 1-40. After the hearing notices and scheduled hearing, Appellants filed written submissions on 14.06.2024 with amended claims 1-4. Instant application was rejected by the impugned order dated 11.07.2024 on ground of lack of inventive step under Section 2(1)(ja) and non-patentability under Section 3(d).

17. First and foremost argument of the Appellants is that Respondent has failed to consider the written submissions dated 14.06.2024 in entirety and this vitiates the order. Appellants brought out in detail how prior arts do not teach or motivate a person skilled in the art to reach the claimed invention and thus the claimed invention does not lack inventive step. Similarly, in the context of the objection under Section 3(d), it was brought out that the Respondent has not provided any information of the 'known substance' or the 'known efficacy' of the 'known substance', which is the fundamental

requirement under Section 3(d). Court finds that none of these submissions, even find a mention in the impugned order, leave alone discussing them. This Court in ***Qualcomm Incorporated v. Controller of Patents and Others, 2023 SCC OnLine Del 4308*** and ***Boehringer Ingelheim Vetmedica GMBH v. Controller of Patents, 2024 SCC OnLine Del 8578,*** has held that orders which do not deal with the submissions advanced by parties and are *ex facie* unreasoned, cannot be sustained in law and that it is incumbent on the concerned authority to deal with the submissions raised by the party, to the extent they are relevant and material. This to my mind is also a facet of principles of natural justice and as rightly flagged by the Appellants an order which is bereft of consideration of the submissions of the Appellants cannot be sustained in law.

18. There is another glaring illegality in the impugned order. The Division Bench of this Court in ***F. Hoffmann (supra),*** has elucidated a five-step test for determining lack of inventive step in a claimed invention and the first step requires the Controller of Patents to identify the person skilled in the art. The impugned order shows that neither of five-steps have been followed by the Respondent and the objection has been dealt with by merely referring to an observation in the judgment that a person skilled in the art is presumed to know not only the state-of-the-art at that time but also to posses understanding better than a person of average knowledge thereof and further, the person should have knowledge that was publicly available along with common sense. Respondent is required to follow the test as laid down and cannot absolve itself of this duty by merely citing paragraphs from the judgement. In the absence of this exercise the conclusion of lack of inventive step cannot be sustained. This Court has consistently held that

while rejecting an invention for lack of inventive step, Controller has to consider three elements: (a) invention disclosed in the prior art; (b) invention disclosed in the patent application; and (c) the manner in which subject invention would be obvious to the person skilled in the art. This means that the Controller has to analyse the existing knowledge and how the person skilled in the art would move from the existing knowledge to the subject invention ***[Ref.: Agriboard International (supra)],*** which has not been done in the present case.

19. As for the objection of non-patentability under Section 3(d), a bare reading of the provision shows that a mere discovery of a new form of a 'known substance' which does not result in the enhancement of 'known efficacy' of that substance or the mere discovery of any new property is not an invention. Therefore, Appellants rightly submit that the most fundamental requirement while raising an objection under Section 3(d) is to provide information to the inventor regarding the 'known substance' or the 'known efficacy' of the said 'known substance'. It is brought forth on behalf of the Appellants that no such information was forthcoming either in the FER dated 07.12.2023 or the hearing notice dated 21.02.2024 or even the extended hearing notices dated 15.03.2024 and 05.04.2024. It was for the first time that the Respondent identified the 'known substance' in the impugned order and observed '*the said compound of Formula II is already disclosed in the cited document D1 as compound no-297 and 298*'. Therefore, as rightly placed by the Appellants, they did not get the opportunity to respond to the objection and contest the same and this is a clear violation of principles of natural justice as held by this Court in ***Otsuka Pharmaceutical Co. Ltd. v. Controller of Patents, 2022 SCC OnLine Del***

4982 and ***Perkinelmer Health Sciences Inc and Others v. Controller of Patents, 2023 SCC OnLine Del 8590.***

20. Reading of the impugned order with respect to the objections under Section 3(d) also reflects that without disclosing the 'known substance' or 'known efficacy' prior to passing of the order, Respondent has refused the application on the ground that the Supreme Court in ***Novartis (supra)*** affirmed that better efficacy in pharmaceutical substance is enhanced therapeutic efficacy as also that solubility is not a factor of therapeutic efficacy. Respondent has also observed that there is no data to exhibit the results of efficacy in case the corresponding active pharmaceutical substance of the prodrug being available inside the body and the C_{max} and AUC values are provided for the prodrug itself, which at the most indicate bioavailability but do not substantiate that the prodrug provides better results to a patient as contemplated in the instant application in comparison to where the actual drug molecule is directly used as a dosage and itself acts as a drug without any conversion *in vivo*. Appellants have seriously contested the interpretation given by the Respondent to the judgment of the Supreme Court as also the enhanced therapeutic efficacy of the claimed invention referring to articles on the subject and the specifications of claims 1-4. Considering that the Respondent has erred in not dealing with the objection under Section 3(d) in the manner it ought to have been by first providing information of 'known substance' prior to passing of the impugned order, Appellants have been deprived of the opportunity to defend the objection. As the impugned order suffers from fundamental errors of following the required tests for determining lack of inventive step under Section 2(1)(ja) as also under Section 3(d) and there are violations of principles of natural

justice, I am of the view that this is a fit case for remand without entering into the merits at this stage.

21. Accordingly, this appeal is partially allowed and the impugned order dated 11.07.2024 is set aside. Respondent is directed to consider Indian Patent Application No. 202117021158 titled *'PRODRUG MODULATORS OF THE INTEGRATED STRESS PATHWAY'* afresh in accordance with law and without being influenced by the earlier order. Needless to state, while reconsidering the application, the Respondent shall grant full opportunity to the Appellants to address on the objections raised under Sections 2(1)(ja) and 3(d) of 1970 Act. All documents on record including response to FER as also written submissions and the judgments relied upon shall be taken into consideration before taking a final decision. The entire exercise will be completed within a maximum period of four months from today. It is made clear that this Court has not expressed any opinion on the merits of the case.

22. Appeal stands disposed of in the aforesaid terms.

JYOTI SINGH, J

JULY 13, 2026
S.Sharma