2023:MHC:5451

WEB COPY

IN THE HIGH COURT OF JUDICATURE AT MADRAS

Judgment reserved on	05.09.2023
Judgment pronounced on	20.12.2023

CORAM:

THE HON'BLE MR. **JUSTICE SENTHILKUMAR RAMAMOORTHY**

(T) CMA (PT) No.150 of 2023

(OA/61/2020/PT/CHN)

Mr.Tony Mon George
Constituted Attorney of ABBVIE Inc.,
1, North Waukegan Road, North Chicago,
Illinois, USA 60064 ... Appellant

Vs.

Deputy Controller of Patents & Designs,
Patent Office Intellectual Property Building,
G.S.T.Road, Guindy,
Chennai 600032 ... Respondent

PRAYER : This Civil Miscellaneous Appeal filed under Section 117A of the Patents Act, 1970, prays to pass an order setting aside the impugned order of the Respondent dated 18th September 2020

https://www.mhc.tn.gov.in/judis

WEB COPY

and pass an order granting a patent on Indian Patent Application No.7096/CHENP/2015.

For Appellant : Ms.Archana Shanker
Mr.Sachin Malik
Mr.N.C.Vishal
Mr.N. Shrivastav
for M/s. Anand and Anand

For Respondent : Mr.K.Subbu Ranga Bharathi,
Central Govt. Standing Counsel &
Mr.K.S.Hariram,
Deputy Controller of Patents

JUDGMENT

BACKGROUND

The appellant challenges the order dated 18 September 2020 of the respondent refusing to grant a patent in respect of Indian Patent Application No.7096/CHENP/2015.

2. The inventor/assignor, Reata Pharmaceuticals Inc., filed Indian Patent Application No.8486/DELNP/2014 for grant of patent in respect of a compound called RTA-408. A patent was granted pursuant thereto by the Indian Patent Office(IN 345058). Thereafter, a PCT application was filed for the claimed invention

https://www.mhc.tn.gov.in/judis

WEB COPY

titled "2,2–Difluoropropionamide Derivatives of Bardoxolone Methyl, Polymorphic Forms and Methods of Use Thereof", which pertains to two polymorphic forms of RTA-408. In the said application, priority was claimed from US application number 61/815,502, i.e. from 24 April 2013. After filing the Indian national phase application derived from the PCT application in the year 2015, the appellant made the request for examination on 11 April 2017. The First Examination Report (FER) was issued on 13 February 2019. After obtaining an extension, the appellant responded to the FER on 11 November 2019. After a hearing on 29 July 2020, the appellant submitted written submissions on 11 August 2020. Eventually, by impugned order dated 18 September 2020, the application for grant of patent was refused. The present appeal arises in the above facts and circumstances.

COUNSEL AND THEIR CONTENTIONS

3. Oral arguments on behalf of the appellant were addressed by Ms.Archana Shanker, learned counsel from M/s.Anand and Anand; and on behalf of the respondent by

https://www.mhc.tn.gov.in/judis

WEB COPY

Mr.Subbu Ranga Bharathi, learned Central Government Standing Counsel, and Mr.K.S.Hariram, Deputy Controller of Patents.

4. Learned counsel for the appellant submitted that the claimed invention is in respect of two polymorphic forms, Forms A and B, of a compound called RTA-408. By pointing out that certain compounds exhibit polymorphic forms, learned counsel submitted that polymorphic forms are crystalline forms as opposed to amorphous forms. She further submitted that the appellant produced two polymorphic forms which exhibit technical advancement over the existing knowledge in as much as they exhibit greater stability and are solvent-free, and that this is in addition to exhibiting superior anti-inflammatory, anti-oxidative and anti-proliferative properties.

5. Her next submission was that a patent was granted by the Indian Patent Office in respect of RTA-408. The publication date in respect of the RTA-408 patent was 31 October 2013, whereas the priority date of the claimed invention is 24 April 2013.

https://www.mhc.tn.gov.in/judis

WEB COPY

After pointing out Section 3 (d) of the Patents Act, 1970 (the Patents Act) does not apply unless the claimed invention relates to a new form of a known substance, learned counsel submitted that RTA-408 does not qualify as a known substance and that the patent relating thereto does not qualify as prior art. As regards the reference in the impugned order to TX-63682 as being a known substance, learned counsel submitted that the claimed invention is not in respect of polymorphic forms of TX-63682. Therefore, even with reference to TX-63682, she submitted that Section 3(d) of the Patents Act is not applicable.

6. According to learned counsel, the respondent committed the error of comparing RTA-408, instead of its polymorphic forms, with the compounds 402-38 and TX-63682. While pointing out that a patent was granted for the claimed invention in multiple overseas jurisdictions such as the USA, Japan, Europe and China, learned counsel submitted that prior arts D2 and D3, which were cited herein by the respondent, were considered in the International Search Report (ISR) in respect of

https://www.mhc.tn.gov.in/judis

WEB COPY

the PCT application and that both prior arts were classified as 'A', which pertains to a document defining the general state of the art which is not considered of particular relevance. She also relied on the written opinion of the International Searching Authority (ISA) in respect of RTA-408 to the effect that the claimed invention satisfies the requirements of novelty, inventive step and industrial application capability.

7. Learned counsel next referred to the impugned order at internal page 7, and submitted that the Deputy Controller differed from the written opinion of the ISA, without assigning cogent reasons, although the ISA considered all the cited prior arts. With reference to D3, if the intention were to identify a compound with low half-maximal inhibitory concentration (IC_{50}) value with regard to inhibition of interferon-gamma ($IFN_{y)}$ induced nitric oxide (NO) production, learned counsel submitted that the person skilled in the art would have selected compounds such as TX-63522, TX-63558, TX-63811, TX- 63914, TX-63925, TX-63928 and TX-63929, which exhibit lower IC_{50} values, and not TX-

https://www.mhc.tn.gov.in/judis

WEB COPY

63682. By relying on the judgment of the Delhi High Court in *F.Hoffmann La Roche Ltd. & another v. Cipla Ltd., 2015 SCC Online Del 13619,* for the test of obviousness, learned counsel submitted that the Deputy Controller did not adhere to the principles laid down therein. Learned counsel, therefore, contended that the rejection under Section 2(1)(ja) was unjustified and effectively unreasoned.

8. On behalf of the respondent, it was submitted that prior art D2 discloses the compound 402-38 and that the only difference between the said compound and the claimed invention is the addition of fluorine atoms. As regards the contention on behalf of the appellant that the polymorphic forms are more stable and solvent-free, the respondent submitted that enhanced stability and the solvent-free nature of crystalline forms of the compound are inherent characteristics, which are not attributable to the appellant, and cannot be termed as a technical advancement.

https://www.mhc.tn.gov.in/judis

WEB COPY

9. The next contention on behalf of the respondent was that TX-63682 is a known substance and, therefore, section 3 (d) is clearly applicable. As between the known substance, TX63682, and the claimed invention, the respondent submitted that the only difference was that there was di-methyl substitution in the claimed invention. Once Section 3(d) applies, unless the patent applicant is able to demonstrate a significant improvement in efficacy, it was submitted that such applicant is not eligible for a patent. In this case, the respondent submitted that the appellant failed to demonstrate that the claimed invention demonstrates significant improvement in efficacy or even technical advancement over the known substance.

10. Even *de hors* Section 3(d), by pointing out that the claimed invention is required to exhibit technical advancement or economic significance or both and that such technical advancement or economic significance should not be obvious to a person skilled in the art, it was submitted on behalf of the respondent that the IC_{50} value of the claimed invention is higher

https://www.mhc.tn.gov.in/judis

WEB COPY

than that of TX-63682, thereby indicating lower effectiveness in inhibiting inflammation.

11. The respondent further submitted that a composition claim is not patent-eligible unless the applicant for patent demonstrates that there is synergy between the ingredients forming the composition and that, as a result, the composition is more than the sum of its parts. Since the composition claim (claim 7) does not satisfy this requirement, it was submitted that it is not patent-eligible as per Section 3(e) of the Patents Act.

12. By way of rejoinder, learned counsel for the appellant submitted that the person skilled in the art would be a solid state chemistry expert and not a medicinal chemist. She further stated that prior art D2 was considered while granting the patent to RTA-408. Because RTA-408 was not a known substance as on 24 April 2013, she reiterated that Section 3 (d) is not applicable. By referring to the order dated 22 August 2019 (at page 274 of the typed set dated 3 August 2023) of the IPAB in *Eisai R & D Management Co.*

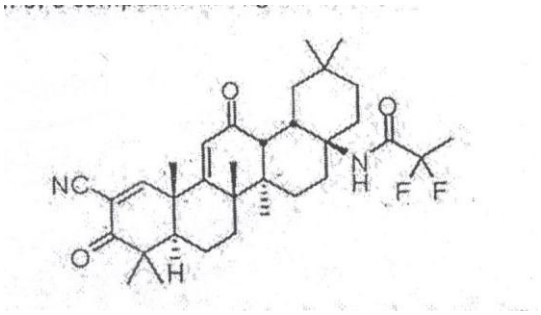
https://www.mhc.tn.gov.in/judis

WEB COPY

Ltd., she submitted that the IPAB concluded that anything published after the priority date cannot be considered as prior art.

DISCUSSION, ANALYSIS AND CONCLUSION:

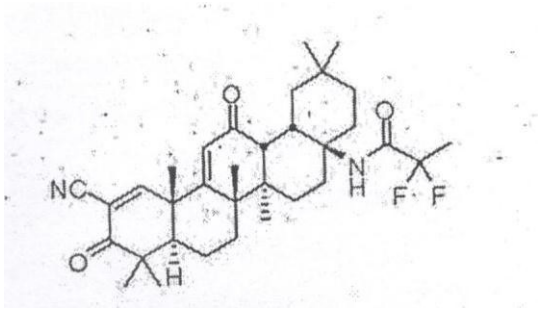
13. At the outset, I set out below the current claims of the appellant:

> *" 1. A polymorphic form of a compound having the formula:*
>
> 
>
>
> *wherein the polymorphic form is crystalline, having an X-ray powder diffraction pattern (CuKa) comprising peaks at about 10.601, 11.638, 12.121, 13.021, 15.418, 15.760, 17.830, 18.753, and 19.671 o 20.*
>
> *2.The polymorphic form as claimed in claim 1, wherein the X-ray powder diffraction pattern (CuKa) is substantially as shown in FIG.53*

WEB COPY

3. The polymorphic form as claimed in claim 1, wherein the melting point is about 181.98°C.

4. A polymorphic form of a compound having the formula:



wherein the polymorphic form is crystalline, having an X-ray powder diffraction pattern (CuKa) comprising peaks at about 7.552, 10.339, 11.159, 12.107, 14.729, 15.329, 15.857, 16.824, 17.994, and 18.344, 19.444, 19.764, 20.801, and 22.414 o 20.

5. The polymorphic form as claimed in claim 4, wherein the X-ray powder diffraction pattern (CuKa) is substantially as shown in FIG.56

6. The polymorphic form as claimed in claim 4, wherein the melting point is about 250.10°C.

7. A pharmaceutical composition comprising: 0.01% to 75% by weight of an active ingredient comprising a polymorphic form of a compound as claimed in any one of claims 1-6, and a pharmaceutically acceptable carrier."

WEB COPY

REJECTION UNDER SECTION 3(d):

14. The first question that falls for consideration is whether Section 3(d) of the Patents Act is applicable. Section 3(d) is set out below:

> *"**3. What are not inventions.** - The following are not inventions within the meaning of this Act,-*
>
> *....*
>
> *(d) **the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance** or the mere discovery of any new property or new use for a known substance or of the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant.*
>
> *Explanation : **For the purposes of this clause, salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance shall be considered to be the same substance, unless***

WEB COPY

they differ significantly in properties with regard to efficacy*; "(emphasis added).*

As is evident from the opening "the following are not inventions" expression, which applies to all clauses [(a) to (p)] of Section 3, the provision incorporates a legal fiction by which claims for patent that fall within the clauses of Section 3 will not qualify as inventions, even if such claims meet the requirements of Section 2(1)(j) of the Patents Act, unless they pass through the exemption filters that are built into some of the clauses therein.

15. The principal clause of Section 3(d) contains about three limbs, which are separated by the disjunctive "or". The three limbs are as under:

(i) 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.

(ii) The mere discovery of any new property or new use for a known substance.

(iii) O*f the mere use of a known process, machine or apparatus unless such known process*

WEB COPY

results in a new product or employs at least one new reactant.

The break-up of Section 3(d) also reveals that both the first and second limbs deal with and govern claims relating to known substances. While the first limb deals with and governs claims relating to new forms of a known substance, the second deals with and governs new properties or new uses thereof. The third limb is clearly inapplicable to this case and the inference that flows from the impugned order is that the respondent relied only on the first and not the second limb.

16. The first limb of the above provision becomes applicable if the claimed invention is a new form of a known substance. In this case, the appellant contended that the claimed invention relates to polymorphic forms of a parent compound known as RTA-408. This parent compound, however, was made known to the public after the priority date of the claimed invention. In this factual context, RTA-408 does not qualify as a known substance for purposes of Section 3 (d). The next question

https://www.mhc.tn.gov.in/judis

WEB COPY

to be considered is whether the polymorphic forms qualify as new forms of either 402-38 or TX 63682, and 402-38 is compared first.

17. When a substance takes two or more crystalline forms with identical chemical composition as the said substance, the crystalline forms are referred to as polymorphic forms. As between the compound 402-38 and the claimed invention, the admitted position is that the claimed invention contains additional fluorine atoms. Therefore, the chemical composition is different and the claimed invention cannot be construed as polymorphic forms of 402-38. Turning to TX-63682, the agreed position is that the structure of the claimed invention contains di-methyl substitution and that the structure differs from TX-63682 in that regard. Therefore, in spite of the structural similarities between the claimed invention and TX-63682, the claimed invention cannot be considered as polymorphic forms of TX 63682 either. Although the Explanation to Section 3(d) also refers to other derivative forms of a known substance such as salts, esters, ethers, metabolites and the like, the respondent cannot and did not place the polymorphic

https://www.mhc.tn.gov.in/judis

WEB COPY

forms of RTA 408 within any such derivative form of 402-38 or TX-63682. Once it is concluded that the claimed invention is not a new form of a known substance, it is not necessary for the appellant to cross the hurdle of Section 3. Nevertheless, the appellant is required to satisfy the requirements of an invention under the Patents Act. For this purpose, apart from novelty and industrial application capability, it is necessary that the claimed invention should exhibit technical advancement and such technical advancement should not be obvious to a person skilled in the art. Whether such technical advancement was demonstrated is examined next.

TECHNICAL ADVANCEMENT AND OBVIOUSNESS

18. Section 2(1)(ja) of the Patents Act defines "inventive step" as under:

> *"inventive step means a feature of an invention that involves technical advance as compared to the existing knowledge or having economic significance or both and that makes the invention not obvious to a person skilled in the art"*

WEB COPY

The technical advancements claimed by the appellant for the polymorphic forms of RTA 408 are *inter alia* : enhanced anti-inflammation activity by suppression of IFN-y induced NO production, as measured by IC_{50} values; enhanced anti-oxidation as measured by the activation of the antioxidant response element (ARE) by testing in two different reporter assays; increased expression of nuclear factor (erythroid-derived)-like 2(nrf2) target genes; increased glutathione levels, as measured by EC_{50} values; greater stability; and solvent-free nature without toxic chemicals. The detailed recitals in this regard are in the complete specification at internal pages 66-78 under the heading "Pharmacodynamics" and reference may be made thereto. As a result, potential use cases in the treatment of multiple diseases are indicated. RTA 408, which possesses all the above attributes except the last two, was assessed for technical advancement and inventive step earlier; the parent compound passed the test and was, therefore, granted a patent. It is instructive to refer to the written opinion of the ISA in this regard, including the discussion therein on D3. RTA 408 is known in the market today as Omaveloxone and judicial notice

https://www.mhc.tn.gov.in/judis

WEB COPY

may be taken of the fact that it was approved by the US FDA for the treatment of Friedriech's Ataxia, which is a genetic, progressive, neuro-degenerative movement disorder.

19. The current claims are made for the two polymorphic forms of RTA-408. Each polymorphic form is identified by the distinct X-ray powder diffraction pattern comprising distinct peaks and melting points. In addition to the technical advancements that are common to the claimed invention and RTA-408, the additional properties claimed for the polymorphic forms are enhanced stability and solvent-free nature thereby reducing toxicity.

20. The respondent countered these contentions by asserting that the IC_{50} value of TX-63682 is lower and, therefore, TX-63682 has greater potency as regards suppression of IFN-y induced NO production. As regards stability and being solvent-free, the respondent contended that the said properties are inherent characteristics of the crystalline forms of any compound.

https://www.mhc.tn.gov.in/judis

WEB COPY

Paragraph 15 of the impugned order, which is of particular relevance, is set out below:

> *"15. The pharmacological/biological activity plays a crucial role since it suggests uses of the compound in a particular medicinal activity. The present and D1, D2 compounds has anti inflammatory activity. It is pertinent to note that the anti- inflammatory activity of TX 63682 (suppression of NO release by RAW 264.7 shows an excellent assay results than the presently claimed polymorphic form compound. The table in page no 46 of D3 discloses the NO IC_{50} of TX63682 is 1.1, relative NO IC_{50} 0.65 are clearly indicates the higher activity of TX63682 than the RTA 408. This coherent thread leading from the prior art by adding a methyl group to arrive at the present claimed compound is obvious to a person skilled in the art. It will be more appropriate, when a more active prior art compound is known and then the comparison of the present compound shall be made with that compound. It is routine to a person skilled in the art to conduct various additional activity assays in pharmacokinetics and pharmadynamics test of similar prior art compounds and its crystals/polymorphs. In fact both the prior art citations are done using the*

WEB COPY

same routine experiments. These routine experiments are employing a common general knowledge of a skilled person in the art and make conventional trial and error experimentations. Moreover, each crystalline form has its own X-ray diffraction pattern. This X-ray diffraction pattern is inherent property of each crystalline compound without an intervention of the applicant. In this regard I differ with the ISA written opinion and the applicant argument that these additional activity in other assays do not considered as technical advance as compared to the existing more anti-inflammatory activity compound Tx63682. It is obvious to a person skilled in the art by reading D2 page 100, VII. Examples and particularly D3 page 38 and 46, crystalline non solvate form cannot be considered as new entity involving inventive since non solvate are do not contain toxic solvents as well as crystalline forms are typically more stable than amorphous form. In view of the above discussion I agree with the examiner's opinion, it is evident that different polymorphic form can be obtained without any inventive merit, by routine techniques. In absence of any superior/ surprising effect compared to the known form of an existing drug, making of a new polymorph of a drug should be considered as obvious

https://www.mhc.tn.gov.in/judis

WEB COPY

to the person skilled in the art in view of documents D2 and particularly D3. Since the polymorphic form compound itself not inventive, the composition using the polymorphic form do not have any significance without any inventive features. Hence the present application amended claims 1-7 are not inventive under section 2(1)(j)(a) of Patent Act 1970."

21. The following conclusions are discernible from paragraph 15 of the impugned order:

(i) D1, D2 and the compound of the claimed invention have anti-inflammatory activity.

(ii) The anti-inflammatory activity of TX 63682, as measured by the IC_{50} value specified at page 46 of D3, is greater than that of the claimed invention.

(iii) It would be obvious to a person skilled in the art to add a methyl group to TX 63682, which would lead to the claimed invention.

(iv) The x-ray diffraction pattern is an inherent property of each crystalline compound, and the crystalline non-solvate form cannot be treated as a new entity.

https://www.mhc.tn.gov.in/judis

WEB COPY

(v) The additional activity in other assays cannot be regarded as an advancement.
(vi) The polymorphic forms of a compound can be discovered without inventive merit.
(vii) Since the polymorphic forms are not inventive, the composition containing the same is not inventive.

Each of the above conclusions should be examined. Conclusion (i) above is unexceptionable because it is a matter of fact and record that the compounds forming the subject of D1, D2 and the claimed invention are *inter alia* anti-inflammatory. However, it bears repetition that D1 does not qualify as prior art and, therefore, cannot form the basis of either novelty or obviousness analysis.

22. As regards conclusions (ii), (iii) and (v), the first aspect to be noticed is that D3 is an invention relating to more than 100 compounds and that TX-63682 is one of the compounds forming the subject of D3. The IC_{50} values of these compounds vary considerably and, as pointed out by the appellant, many compounds of prior art D3, such as TX-63522, TX-63558, TX-63811,

https://www.mhc.tn.gov.in/judis

WEB COPY

TX- 63914, TX-63925, TX-63928 and TX-63929, have a lower IC_{50} value than TX-63682. The second aspect to be noticed, in this regard, is that the complete specification of D3 contains comparisons between the IC_{50} values of the compounds forming the subject of D3 invention and RTA 402 in the section bearing the heading "III. Biological Activity" at internal pages 38-75 thereof. From an obviousness analysis perspective, the impugned order contains no reasons as to why a person skilled in the art would pick out the compound TX-63682 from the 100+ compounds in D3 and arrive at RTA-408 by adding a methyl substituent in position 4a especially when there are many other compounds in D3 with a lower IC_{50} value. Without the benefit of hindsight and the resultant recognition of TX-63682 as a structural analogue, it does not appear possible.

23. Apart from the above, as discussed earlier and in the written opinion of the ISA with regard to the RTA-408 compound, enhanced anti-inflammation, as measured by IC_{50} values, is only one of the claimed technical advancements for the claimed

https://www.mhc.tn.gov.in/judis

WEB COPY

compound, and the impugned order does not discuss the other claimed technical advancements such as ARE activation, increased expression of nrf2 target genes, etc. While conclusion (v) brushes aside the other claimed advancements, the said conclusion is not supported by reasons.

24. Turning to conclusions (iv) and (vi), these conclusions are untenable because RTA 408 is not a known substance and, therefore, the polymorphic forms thereof cannot be treated as obvious. Besides, the x-ray powder diffraction pattern is a means to identify the polymorph and not a technical advancement. In paragraph 18 above, the asserted advancements over the existing knowledge is set out. Since Forms A and B are not polymorphic forms of a known substance for reasons discussed earlier, Section 3(d) does not apply and enhanced efficacy over the known substance need not be shown. I am conscious that it is prudent to tread with circumspection while considering a subsequent and separate patent claim for polymorphic forms because of the potential for ever-greening. On the facts of this case, however, I

https://www.mhc.tn.gov.in/judis

WEB COPY

find that patent protection, if granted, only exceeds that of the parent compound by about one year. Although D3 did not qualify as prior art when RTA 408 was granted a patent, for reasons set out in the preceding paragraphs, D3 does not detract from the technical advancement of the claimed invention or render it obvious. In those circumstances, the polymorphic forms are also entitled to a patent provided there is clear identification and enablement. In the claims, each polymorphic form is identified by the distinct x-ray powder diffraction pattern and melting point. The methods of production of Forms A and B are also fairly described in internal pages 90 and 91 of the complete specification. Therefore, there is sufficient merit in claims 1-6.

25. All that remains is the composition claim. As regards this claim, the appellant has not asserted or demonstrated any synergy between the ingredients. Since there is no proof of the composition being more than the sum of its parts, the composition claim fails the Section 3(e) test. Reference may be made to the judgment of this Court in *Novozymes Krogshoejvej v. Assistant*

https://www.mhc.tn.gov.in/judis

WEB COPY

Controller of Patents, 2023/MHC/4261, with regard to the interpretation of Section 3 (e) of the Patents Act.

26. For reasons discussed above, Patent Application No.7096/CHENP/2015 shall proceed to grant on the basis of claims 1-6, i.e. all current claims excluding claim 7. (T) CMA(PT)No.150 of 2023 is partly allowed on the above terms without any order as to costs.

20.12.2023

Index : Yes/No

Internet : Yes/No

Neutral Citation : Yes/No

kal

https://www.mhc.tn.gov.in/judis

WEB COPY

SENTHILKUMAR RAMAMOORTHY J.

kal

Pre-delivery judgment made in

(T) CMA (PT) No.150 of 2023

(OA/61/2020/PT/CHN)

20.12.2023