Resverlogix Corp Vs Deputy Controller Of Patents & Designs

Court: Intellectual Property Appellate Board, Chennai Circuit Bench At Kolkata

Date of Decision: Feb. 13, 2021

Acts Referred: Indian Patents Act, 1970 â€" Section 2(1)(ja), 3(d), 3(d), 15, 117A

Hon'ble Judges: Dr. B.P. Singh, Technical Member; Manmohan Singh, J

Bench: Division Bench

Advocate: Archana Shankar, Dr. Sachin Malik

Final Decision: Allowed

Judgement

1. The present appeal is filed under Section 117A of the Indian Patents Act, 1970, against the order dated 30/07/2019, passed by the Respondent,

being the Deputy Controller of Patents & Designs, under Section 15 of the Indian Patents Act, 1970, refusing to grant the AppellantÃ¢â‚¬â„¢s Indian

patent application no. 4764/KOLNP/2011.

2. The invention as explained by the appellant is under:

The claims of the present application are directed to novel synthetic quinazolone compounds as claimed in claims 1 and

2. The patent specification (Annexure P2 at page 50 of the Appeal Book, internal page 1 of the specification) relates to novel inflammatory agents for

regulating interleukin-6 (IL-6) and/or vascular cell adhesion molecule (VCAM-1) and their use for treating and/or preventing cardiovascular and

inflammatory diseases.

Ã, The chemical structures of compounds of at least claim 1 are as follows:

5-(2-dimethylamino-ethoxy)-2(4-hydroxy-3,5-dimethylphenyl)- 7-methoxy-3H-quinazolin-4-one;

O

NH

OÃ, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, O

N

7-(2-benzyloxy-ethoxy)-2-(4-hydroxy-3,5-dimethyl-phenyl)-5- methoxy-3H-quinazolin-4-one;

OÃ, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, O

NH

O

O

2-(4-(2-(benzyloxy)ethoxy)-3,5-dimethylphenyl)-5,7- dimethoxypyrido[2,3-d]pyrimidin-4(3H)-one;

OÃ, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, O

O

O

2-[4-(2,3-Dihydroxy-propoxy)-3,5-dimethyl-phenyl]-5,7- dimethoxy-3H-quinazolin-4-one;

OH

O

OÃ, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, O

7-(2-benzyloxy-ethoxy)-2-(2-hydroxymethyl-benzofuran-5-yl)- 5-methoxy-3H-quinazolin-4-one;

OÃ, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, O

OÃ, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, OÃ, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, Ã, OH

The Appellant in the patent specification has extensively provided exemplary embodiments, including methods and intermediates for preparing

compounds of the present invention, with specific compounds disclosed therein at pages 79-82 of the appeal book, internal pages 30-33 of the

specification; pages 89-98 of the appeal book, internal pages 40-49 of the specification; pages 108-178 of the appeal book, internal pages 59-129 of the

specification.

The Appellant at pages 180-182 of the Appeal Book (internal pages 132-133) has described a biological study to measure the transcriptional inhibition

of IL-6 following treatment with compounds of the present invention, along with the results of the same in Table 2.

Similarly, Appellant at pages 182-185 of the Appeal Book (internal pages 134 137) have disclosed an assay to quantify transcriptional inhibition of

VCAM-1 following treatment with compounds of the present invention, with results shown in Table 3.

3. It is the case of the appellant that:

4. The RespondentÃ¢â‚¬â„¢s order of one page is a flawed order and has refused the application on the ground of: that the claimed subject matter does

not reflect any technical advancement over the prior art and therefore lacks inventive step; and that the claimed compounds are considered derivative

of known compound without enhancement of known efficacy.

Ã‚

It is submitted that the applicant has been granted patents in several countries for the said compounds.

Copies of granted EP patent Ã¢â‚¬Ëœ086 and updated statement and undertaking on Form 3 is also enclosed. It is submitted that EP 086 includes compound

claims

It is submitted that the order of the Respondent is not a reasoned order. It is further submitted that the Respondent had clearly erred in appreciating

and understanding the invention and has not applied the test of inventive step analysis under Section 2(1)(ja).

We would like to draw the HonÃ¢â‚¬â„¢ble BoardÃ¢â‚¬â„¢s attention to the first examination report (Annexure P3, at pages 209-213 of the Appeal Book),

wherein the Respondent with regard to inventive step cited documents D1 and D2 ONLY.

The Respondent did not identify any reason as to how documents D1 (WO2007016525) and D2 (WO2008092231) render the subject matter of the

present application as lacking in inventive step and simply stated that documents D1/D2 presents maximal structural similarity since compounds of

D1/D2 have some core moiety as that of the alleged invention.

In the hearing notice (Annexure P5 at pages 390-391 of the Appeal Book), the Respondent waived off the objection with regard to document D1 and

cited document D3 (US20080188467A1) instead along with D2.

However, in the impugned order, the Respondent does not refer to D3 but only refers to document D1 and D2, whereas in the hearing notice objection

with regard to D1 was waived and D2 and D3 were only cited.

Ã, It is further submitted that the Respondent failed to adopt the inventive step analysis that has been provided by the higher authorities and that were

extensively referred to by the Appellant in the written submissions pursuant to the hearing before the respondent, at Annexure P6 from page 397

onwards.

Ã, With regard to the prior art documents referred to in the hearing notice and impugned order, it is submitted that documents D1 and D2 are non-

analogous art as they describe regulating the expression of ApoA-I, not IL-6.

Ã, Thus, the primary receptor discussed in both D1 and D2 is distinct from the target of this invention (IL-6), as further evidenced by the distinct

indications described (e.g., treating metabolic conditions such as cardiovascular diseases and/or inflammatory disorder). Even otherwise, the

compounds cited by the Respondent from documents D2 and D3 in the hearing notice are not even structurally similar as oppose to the present

invention, notwithstanding as to how the Respondent identified the said compounds from the prior art.

Ã, Contrary to the RespondentÃ¢â‚¬â„¢s assertion that compounds of D2 show IL-6 inhibition, it is submitted that throughout the document D2 only talks

about the target ApoA-I. The premise of D2 revolves around developing compounds that regulate expression of ApoA-I can be seen in the following

paragraphs and thus clearly a non-analogous art.

Ã¢â‚¬Å“[001] and [007] The present disclosure relates to compounds, which are useful for regulating the expression of apolipoprotein A-I (ApoA-I), and

their use for the treatment and prevention of cardiovascular disease and related disease states, including cholesterol- or lipid-related disorders, such as,

for example, atherosclerosisÃ¢â‚¬â€‹

Ã, For instance, based on example 33 of D2 and example 48 of the instant invention as given below, the HonÃ¢â‚¬â„¢ble Board will appreciate that

example 33 of D2 has a phenyl group whereas in example 48 the equivalent substituent is a hydrogen.

Ã,

Additionally, and as shown below, Example 4 of D2 and Example 1 of the instant invention as structurally different.

Similarly, D3 is a non-analogous art as document D3 also focuses on the target ApoA-I. The premise of D3 revolves around developing compounds

that regulate expression of ApoA-I as can be seen in the following paragraphs.

Ã¢â‚¬Å“[0001] The present disclosure relates to compounds, which are useful for regulating the expression of apolipoprotein A-I (ApoA-I), and their use

for treatment and prevention of cardiovascular disease and related disease states, including cholesterol- or lipid-related disorders, such as, for example,

atherosclerosis.Ã¢â‚¬â€‹

Contrary to the RespondentÃ¢â‚¬â„¢s assertion, D2 and D3 only relate to the target ApoA-I. In contrast, the claimed compounds are IL-6 inhibitors.

Accordingly, D2 and D3 are non-analogous citations and therefore do not qualify as relevant prior art.

Ã, Furthermore, Example 57 of D3 and Example 57 of the present invention also are structurally different.

It is submitted that the intra-molecular hydrogen bonding that is possible in Example 57 of D3 is not possible in Example 57 of the present invention.

Ã, The Appellant provided the example of Mirtazapine and Mianserin, which comprises a simple isosteric replacement of an aromatic methine group

(CH) in mianserin with a nitrogen to give a pyridine ring (mirtazapine). This modification has profound effects on the compoundÃ¢â‚¬â„¢s physiochemical

properties, pharmacokinetics, mechanisms of action, and antidepressant activities.

Ã, It is further submitted that the Respondent has not provided any reason for selecting compound 33 from D2 among 40 exemplified compounds. The

said selection is clearly based on hindsight and structure similarity, which is impermissible in an obviousness analysis. As shown below, the most active

compound in D2Ã¢â‚¬â„¢s ApoA-I ELISA assay is Example 20. By contrast, no specific activity data is provided for compound 33, and compound 4 of

D2 exhibits low activity (as evidenced by a relatively high EC50 in the ApoA-I ELISA assay)

The Hearing Notice states that it would be obvious to replace a hydrogen atom in D2's Example 4 with a -CH2N(CH3)2 group to arrive at Applicant's

Example 1, and the skilled person would expect that such a modification would result in a compound having similar properties. Applicant respectfully

disagrees. A person of ordinary skill in the art would recognize that such a replacement would result in different functionality. For instance, a skilled

artisan would recognize that the -N(CH3)2 moiety will alter the overall pKa1 profile of the compound and also provide the compound with additional

modes of interaction, such as, for example, hydrogen bonding. This, in turn, would influence the compound's ability to interact with its environment,

such as the compound's binding to a biological target. Moreover, Appellant submits that neither D2 nor D3 provides any guidance to make such a

modification nor any indication that such a compound would maintain the activity of Example 4 of D2.

Similarly, the replacement of -OCH2CH2OH in D3's Example 57 by a -CH2CH2CH2OH moiety of Applicant's Example 57 could also have a

profound effect on the compound's properties. For example, the

hydrogen of the hydroxy group on the ethoxyhydroxy side chain of Example 57 of D3 can engage in intramolecular hydrogen bonding with the lone

pair of the oxygen of the same group, which is directly attached to the rest of the molecule. This type of interaction is not possible with the -

CH2CH2CH2OH side chain of AppellantÃ¢â‚¬â„¢s Example 57 because the oxygen in the side chain of D3's Example 57 has been replaced by a

methylene (-CH2-) unit, which is not capable of engaging in hydrogen bonding. Accordingly, this renders the hydrogen of the hydroxyl group available

for other interactions, such as intermolecular hydrogen bonding (e.g., interacting with other compounds, solvent, biological targets, etc.). This in turn

can have a profound effect on the compound's biological activity (e.g., inhibition of IL-6 transcription). Moreover, neither D2 nor D3 provides any

guidance to make such a modification nor any indication that such a modification would at least maintain the activity of D3's Example 57.

Ã, The Respondent has incorrectly applied the test of Section 3(d) as Section 3(d) does not apply to a new chemical entity.

Ã, In the Hearing Notice, the Respondent states that the compounds as claimed do not meet the requirement under Section 2(1)(ja). This is clearly an

error as the Respondent has himself acknowledged that the compounds are novel and has stated the same in his order.

Ã, Thus, on one hand, the Respondent states that Section 3(d) is applicable because it is new use of a known substance while holding the compounds

as being novel and on the other hand states that the claims are not new or merely a derivative of a known substance. This is a self-contradicting order.

Further, the Respondent relies on EP and US prosecution to state that in EP and US, use for treatment or method for treatment claims have been

granted while no compound claims have been granted. This statement is outdated. Compound claims, with no use limitation, have granted in Europe, in,

e.g., claims 1 and 2 of EP Patent No. 3,431,086. In fact, all the compounds listed in pending claim 1 of the instant application have been patented as

part of claim 1 of EP Patent No. 3,431,086.

Ã, In essence, the order of the Respondent appears to be based on an evolving EP and US position that reflects distinct strategic considerations made

in each jurisdiction.

Ã, It is further submitted that there is no known substance with known efficacy. For Section 3(d) to apply, the following criteria have to be met:

(a) That the claimed invention is a new form of a known substance or a derivative of a known substance; AND

(b) That the said KNOWN SUBSTANCE should have KNOWN EFFICACY.

Ã, Further, it is submitted that the term Ã¢â‚¬Ëœderivativeâ€™ used in the explanation part of Section 3(d) is not to be confused with the term

Ã¢â‚¬Ëœderivativeâ€™ used in the context of organic chemistry. Derivative compounds as used in the organic chemistry are different chemical compounds

and are thus different substances. They are new chemical entities. The expression Ã¢â‚¬Ëœderivativeâ€™ used in section 3(d) has to be given a meaning

such that it falls within the same category as Ã¢â‚¬Ëœsalt, ester,

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ether, polymorph, metabolite, pure form, particle size, isomer, mixture of isomers, complex or combinationÃ¢â‚¬â„¢.

Ã, This is in accordance with the legal principle Ã¢â‚¬Ëœejusdem generisÃ¢â‚¬â„¢, the literal translation of which is Ã¢â‚¬Å“of the same kindâ€Ÿ. Under the law of

interpretation of statutes, this expression means that where there is a list of specific classes of persons or things followed by a general term, then the

general term will be given a meaning so as to extend it to apply to the same kind of persons or things specifically listed.

Ã, In this regard, just by way of a simple example, even the Division Bench of the HonÃ¢â‚¬â„¢ble Delhi High Court in Roche vs Cipla did not hold

Erlotinib, the claimed invention as being a derivative of a prior art compound even when there was a high structural similarity. The court dealt with this

issue under Ã¢â‚¬Å“INVENTIVE STEPÃ¢â‚¬â€‹ and NOT Section 3(d) and treated Erlotinib as a New Chemical entity.

Therefore, the claimed compounds do not fall within the ambit of section 3(d).

Even otherwise, the specification provides experimental evidence showing that each of the claimed compounds is capable of inhibiting â‰¥ 20% of IL-6

mRNA concentration in vitro. See specification at example 59.

In light of our above submissions the amended claims do not fall within the scope of section 3(d)

5. We have noted that the instant application was filed initially with 46 claims and after the First Examination Report all other claims were deleted

retaining claims 39-41 and renumbering them as claims 1-

3. While claims 1-2 were oriented towards Ã¢â‚¬Å“A compoundÃ¢â‚¬Â¦Ã¢â‚¬, the last claim is an application claim, claiming Ã¢â‚¬Å“CompositionÃ¢â‚¬ comprising one of

the claimed compounds.

6. We have also noted that First Examination Report carried the main objections as under:

Claim(s) (39-41) lack(s) inventive step, being obvious in view of teaching (s) of cited document(s) above under reference for the following reasons:

Both the documents (D1-D2) { D1 WO2007016525 A2 ; D2 WO2008092231 A1} discloses structurally similar compound having the same core

moiety as that of the present alleged invention (claim 39-41). The present compounds are only differs in the substituent in the core moiety. Thus, the

technical problem underlying the present application has to be seen the provision of further alternate compounds having an unexpected effect with

regard to the D1 and/or D2. As the applicant has not furnished any evidence for a surprising effect over D1 and/or D2 in form of comparative data

between a compound of the present application and one of D1/D2 presenting maximal structural similarity to show convincingly that the unexpected

effect indeed has its origin in the distinguishing feature, the subject matter of the claim 39- 41, does not meets the requirement of section 2(1)(ja) of

the Patent Act.

Claim(s) (Claim 1-45) are statutorily non-patentable under the provision of clause (d & i) of Section 3 for the following reasons: 1. Without prejudice

to the objection of section 2(1)(ja) of the Patent Act, the subject matter of claim 39-41 is not allowable u/s 3(d) of the Patent Act for the reason as

mentioned above. 2. Method of treatment: Claim 1-38 & 42-45 The subject matter of claim 1-38 & 42-45 refers to a method treatment which is not

allowable u/s 3(i) of the Act. Even if the applicant amend the claims by changing the preamble, then also the said claims will not be allowable as the

scope of the claims will be changed.[Emphasis added]

7. The final hearing notice issued after consideration of the response to FER contained the following main objections:

Ã, Invention u/s 2(1)(j)

D2: WO2008092231 A1 (as that of FER) D3:

US20080188467A1 (07/08/2008) Few selected compounds have been claimed in the amended set of claims. The selected compounds are structurally

almost identical with the example of D2 or D3. The present compounds differ in the substituent on the Ã¢â‚¬ËœOÃ¢â‚¬â„¢ atom of the phenyl ring (e.g.

Ã¢â‚¬"OCH3 of the example 4 of D2 has been replaced by the Ã¢â‚¬"O(CH2- CH2-N(CH3)2 in example 1 of the present invention or Ã¢â‚¬"O-CH2-CH2-OH

of the example 57 of D3 has been replaced by the Ã¢â‚¬"CH2-CH2-CH2-OH in example 57 of the present invention). Regarding this difference in

chemical structure, the applicant has argued that the present compounds are capable of inhibiting IL-6 instead of ApoA of the prior art. But as the

present claimed compounds are structurally identical (almost), the office thinks that the present claimed compounds will also exhibits ApoA activity

and the prior art compounds will also show IL-6 inhibition property. Moreover, the applicant has not furnished any such evidence. Therefore, the

compounds as claimed in claims 1-3 does not meets requirements of section 2(1)(ja) and not allowable u/s 3(d) [new use of known substance] of The

Patent Act.

Other Requirement(s)

The compounds as claimed in revised claims 1-3 are either not new or merely new derivatives which can be prepared very easily by a person skilled

in the art. The corresponding application filed in EPO or USPTO revealed that only 'use for treatment' or 'method of treatment' claims are granted and

no compound claim has been granted.

8. It is worth noting here that while in FER the Respondent relied on two documents i.e. D1 WO2007016525 A2 ; D2 WO2008092231 A1 for his

objection of lack of inventive step but during hearing notice he chose to ignore D1 and along with D2 cited one more document D3

US20080188467A1, for proving the lack of inventive step. Not surprising, all the documents were cited in International Search Report (ISR). The two

final citations are shown herein below:

9. It is evident that ISR did not hold any of the documents relevant for claims 39-41, as finally retained by the appellants. Secondly, very interestingly,

the Respondent holds in category Ã¢â‚¬Å“other requirementsÃ¢â‚¬ of his hearing notice that no compound claim is granted in other jurisdiction. His statement

compelled us to review the grant in other jurisdiction and found his statement is not wholly true.

10. LetÃ¢â‚¬â„¢s have a look on the order of the respondent:

Ã, Reason for Refusal:- The subject matter of revised claims 1-3 that filed after hearing of the instant patent application provides novel synthetic

quinazolone compounds, as well as

Ã,

pharmaceutical compositions comprising those compounds. The cited documents D1 and D2, as explained in detail in the hearing letter / FER also

reveal similar type of compounds with some alteration in the substituent groups / moieties only leaving the main backbone structure intact. The claimed

compounds, which are derived from known prior compounds, are considered as novel. However, preparation of such derivative compounds in the field

of new organic chemistry is well-known to a person skilled in the art. In view of the above, the claimed compounds, although novel, are considered as

obvious, particularly in the absence of enhancement of therapeutic efficacy. The complete specification is silent regarding the results of comparative

efficacy data of the present and prior compounds, rendering the claimed invention also not patentable under Section 3(d) of the Patents Act.

Ã, Opinion Ã¢â‚¬"The claimed subject matter does not reflect any technical advancement over prior art and therefore, lacking in inventive step. The

claimed compounds are considered as mere derivative of known compounds without any enhancement of therapeutic efficacy and therefore, also not

patentable u/s 3(d) of the Ã¢â‚¬ËœAct. The application is refused for grant of patent under section 15 of the Ã¢â‚¬ËœAct.

11. It is evident that while in the hearing notice, the respondent relied on document D2 and D3 his refusal order is based on document D1 and D2. It is

known that document D1 was dropped by the Respondent at hearing notice stage, after having used in FER. Hence refusing the case based on a

document which was not even discussed in hearing is totally against natural justice and cannot stand scrutiny of law.

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12. Further, the order is a classic example of non-speaking order and does not give any reasoning whatsoever to substantiate his contention. He

agrees that the claimed compounds are novel. But then goes on to say that such preparation of such derivative compounds in the field of new organic

chemistry is well-known to a person skilled in the art. It is just a subjective statement of the respondent. The 'obviousness' has to be strictly and

objectively judged Biswanath Prasad Radhey Shyam vs Hindustan Metal Industries Ltd (AIR 1982 SC 1444). It is noticed that the Respondent has not

only ignored the principles of determination of inventive step as enshrined in the Manual and Guidelines at IPO; but ignored several judicial

pronouncements on the subject and makes a stray statement which is not tenable in eye of law.

13. The objection under section 3(d) is also not maintainable considering the arguments of the appellant. The respondent has failed to prove that the

claimed compound is Ã¢â‚¬Å“discovery of new form of known substanceÃ¢â‚¬â€‹ a basic requirement for application of the provisions of section 3 (d).

14. We have seen that the compound claims are granted in other jurisdictions, after having considered all the mentioned prior arts.

15. We are therefore convinced by the arguments and documentary evidences submitted by the appellant that both the objections taken by the

respondents in his refusal order are not sustainable.

16. We set aside the impugned order of Respondent dated 30/07/2019 and direct the respondent to grant the patent on existing set of claims within 4

weeks from the issuance of this order.

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17. Keeping in view the above, the instant appeal is allowed. No cost.