IN THE HIGH COURT OF DELHI AT NEW DELHI

% Judgement reserved on: 18.05.2026
Judgment delivered on: 23.07.2026

\+ C.A.(COMM.IPD-PAT) 37/2023

ARRAY BIOPHARMA INC .....Appellant

versus

DEPUTY CONTROLLER OF PATENTS
AND DESIGNS .....Respondent

Advocates who appeared in this case:

For the Appellant: Ms. Archana Shankar and Mr. Devender Rawat, Advocates.

For the Respondent : Mr. Rohan Jaitley, CGSC with Mr. Varun Pratap Singh, Mr. Akshay Sharma, Mr. Dev Pratap Shahi and Mr. Yogya Bhatia, 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 30.06.2023 (hereinafter referred to as '*impugned order*') under Section 15 of the Act refusing the Patent Application No. 450/DELNP/2015 titled "*PHARMACEUTICAL COMBINATION COMPRISING A B RAF INHIBITOR AN EGFR INHIBITOR AND OPTIONALLY A PI3K ALPHA INHIBITOR*" (hereinafter referred to as "*subject application"*) on the ground of lack of inventive step under Section 2 (1) (ja) of the Act and non patentability under Sections 3(d) and 3(i) of the Act.

2. The facts as culled out from the appeal and germane, are as under:-

2.1. It is the case of the appellant that the subject patent traces its origin to a priority application filed on 07.08.2012 (US 61/680,473), followed by an international PCT application (PCT/US2013/053619) on 05.08.2013, which was published as WO2014/025688 on 13.02.2014. The corresponding Indian patent application was filed on 19.01.2015 and was published under Section 11A of the Act on 26.06.2015. A request for examination was subsequently filed on 01.08.2016.

2.2. The appellant submits that the Indian Patent Office issued the First Examination Report (hereinafter referred to as *"FER"*) on 24.08.2018, to which a response was duly filed on 06.02.2019. Thereafter, a hearing notice dated 25.09.2020 fixed the matter for hearing on 19.10.2020. The appellant sought an adjournment on 14.10.2020, following which the hearing was rescheduled to 19.11.2020. A second adjournment request was filed on 12.11.2020, resulting in the hearing being further rescheduled to 21.12.2020, and subsequently by the Controller to 05.01.2021.

2.3. The appellant submits that the hearing under Section 15 of the Act was conducted on 05.01.2021, after which written submissions were filed on 20.01.2021. Following a considerable lapse of time, another hearing notice dated 10.03.2023 fixed the matter for 17.03.2023. The appellant sought an adjournment on 14.03.2023, and the respondent thereafter rescheduled the hearing to 21.03.2023, citing an incorrect prior art citation.

2.4. The appellant submits that, after the rescheduled hearing, a petition under Rule 138 was filed on 30.03.2023 seeking a one-

month extension of time to file hearing submissions. The hearing submissions were thereafter filed on 01.05.2023, thereby placing the appellant's substantive response and supporting material on record for consideration by the Patent Office.

2.5. It is the case of the appellant that, notwithstanding the prosecution history and the submissions made, the Controller passed the impugned order on 30.06.2023 under Section 15 of the Patents Act refusing the grant of the patent. Subsequently, on 18.08.2023, Form-6 was filed to record Array BioPharma Inc. as the applicant on record.

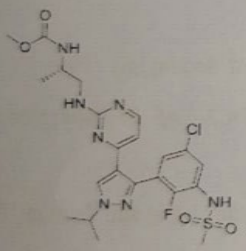
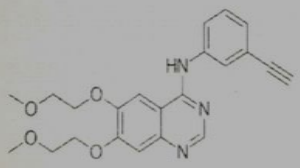
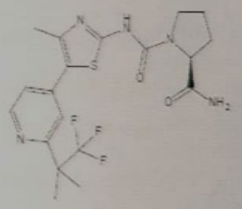
2.6. Hence the present appeal.

CONTENTIONS OF APPELLANT

3. Ms. Archana Shankar, learned counsel appeared for the appellant and submits as under:

3.1. At the outset, learned counsel submits that the Claim 1 of the subject application is in relation to a pharmaceutical combination. It is stated that the claims of the subject application are directed to a combination of 2/3 specific drugs having a specific structure and formula with different mechanism of action. It is stated that the dual combination comprises (a) compound A (encorafenib) which is a B-Raf Inhibitor and (b) Cetuximab/Erlotinib (EGFR Inhibitor), while the triple combination comprises (a) compound A (encorafenib) which is a B-Raf Inhibitor and (b) Cetuximab/Erlotinib (EGFR Inhibitor) and (c) compound B (PI3K-α Inhibitor). A table demonstrating how the specific compound i.e. compound A (B-Raf Inhibitor), compound B (PI3K - Inhibitor) and Erlotinib/Cetuximab (EGFR Inhibitor) are used in the said combination and relied upon

by the appellant is given below:

COMPOUND A Impugned Application	ERLOTINIB / TARCEVA Impugned Application	COMPOUND B Impugned Application
 b RAF inhibitor	 EGFR Inhibitor: Erlotinib	 PI3K-α inhibitor

3.2. Predicated upon the aforesaid combination of specific compounds, the learned counsel would assert that the data which has been collated from the tests conducted in respect of each of such combinations has revealed and demonstrated technical advancement/synergistic effect. In order to further clarify, learned counsel would submit that the data in the Complete Specifications (hereinafter referred to as '*CS*'), also provides that the said dual/triple combination of the specific drugs having three different mechanism of actions as per the claimed invention is the synergistic combination that improves the therapeutically relevant selectivity. It is contended that the data clearly demonstrates surprising and unexpected therapeutic benefits. In that, not only does the combination demonstrate a synergistic therapeutic effect with regard to alleviating, delaying progression of or inhibiting the symptoms but also in fewer side effects, more durable response, an improved quality of life or a decreased morbidity, in comparison to the monotherapy applying one of the pharmaceutically therapeutic

agents.

3.3. Dilating further on the aforesaid, learned counsel referred to the clinical studies contained in the CS which have been verified as two Phase Ib and Phase II clinical trial studies. She would submit that Examples 2 & 3 in the CS provide the data from the clinical studies. Learned counsel relied upon the following table to substantiate her arguments:-

Grp	n	Treatment Regimen				Mean Volume, mm^3			T/C or T/T_0	Statistical Significance					Regressions		Mean BW Nadir	Deaths	
		Agent	mg/kg	Route	Schedule	Day 1	Day 29	Change		vs G1	vs G2	vs G3	vs G4	vs G8	PR	CR		T R	N T R
1	10	Vehicle 1 Vehicle 2	--- ---	po po	bid x 28 qd x 28	122	1065	943	---	---	---	---	---	---	0	0	-0.6% Day 8	0	0
2	10	Cpd. A	20	po	bid x 28	122	1016	894	95%	ns	---	---	---	---	0	0	-0.1% Day 8	0	0
3	10	Cpd B	25	po	qd x 28	122	660	538	57%	ns	---	---	---	---	0	0	-2.5% Day 8	0	0
4	10	Cetuximab	20	ip	biwk x 4	125	955	830	88%	ns	---	---	---	---	0	0	-1.2% Day 8	0	0
5	10	Cpd. A Cpd. B	20 25	po po	bid x 28 qd x 28	125	491	366	39%	ns	ns	ns	---	***	0	0	-0.7% Day 4	0	0
6	10	Cpd.A Cetuximab	20 20	po ip	bid x 28 biwk x 4	125	239	114	12%	**	**	---	**	ns	0	0	---	0	0
7	10	Cpd B Cetuximab	25 20	po ip	qd x 28 biwk x 4	125	584	459	49%	ns	---	ns	ns	***	0	0	-1.4% Day 4	0	0
8	10	Cpd A Cpd. B Cetuximab	20 25 20	po po ip	bid x 28 qd x 28 biwk x 4	123	120	-3	-2%	***	***	**	***	---	0	0	---	0	0
9	10	Paclitaxel	30	iv	qod x 5	122	229	107	11%	**	---	---	---	---	0	0	-10.1% Day 11	0	0

3.4. Pointing out to Group 6 in the aforesaid table, she would contend that Compound A in dual combination with Cetuximab slowed down the tumor progression to 12% and indicated significant inhibition. It was stated that the said combination showed significant improvement upon Compound A monotherapy in Group 2 (95%) and Cetuximab monotherapy in Group 4 (88%). Referring to Group 8 of the aforesaid table, it is contended that Compound A, Compound B and Cetuximab in triple combination resulted in tumor progression as well as tumor regression by (-)2%. According to her, this treatment immensely improved the treatment over and above Compound A monotherapy in Group 2 (95%), Compound B monotherapy in Group 3 (57%) and Cetuximab monotherapy in

Group 4 (88%). For clarification, learned counsel would submit that the lesser percentage is indicative of significant slowing down of progression of the tumor. In other words, appellant asserts that the data is clear indicator of surprising and unexpected properties of the claimed invention using 2 or 3 specific drugs in comparison to the Compound A alone being administered, or Compound B alone or EFGR alone as also Compound A+B or Compound B+Cetuximab.

3.5. It is thus contended that the respondent neither appreciated nor considered the aforesaid data nor analysed its synergistic surprising effects.

3.6. It was next contended that the claim is a combination product and not a method of treatment to fall under the exception stipulated under Section 3(i) of the Act and the claimed invention has to be assessed as a whole. Learned counsel would contend that in order to appreciate the claimed invention the nature and scope of the same must be determined by reading the claims, the complete specifications and all the disclosures as a unified whole. It is stoutly contended that the present claims are product claims directed to a "pharmaceutical combinations" and not to a method of treatment of human beings as has been incorrectly assessed by the respondent. It is submitted that the erroneous conclusion is based on incorrect characterisation of the invention by fragmenting the claim language and reading individual portions of the specifications in isolation. In other words, the subject matter which is excluded by Section 3(i) of the Act is the process and not a product or a combination or even a pharmaceutical entity.

3.7. It is emphasized that Claim 1 of the subject application

provides for a functional descriptor of the claimed pharmaceutical combination as a product and not as a method step. It only describes a range of ways in which the constituent actives may be administered without transforming the product into a method. The appellant relied on the judgment in the case of ***Nestle SA vs. Controller of Patents & Designs [CA (COMM).IPD-PAT) 22/2022]*** particularly upon para 14 & 15 to submit that the mere use of the expression "treatment" in a claim need not necessarily render it as a method of treatment proscribed under Section 3(i) of the Act. It was further stated that the expression "composition for the treatment", was held to be used for defining the combination and not for claiming a method of treatment. For similar reasons, the appellant also relied upon the judgment in ***Medilabo RFP Ink Inc. vs. Controller of Patents, (CA (COMM).IPD-PAT) 16/2024*** of this Court.

3.8. It was emphasized that the clinical trial data and dosing schedules in the CS demonstrates the clinical efficacy of the combination, the synergistic interaction of the specific compounds as a defined combination product. These are evidence of the combination utility under Section 2(1)(ac) and not a definition of the claimed invention. Learned counsel would submit that the use of the terms "treatment" or "administration" in the claim would neither alter nor display the inventive concept since the inventive concept resides in the combination itself.

3.9. Learned counsel heavily relied upon the counterpart EP patent number 2882440 where similar combination products were not considered as methods for treatment. In order to substantiate the similarity of objections in the European Patent Convention and the

proscription in Section 3(i) of the Act, learned counsel referred to Article 53(c) of the EP Convention wherein methods for treatment of the human etc., are non patentable, yet, the European Counterpart of the claimed invention was granted patent. Learned counsel has relied upon the following table in order to substantiate the aforesaid contentions:

Particulars Cited prior arts				
Country AU 2013299841	**EP2882440B1**	**US9474754 B2**	**ISR**	**Indian patent office**
WO 2011/046894	WO2011/046894	WO 2011/046894;	WO 2011/046894	WO2011/046894 (D3);
WO 2010/029082 A 1;	WO-A1-2010/029082;	WO 2010/029082;	WO 2010/029082 A1;	WO/2010/029082 (*Caravatti et al.*- D4)
WO 2011/025927 A1;	WO-A1‖ 2011/025927;	WO 2011/025927;	WO 2011/025927 A1;	W02011/025927 (*D1-Huang et al.)*
WO 2011/028540 A1	WO-A1-2011/028540	WO 2011/028540	WO 2011/028540 A1;	WO 2011/028540 (*D2 Hatzivassiliou et al)* same as *IPD 2* 1403/DELNP/2012;
-	WO-A1-2013/070996	-	WO 2013/070996 A1	-
-	-	WO 2008/124161 A1	-	-
-	-	WO 2012062694	-	
-	-	WO 2013/070998	-	

3.10. To lend credence to the aforesaid submissions, learned counsel relied upon the decision of the Intellectual Property Appellate Board (IPAB) in the case of ***Ranbaxy Laboratories Ltd. vs. The Controller of Patents & Designs (OA)/15/2011/PT/MUM)*** particularly para 3 to submit that the combination of 2 or more actives are permitted and the inventive concept/unexpected technical advantages is based on the final outcome and effect of the said combination. Thus, according to the learned counsel, the finding of the respondent that the claimed invention is a method of treatment of human beings and non patentable under Section 3(i) of the Act is not only erroneous but

also unfounded.

3.11. The learned counsel next contended that the conclusion of the respondent of the claimed invention being non patentable under Section 3(d) of the Act also is erroneous and contrary to the facts on record. It was contended that the provisions of Section 3(d) of the Act are not attracted to a combination of independent Active Pharmaceuticals Agents (APA).

3.12. Ms. Shankar stoutly contended that the claimed combination of 2 or 3 pharmacologically active specific agents i.e. a B-Raf Inhibitor, an EFGR Inhibitor and an optional PI3K-α is not a new form, salt, ester, ether, polymorph, metabolite, isomer, or derivative of any known substance referred to in the prior art. In fact, according to the appellant the claimed invention is a combination of distinct and independent APA. She relied upon the judgment of IPAB in ***Ajantha Pharma Ltd. vs. Allergan Inc. & Ors. (Order No.173/2013)*** where, it is stated that, the Board held that a combination of two active drugs cannot be considered derivatives of each other and that the "combination" referred to in the Explanation to Section 3(d) can only mean a combination of two or more derivatives enumerated in the Explanation or a combination of one or more such derivatives with the known substance itself and not a combination of two independent active substances. Based on such analysis, the objection under Section 3(d) was rejected by the IPAB.

3.13. Thus, according to the learned counsel, it would follow from the aforesaid decision of the IPAB that a combination of two or more independent APA, each with its own distinct chemical identity, mechanism of action and therapeutic profile, would clearly fall

outside this Court and ambit of Section 3(d) of the Act. To the same effect, reliance was placed on the judgment of the Calcutta High Court in ***Topotarget UK Ltd. vs. Controller General of Patents & Designs, Mumbai & Ors., (IPDPTA/50/2023).***

3.14. In the alternative, learned counsel would contend that without prejudice even assuming that Section 3(d) is applicable, the threshold of enhanced therapeutic efficacy in any case is satisfied having regard to the data placed on record by the appellant. Learned counsel places reliance on the table referred to in para 3.3 above.

3.15. So far as the objections under Section 10 (4) of the Act are concerned, learned counsel would submit that the appellant has discharged its disclosure obligations fully and completely. It is asserted that the CS not only discloses the invention, its operation but also the best method known to the appellant for performing it. The clinical trial data contained in the CS clearly demonstrates the technical advancement achieved in the combinations disclosed. As such, the disclosure, according to the appellant, is not merely perfunctory or inadequate but exemplary.

3.16. Relying upon ***Topotarget*** *(supra)*, learned counsel would contend that the Court has clarified the scope of the requirement of the disclosure as contemplated in Section 10(4) of the Act in the context of pharmaceutical combination patents. It was stated that in para 15, it was held that while Section 10(4) requires full and particular description of the invention and its best method of performance, the said requirement does not necessitate that the CS should contain illustrative examples for every conceivable embodiment or specific combinations falling within the scope of the

claims. It was further held that the findings of insufficiency of disclosure and lack of inventive steps in the same order are not only contradictory but also irreconcilable.

3.17. Learned counsel next referred to the objections sustained by the respondent in respect of Section 2(1)(ja) of the Act. At the outset, learned counsel vehemently submitted that the impugned order does not contain any analysis on the question of inventive steps. Equally, it neither identifies the closest prior art document nor articulates the technical problem that the claimed invention solves over the closest prior art. According to her, the inventive step of the present combination is clearly demonstrable and discernible from the unexpected technical advantage brought out in the clinical trial data set out in the CS. In reiteration of the earlier submissions, learned counsel would submit that the inventive step is established by the fact that the dual combination demonstrates a 12% reduction in the tumor progression and the triple combination has achieved tumor regression of (-)2%. It is stated that this unexpected result, which was unforeseeable from the prior art, itself is a conclusive evidence of inventive step under Section 2(1)(ja) of the Act and constitutes technical advancement.

3.18. Distinguishing the 4 prior arts i.e. D1 to D4, learned counsel would submit as under:

- Cited Document D1 is directed to a new chemical entity in the B-Raf inhibitor class. The only combination disclosed in document D1 is at paragraph 43 and Figure 1 which is a combination of a specific Compound 9 (B-Raf inhibitor- Methyl N-[(2S)-1-({4-[3-(5-chloro-2-fluoro-3-methanesulfonamidophenyl)-1-(propan-2-yl)-1H-

pyrazol-4-yl]pyrimidin-2-yl}amino)propan-2-yl]carbamate) with Compound A3 (a MEK inhibitor). Document D1 contains no disclosure of, and provides no teaching towards, any combination involving an EGFR inhibitor or a PI3K-α inhibitor.

- A Person Skilled in the Art from D1 would not be motivated to replace the Braf inhibitor of D1 with B- Raf inhibitor Compound A (INN Encorafenib) as claimed in the present invention and also replace the MEK inhibitor of D1 with 2 other specific actives (PI3K and EGFR) of the present invention because none of the other cited prior arts teach the said specific actives with 2 different mechanism of action Erlotinib/Cetuximab and PI3K-α inhibitor (INN alpelisib).
- It is submitted that the Document D2/IPD2 must be read and understood as a whole and it is not a combination patent. This prior art is directed to prognostic methods for identifying tumours which are not susceptible to B-Raf inhibitor treatment by detecting mutations in a K-ras gene or protein.
- Figures 34A and 34B of D2, which the Controller relied upon, relate to a specific B-Raf inhibitor in the context of this prognostic teaching and the document do not disclose/suggest/teach any combination of a B-Raf inhibitor with an EGFR inhibitor or a PI3K-α inhibitor as claimed in the present application.
- Document D3 discloses two specific compounds none of which is the specific actives with 3 mechanism of actions as recited in claim 1 of the present application. D3 does not disclose:

> "• *The B-Raf inhibitor in D3 (Compound A of D3) is not Encorafenib : the specific B-Raf inhibitor of the present invention.*
>
> • *The PI3K inhibitor in D3 (Compound B of D3) is not Alpelisib — the specific PI3K-α inhibitor of the present invention.*

- *D3 contains no disclosure whatsoever of an EGFR inhibitor; neither Erlotinib nor Cetuximab nor any other EGFR inhibitor appears anywhere in D3.*

- *D3 accordingly contains no disclosure of the dual combination (B-Raf + EGFR) or the triple combination (B-Raf + EGFR + PI3K-α) that forms the subject matter of the present invention."*

- Cited document D4 is directed solely to a novel PI3K inhibitor as a chemical entity. D4 addresses a different technical problem i.e. the identification and characterisation of PI3K inhibitors and compared to the present invention it is a non-analogous prior art.

3.19. Predicated upon the aforesaid distinction drawn, learned counsel would forcefully contend that none of the aforesaid documents whether considered independently or a combination disclose or suggest, (a) the specific B-Raf Inhibitor Encorafenib (Compound A of the present invention); (b) the specific EGFR Inhibitors Erlotinib or Cetuximab (Compound 2 of the present invention); (c) the specific PI3K-(put alfa mark) Inhibitor Alpelisib (Compound 3 of the present invention) or (d) the dual combination of Encorafenib with Erlotonib/Cetuximab, or the triple combination of all three agents together.

3.20. Ms. Shankar would submit that by reading D1, D2, D3 and D4 as of the priority date, a person skilled in the art would have no motivation let alone a reasonable expectation of success to select these specific agents from the vast landscape of B-Raf Inhibitors, EGFR Inhibitors and PI3K Inhibitors available and combine them in a precise manner as put forth in the claimed invention. It was asserted that no document in the prior art discloses the specific agents as claimed. The learned counsel referred to and relied upon the Guidelines for Examination of Patent Applications in the Field of

Pharmaceuticals, October, 2014 (Clauses 7.2 and 7.6) as well as MANUAL OF PATENT OFFICE PRACTICE AND PROCEDURE Version 3.0 dated 26th November, 2019. Clauses 7.2 of the Guidelines is reproduced as follows:

> ***"Guidelines for Examination of Patent Applications in the Field of Pharmaceuticals:***
> *7.2 .....A generic disclosure in the prior art may not necessarily take away the novelty of a specific disclosure. A specific disclosure in the prior art takes away the novelty of a generic disclosure."*

3.21. Learned counsel also relied upon the judgments in ***Biomoneta Research Pvt. Ltd. Controller General of Patents & Designs and Anr., (2023/DHC/001816)*** particularly para 64, ***Groz-Beckert KG vs. Union of India and Others (2023 SCC OnLine Cal 111)*** particularly para 7, ***Guangdong Oppo Mobile Telecommunications Corp. Ltd. vs. The Controller of Patents and Designs (AID No.20 of 2022)*** particularly para 12 & 13, ***Titan Umreifungstechnik Gmbh and Co. KG vs. Assistant Controller of Patents and Designs and Anr. (2023:DHC:3832)***.

3.22. As a concluding argument, Ms. Shankar, learned counsel submitted that each of the prior art documents D-1 to D-4 were cited in the counterpart patent granted in Australia, Canada, EP and USA. She would submit that though the said grant of patent may not be binding upon the Indian Patent Office on the ground of territoriality, however, such grant would surely have a persuasive value. She would emphasize that in each of the said jurisdictions and for the same combination product, the very same prior arts having been cited, tested and distinguished granting patent which is the subject matter of the subject application needs to be appreciated and rightly considered by this Court. Additionally, she relies on the judgement of this Court

in ***Biomoneta Research*** *(supra)* and ***Nestle SA*** *(supra)* and the judgment of the Madras High Court in ***Shaperon Inc. v. Assistant Controller of Patents and Designs*** [(T) CMA(PT) No.46/2023].

3.23. On the basis of the aforesaid arguments, she prays that the impugned order may be set aside and the subject patent application be allowed and patent be granted.

CONTENTIONS OF THE RESPONDENT.

4. Mr. Rohan Jaitley, learned CGSC, appearing for the respondent, refutes the submissions made on behalf of the appellant and supports the analysis and findings recorded in the impugned order. He submits as under:

4.1. At the outset, Mr. Jaitley, learned CGSC would contend that the claimed invention is a method of treatment contrary to the submissions made by the appellant, and thus, barred under the provisions of Section 3(i) of the Act. He draws attention of the phrase "for simultaneous, separate or sequential administration" is not a statement as to what is a pharmaceutical product, but a description of therapeutic protocol and is a treatment schedule which is non-patentable. He would urge that the title of the application itself would suggest that it is directed at the therapeutic use combination rather than any fixed formulation. He would also contend that the CS itself demonstrates that the inventive contribution is the therapy by itself and not any physical product. He would invite attention to the elaborate Phase Ib and Phase II clinical trial protocol defining the patient population selection criteria, dose escalation schedules, and treatment duration clearly depicts a treatment methodology and definitely not a pharmaceutical product. Further, according to him, the details such as "*Compound A: Capsule*

for oral use as assigned once or twice daily; Compound B: Tablet for oral use once or twice use daily; Cetuximab: Intravenous Infusion 400mg/m2/250mg/m2 subsequent" is a clear and undoubted pointer that this is a clinical treatment protocol and not a product specification.

4.2. He would also contend that even otherwise there is nothing novel about any physical product in the present subject patent application. He would assert that Compound A is a known compound; Cetuximab is a known drug; Erlotinib is a known drug, Compound B is a known compound and all are available in a pharmacy which can be obtained by any person separately. Moreover, according to him, the appellant has not claimed any new physical product rather, what is claimed is the idea of giving these three known compounds/drugs to the same patient in sequence or simultaneously. Consequently, it is apparent that this is a treatment process and a therapy which is why the objections under Section 3(i) have not been met with by the appellant either before the respondent or even before this Court.

4.3. Learned CGSC would next contend that the claimed invention does not involve any inventive step as envisaged under Section 2(1)(ja) of the Act. He would emphasize that what the appellant has actually done is mosaicing and combining the teachings from the multiple prior art documents D-1 to D-4 and presented the same as the new invention which in view of the teachings in the prior arts document render the claim obvious. According to him, there is a clear motivation to combine them and a reasonable expectation of success. In order to justify the aforesaid submission, the learned

CGSC relied on the following table:

Label	Document Name	Subject Matter	Role in Analysis
D1	WO2011/025927 (Huang et al.)	B-Raf kinase inhibitors including Compound A (ENCORAFENIB) specifically. Discloses use in colorectal cancer.	Specifically discloses Compound A and its use for BRAF-mutant cancer. The only 'difference' between D1 and the claim is the EGFR inhibitor partner.
IPD2	WO2011/028540 / 1403/DELNP/2012 (Hatzivassiliou)	Discloses synergistic combination of a B-Raf inhibitor and EGFR inhibitor (erlotinib/cetuximab) for BRAF V600E cancers. Fig 32C: synergy of B-Raf inhibitor + erlotinib.	Specifically names erlotinib and cetuximab as combination partners for B-Raf inhibitors in BRAF V600E cancers. Provides in vivo data (Fig 34A/34B) showing efficacy of RAF inhibitor + erlotinib in the same colorectal xenograft model.
D3	WO2011/046894 (correctly cited)	MEK inhibitor + PI3K inhibitor combination.	Less relevant — but the Appellant's argument on D3 is moot given the strength of D1 + IPD2 + correct D4.
D4 (correct)	WO2010/029082 (Caravatti et al.)	Discloses synergistic combination of B-Raf inhibitor (Compound A specifically) + PI3K inhibitor (Compound B specifically) for BRAF-mutant colon cancer. Page 4 and 17: can be used WITH EGFR inhibitors erlotinib, cetuximab, panitumumab by name.	THE MOST IMPORTANT PRIOR ART. Discloses the triple combination explicitly — Compound A + Compound B + named EGFR inhibitors — for the same cancer.

4.4. On the basis of the aforesaid tables, learned CGSC would submit as under:

4.4.1. Prior arts D-1 and D-2 specifically disclose the specific B-Raf inhibitor of the claimed invention and generally disclose the combination with growth fact inhibitors and PI3K inhibitor.

4.4.2. Para 53-55 of the document at pg.308-310 of the appeal paperbook discloses the compounds that can be used in combination with one or more therapeutics such as growth factor inhibitors and PI3K inhibitors. The present subject application is covered by the prior art document D-2. In that, para 71 of the said document discloses of inhibitors of EGFR signalling like Erlotinib (TARCEVA), Gefitinib (IRESSA),

Lapatinib, Pelitinib, Cetuximab, Panitumumab, Zalutumumab, Nimotuzumab and Matuzumab.

4.4.3. If D-1, IPD-2 and D-4 are read together, person skilled in the art (PSITA) working on the B-Raf mutant colorectal cancer, would have been motivated to use the triple combination of compound A (encorafenib), EGFR inhibitor (Erlotinib/Cetuximab) and Compound B as the teaching is specifically taught and supported by experimental synergy data. This combined teaching has not been refuted by the appellant. All individual elements are known, combination thereof is specifically taught and the synergy is already demonstrated in the prior art for the same cancer in the same models.

4.5. In addition to the aforesaid argument, learned CGSC vehemently contended that the subject patent application is in the nature of ever greening of the compounds and the patents. He would contend that no monopoly should be granted for the reason that the invention is not a pharmaceutical product rather is a therapeutic regimen combining three separately available drugs and hence, non-patentable under Section 3(i) of the Act unlike the product saving carved out in European Patent Convention Article 53(c). He would contend that such an exception was not carved out deliberately by the legislature which was confirmed by the Supreme Court in ***Novartis AG v. Union of India: (2013) 6 SCC 1***.

4.6. Even on the merits of the inventive step, learned counsel would contend that the claimed combination is obvious over the prior art. In that, D-1 discloses compound A, specifically for B-Raf V600E Colorectal Cancer; IPDII discloses combining B-Raf

inhibitors with Cetuximab and Erlotinib for the same cancer with *in vivo* data from the same animal model. The Correct D-4 discloses the triple combination of Compound A, Compound B and EGFR inhibitors including Erlotinib and Ceturimab by name with synergic data. According to learned counsel, a person skilled in the art reading these documents would have every reason and expectation to combine these 3 known drugs for B-Raf mutant Colorectal Cancer. Predicated on the aforesaid, learned CGSC would emphatically submit that the results placed on record by the appellant are neither surprising nor unexpected. The prior arts already disclose synergy for this combination.

4.7. Learned CGSC next forcefully contended that even otherwise "public interest" constitutes an independent and compelling reason warranting refusal to grant patent. He relies upon the judgment of this Court in ***Zydus Lifesciences Ltd. v. ER Squibb & Sons LLC*****,** Neutral Citation: **2026:DHC:178-DB,** which according to him recognized that public interest in access to life saving medicines and health of the community is a paramount consideration that the Courts and the Controller must weigh while adjudicating pharmaceutical patent claims and that a grant of monopoly over a cancer treatment combination available to the patients would be contrary to such public interest. In other words, he would submit that a combination of three drugs already independently available for the treatment of Colorectal Cancer would directly impair patient access and the contrary to public interest. In that view of the matter, learned counsel would pray that the appeal be dismissed.

ANALYSIS AND CONCLUSION

5. This Court has heard the arguments of Ms. Shankar learned counsel for the appellant and Mr. Rohan Jaitley, learned CGSC for the respondent and examined the record.

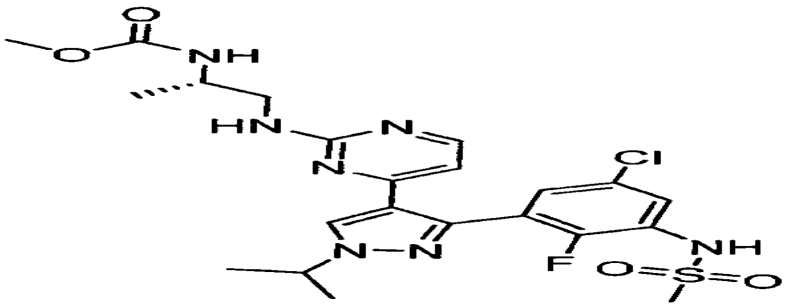
6. Before adverting to the merits of the appeal, it would be apposite to understand the nature of the claimed invention. The CS of the subject application, claims that the present invention pertains to a combination of a B-Raf kinase inhibitor and an Epidermal Growth Factor Receptor (EGFR), which is also known as ErbB-1 or HER-1 inhibitor and, optionally a third inhibitor, a phosphatidylinositol 3-kinase (PI3-kinases or PI3K), and is used for the treatment of proliferative diseases. The field of invention of the subject application is reproduced as follows:

> *"FIELD OF THE INVENTION*
> *A combination of a B-Raf kinase inhibitor and an epidermal growth factor receptor (EGFR also known as ErbB-1 or HER-1) inhibitor and, optionally, a phosphatidylinositol 3-kinase (PI 3-kinases or PI3K) inhibitor which is used for the treatment of proliferative diseases. This invention also relates to the uses of such a combination in the treatment of proliferative diseases; to pharmaceutical compositions of the combination of agents and methods of treating a subject suffering from a proliferative disease comprising administering a therapeutically effective amount of such a combination to the subject."*

7. The present invention under the subject application is useful for separate as well as simultaneous/ sequential administration to a subject who requires it for the treatment or prevention of a proliferative disease. For better understanding, the summary of the invention is reproduced as follows:

> *"SUMMARY OF THE INVENTION*
> *The present invention relates to a therapeutic combination comprising: (a) a B-Raf inhibitor, (b) an EGFR inhibitor and, optionally, (c) a PBK inhibitor, useful for separate, simultaneous or sequential administration to a subject in need thereof for treating or preventing a proliferative disease. The present invention especially relates to a therapeutic combination*

comprising: (a) a B-Raf inhibitor of the formula"



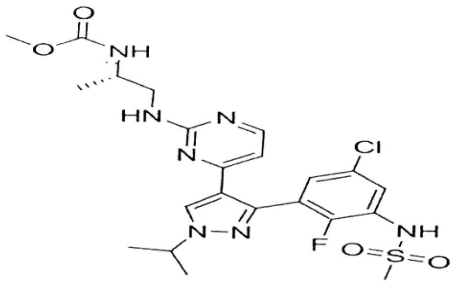
or a pharmaceutically acceptable salt thereof (hereinafter referred to as Compound A), (b) an EGFR inhibitor, and, optionally, (c) a PI3K inhibitor.

8. The dual combination claimed under claim 1 of the subject application comprises B-Raf inhibitor Compound A (Encorafenib) which is a B-Raf Inhibitor and Cetuximab/Erlotinib (EGFR inhibitor). Further, optionally, claim 1 also claims a triple recombination of the compounds. The triple recombination comprises of Compound A (Encorafenib) which is a B-Raf inhibitor, Cetuximab/Erlotinib (EGFR inhibitor), and the third compound which is Compound B (PI3K-α inhibitor). Claim 1 of the present invention is as follows:

We claim:

1. A pharmaceutical combination comprising:

(a) a B-Raf inhibitor of the formula

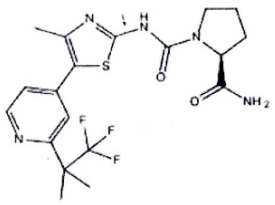


(Compound A)

or a pharmaceutically acceptable salt thereof,

(b) an EGFR inhibitor, wherein the EGFR inhibitor is cetuximab or erlotinib and, optionally,

(c) a PI3K-a inhibitor, wherein the PI3K-a inhibitor is a compound B of Formula (Compound B)



(Compound B)

or a pharmaceutically acceptable salt thereof

for simultaneous, separate or sequential administration.

2. A combination as claimed in claim 1 wherein the EGFR inhibitor is erlotinib.

3. A combination as claimed in claim 1, wherein the EGFR inhibitor is cetuximab.

4. A combination as claimed in claim 1 wherein the EGFR inhibitor is cetuximab.

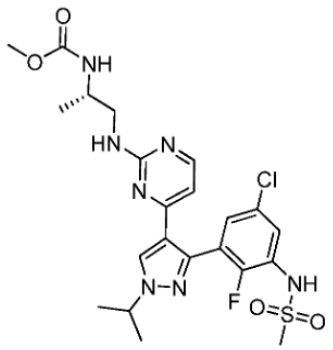
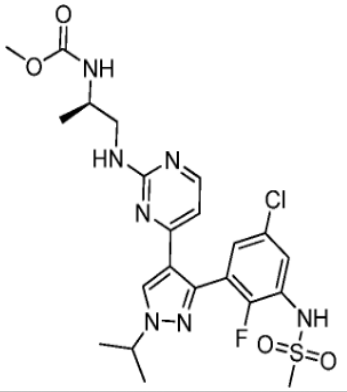
9. Having noted the invention claimed, it may be necessary for this Court to now examine the prior arts which were relied upon by the respondent in the impugned order to refuse grant of patent.

PRIOR ART D1

10. The claimed invention under the Prior art D1 (W02011025927) provides a novel class of compounds of formula I and pharmaceutical compositions comprising such compounds and methods of using these

compounds to treat/ prevent diseases associated with abnormal/deregulated kinase activity, specifically diseases/disorders that involve abnormal activation of B-Raf.

11. D1 discloses compounds of Formula I. The specific compounds 9, 20 disclosed in Table 1 of D1 which are reproduced as follows:

9		0.002	0.0003	^{1}H NMR 400 MHz (CD_3OD) δ 8.41 (s, 1H), 8.08 (d, *J*= 5.6 Hz, 1H), 7.57 (dd, *J*= 6.4, 2.6 Hz, 1H), 7.34 (dd, *J*= 5.6, 2.6 Hz, 1H), 6.65 (brs, 1H), 4.63 (hept, *J*= 6.8 Hz, 1H), 3.62-3.68 (m, 1H), 3.57 (s, 3H), 3.40-3.44 (m; 1H), 3.32-3.36 (m, 1H), 3.00 (s, 3H), 1.58 (d, *J*= 6.8 Hz, 6H), 1.02 (d, *J*= 4.8 Hz, 3H).MS *m/z* 540.1 (M + 1)
20		0.007	0.0008	MS *m/z* 540.2 (M + 1)

12. D1 under Para [0027] and [0047] discloses B-raf kinases which can be used to treat kinase-related diseases. D1 under para [0047] also discloses that the development of a kinase inhibitor for B-Raf leads to a new therapeutic opportunity for treatment of several types of human cancers such as metastatic melanomas, solid tumours, brain tumours such as Glioblastoma multiforme (GBM), etc. The relevant paras are reproduced

as follows:

> *"[0027] The present invention provides compounds, compositions and methods for the treatment of kinase related disease, particularly B-Raf kinase related diseases; for example, metastatic melanomas, solid tumors, brain tumors such as Glioblastoma multiform (GBM), acute myelogenous leukemia (AML), prostate cancer, gastric cancer, papillary thyroid carcinoma, ovarian low-grade carcinoma, and colorectal cancer.*
>
> *[0047]* ***Therefore, development of a kinase inhibitor for B-Raf provides a new therapeutic opportunity for treatment of many types of human cancers, especially for metastatic melanomas, solid tumors, brain tumors such as Glioblastoma multiform (GBM), acute myelogenous leukemia (AML), lung cancer; papillary thyroid carcinoma, ovarian lowgrade carcinoma, and colorectal cancer****. Several Raf kinase inhibitors have been described as exhibiting efficacy in inhibiting tumor cell proliferation in vitro and/or in vivo assays (see, for example, U.S. Pat. Nos. 6,391,636, 6,358,932, 6,037,136, 5,717,100, 6,458,813, 6,204,467, and 6,268,391). Other patents and patent applications suggest the use of Raf kinase inhibitors for treating leukemia (see, for example, U.S. Patent Nos. 6,268,391, 6,204,467, 6,756,410, and 6,281,193; and abandoned U.S. Patent Application Nos. 20020137774 and 20010006975), or for treating breast cancer (see, for example, U.S. Patent Nos. 6,358,932, 5,717,100, 6,458,813, 6,268,391, 6,204,467 and 6,911,446). Data demonstrates that Raf kinase inhibitors can significantly inhibit signaling through the MAPK pathway, leading to dramatic shrinkage in B-Raf (V600E) tumors."*

[emphasis suppled]

13. Para 50 of D1 discloses that compounds of the invention need to be administered in therapeutically effective amounts, via any of the usual and acceptable modes known in the art, either singly or in combination with one or more therapeutic agents. Para 53 to 55 of D1 also discloses the same issue. Para 61 notes that such administration provides therapeutically effective levels of the 2 compounds in the body of the patient. For the purpose of convenience, the contents of para [0050] and para [0053] to [0055] and [0061] are reproduced as follows:

> *"[0050] In general, compounds of the invention will be administered in therapeutically effective amounts via any of the usual and acceptable modes known in the art, either singly or in combination with one or more therapeutic agents. A therapeutically effective amount may vary widely depending on the severity of the disease, the age and relative health of the*

subject, the potency of the compound used and other factors. In general, satisfactory results are indicated to be obtained systemically at daily dosages of from about 0.03 to 30mg/kg per body weight. An indicated daily dosage in the larger mammal, e.g. humans, is in the range from about 0.5mg to about 2000mg, conveniently administered, e.g. in divided doses up to four times a day or in retard form. Suitable unit dosage forms for oral administration comprise from ca. 1 to 500mg active ingredient.

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

[0053] Compounds of the invention can be administered in therapeutically effective amounts in combination with one or more therapeutic agents (pharmaceutical combinations). For example, synergistic effects can occur with other anti-tumor or antiproliferative agents, for example, mitotic inhibitors, alkylating agents, anti-metabolites, intercalating antibiotics, growth factor inhibitors, cell cycle inhibitors, enzymes, topoisomerase inhibitors, biological response modifiers, antibodies, cytotoxics, antihormones, anti-androgens, an anti- angiogenesis agent, kinase inhibitor, pan kinase inhibitor or growth factor inhibitor.

[0054] Compounds of the invention can be administered in therapeutically effective amounts in combination with one or more suitable excipients selected from com starch, potato starch, tapioca starch, starch paste, pre-gelatinized starch, sugars, gelatin, natural gums, synthetic gums, sodium alginate, alginic acid, tragacanth, guar gum, cellulose, ethyl cellulose, cellulose acetate, carboxymethyl cellulose calcium, sodium carboxymethylcellulose, methyl cellulose, hydroxypropyl methylcellulose, microcrystalline cellulose, magnesium aluminum silicate, polyvinyl pyrrolidone, talc, calcium carbonate, powdered cellulose, dextrates, kaolin, mannitol, silicic acid, sorbitol, agar-agar, sodium carbonate, croscarmellose sodium, crospovidone, polacrilin potassium, sodium starch glycolate, clays, sodium stearate, calcium stearate, magnesium stearate, stearic acid, mineral oil, light mineral oil, glycerin, sorbitol, mannitol, polyethylene glycol, other glycols, sodium lauryl sulfate, hydrogenated vegetable oil, peanut oil, cottonseed oil, sunflower oil, sesame oil, olive oil, com oil, soybean oil, zinc stearate, sodium oleate, ethyl oleate, ethyl laureate, silica, and combinations thereof.

[0055] An embodiment of the invention is a method of claim 12 or 13, further comprising administering to the subject an additional therapeutic agent. The additional therapeutic agent comprises an anticancer drug, a pain medication, an antiemetic, an antidepressant or an anti-inflammatory agent. Further, the additional therapeutic agent is a different Raf kinase inhibitor or an inhibitor of MEK, mTOR, HSP90, AKT, PI3K, CDK9, PAK, Protein Kinase C, a MAP kinase, a MAPK Kinase, or ERK and is administered to the subject concurrently with a compound of the invention.

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

[0061] The term "pharmaceutical combination" as used herein means a

product that results from the mixing or combining of more than one active ingredient and includes both fixed and non-fixed combinations of the active ingredients. The term "fixed combination" means that the active ingredients, e.g. a compound of Formula I and a coagent, are both administered to a patient simultaneously in the form of a single entity or dosage. The term "non-fixed combination" means that the active ingredients, e.g. a compound of Formula I and a co-agent, are both administered to a patient as separate entities either simultaneously, concurrently or sequentially with no specific time limits, wherein such administration provides therapeutically effective levels of the 2 compounds in the body of the patient. The latter also applies to cocktail therapy, e.g. the administration of 3 or more active ingredients."

14. It is to be noted that compound A of claimed invention is disclosed in para 43 of D1 as compound 9, namely, ((S)-methyl 1-(4-(3-(5-chloro-2-fluoro-3-(methylsulfonamido)phenyl)-1-isopropyl -lH-pyrazol-4-yl)pyrimidin-2-ylamino)propan-2- ylcarbamate).

15. Additionally, it would be significant to note that para 55 of D1 specifies the additional inhibitor as an inhibitor of MEK, mTOR, HSP90, AKT, CDK9, PAK, Protein Kinase C, a MAP kinase, a MAPK Kinase, or ERK, including the PI3K inhibitor, however does not at all disclose PI3k-α inhibitor which is specified in Claim 1 of the claimed invention.

PRIOR ART D2

16. Prior art D2 or IPD2 (1403/DELNP/2012) is titled as "*DETERMINING SENSITIVITY OF CELLS TO B-RAF INHIBITOR TREATMENT BY DETECTING KRAS MUTATION AND RTK EXPRESSION LEVELS*" and pertains to cancer diagnostics and therapies and specifically to the detection of mutations or RTK overexpression that are diagnostic and/or prognostic and correlating the detection with treatment of cancer.

17. Under para 56, D2 discloses administering an effective amount of an inhibitor of EGFR signaling in combination with a B-Raf inhibitor. For the purpose of clarity, para 56 is reproduced as follows:

> *"[0056] In one embodiment, the subject matter disclosed herein relates to a method of identifying a patient nonresponsive to treatment with a B-Raf inhibitor, comprising determining the presence or absence of a K-ras mutation, whereby the presence of a K-ras mutation indicates a patient will not respond to said B-Raf inhibitor treatment. In one example, the method further comprises administering an effective amount of a MEK or ERK inhibitor to said nonresponsive patient. In another example, the method further comprises administering an effective amount of an inhibitor of EGFR signalling. In another example, the method further comprises administering an effective amount of an inhibitor of EGFR signaling in combination with a B-Raf inhibitor."*

18. Further, under para 71 and 72, D2 notes that EGFR signalling is known in the art and includes erlotinib (TARCEVA®), gefitinib (IRESSA®), Cetuximab etc., among others. Para 71 of D2 also discloses erlotinib/ Cetuximab. Further, para 72 discloses some B-Raf inhibitors, but the inhibitor Encorafenib is not disclosed in D2. The paragraphs 71 and 72 and other relevant para 69 and 70 are reproduced as follows:

> *"[0069] In certain embodiments, for those samples, tumors, cancers, subjects or patients determined to be unresponsive to a B-Raf inhibitor, the methods further comprise administering an effective amount of a ERK inhibitor to said unresponsive samples, tumors, cancers, subjects or patients. In another example, the method further comprise_s administering an effective amount of an inhibitor of EGFR signaling. In another example, the method further comprises administering an effective amount of an inhibitor of EGFR signaling in combination with a B-Raf inhibitor.*
> *[0070) EGFR signaling can be inhibited by a variety of methods, including inhibiting EGFR kinase activity, binding to the extracellular domain of EGFR to inhibit activation or by inhibiting the activity and signaling of EGF ligand.*
> *[0071) Inhibitors of EGFR signaling are known in the art and include, for example, erlotinib (TARCEVA®), gefitinib (IRESSA®), lapatinib, pelitinib, Cetuximab, panitumumab, zalutumumab, nimotuzumab and matuzumab, and those described in U.S. Pat. No. 5,747,498.*
> *[0072] B-Raf inhibitors are known in the art and include, for example, sorafenib, PLX4720, :PLX-3603, GSK2II8436, GDC-0879, N-(3-(5-(4-chlorophenyl)-I H-pyrrolo[2,3-b]pyridine-3-carbonyl)-2,4-difluorophenyl)propane-l-sulfonamide, and those described in WO2007/002325, WO2007/002433, WO2009111278, WO2009111279, WO2009ll1277, WO20091 l 1280 and U.S. Pat. No. 7,491,829.*

19. Additionally, para [0019] of the D2 specifies that the invention therein, relates to methods of treating a tumour which is non-responsive to

B-Raf inhibitor treatment. The said para further specifies that the methods include administering a B-Raf inhibitor in combination with an EGFR inhibitor. Further, it is important to note that although para 71 of D2 specifies the inhibitor erlotinib/ Cetuximab individually, however, not the combination thereof. It is observed in paragraph 19 of D2 that EGFR inhibitors are mentioned in combination with B-raf inhibitor, but it is only EGFR inhibitors in general and not erlotinib/ Cetuximab specifically. Further, the para [0019] only notes the B-raf inhibitor, and does not specify the B-raf inhibitor, which is claimed in the present invention. Further, the para [0072], while disclosing the various types of B-Raf inhibitors, also does not specify Encorafenib/Compound A of the present invention.

20. D2 under para 51, specifies the combination of the *RAF inh a* and Erlotinib (Tarceva) administered to Mice and notes the increased efficacy. As given under para [0041] of D2, the RAF inhibitor used in para 51 is *RAF inh a* which is 2,6-difluoro-N-(3-methoxy-IH-pyrazolo[3,4-b]pyridin-5-yl)-3- (propylsulfonamido)benzamide). The said *RAF inh a* is different from the Encorafenib as claimed under claim 1 of the claimed invention of the subject application.

PRIOR ART D3

21. The invention under prior art D3 (WO 2011/046894 Al) relates to a method of treating cancer in a mammal and to combinations useful in such treatment. In particular, the method relates to a novel combination comprising the B-Raf inhibitor: N-{3-[5-(2-amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol -4-yl]-2-fluorophenyl}-2,6-difluorobenzenesulfonamide, (or it's pharmaceutically acceptable salt or solvate thereof), and the PI3K inhibitor:2,4-difluoro-N{2-(methyloxy)-5-[4-(4-pyridazinyl)-6 -quinolinyl]-3-pyridinyl}benzenesulfonamide, (or it's

pharmaceutically acceptable salt thereof), or pharmaceutical compositions comprising the same, as well as methods of using such combinations in the treatment of cancer. Under Table 1, the D3 discusses the following:

Table 1. Scores Panel of colon cancer cell lines used in combination studies.

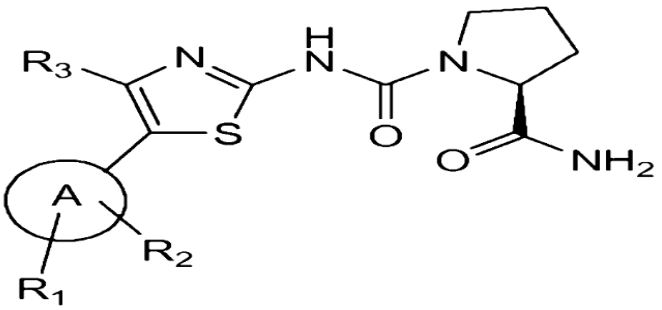
Cell Line	Diagnosis/Histology	KRAS	PIK3CA	BRAF	PTEN
HT29	Carcinoma	WT	1345C>A	1799T>A	WT
SW948	Adenocarcinoma	182A>T	1624G>A	WT	WT
T84	Carcinoma	38G>A	1624G>A	WT	WT
HCT15	Adenocarcinoma	38G>A	1633G>A	WT	WT
HCT8	Adenocarcinoma	38G>A	1633G>A	WT	WT
DLD1	Carcinoma	38G>A	1633G>A	WT	WT
NCIH508	Adenocarcinoma	WT	1633G>A	1786G>C	WT
LS174T	Adenocarcinoma	35G>A	3140A>G	WT	WT
HCT116	Carcinoma	38G>A	3140A>G	WT	WT
RKO	Carcinoma	WT	3140A>G	1799T>A	WT
SW1463	Carcinoma	34G>T	WT	WT	WT
SW837	Adenocarcinoma	34G>T	WT	WT	WT
SW1116	Carcinoma	35G>C	WT	WT	WT
SW480	Adenocarcinoma	35G>T	WT	WT	WT
SW403	Carcinoma	35G>T	WT	WT	WT
NCIH747	Adenocarcinoma	38G>A	WT	WT	WT
LS1034	Adenocarcinoma	436G>A	WT	WT	WT
HCC2998	Carcinoma	436G>A	WT	WT	WT
NCIH716	Adenocarcinoma	WT	WT	WT	WT
NCIH630	Adenocarcinoma	WT	WT	WT	WT
KM12	Adenocarcinoma	WT	WT	WT	800delA, 385G>T
SW48	Adenocarcinoma	WT	WT	WT	WT
COLO320DM	Adenocarcinoma	WT	WT	WT	WT
COLO205	Adenocarcinoma	WT	WT	1799T>A	WT
SW1417	Adenocarcinoma	WT	WT	1799T>A	WT

Table 1 key
Cell Line = Cell line name
Diagnosis/Histology = Pathological diagnosis of tissue
KRAS/BRAF/PIK3CA/PTEN = Mutation status. WT = Wild Type

22. Page 4 of the D3 specifies that Inhibitor PI3K isoforms, particularly PI3K-α, are known to be useful in the treatment of cancer. It is important to note that the invention under D3, is a combination of B-Raf inhibitor dabrafenib not encorafenib on one hand, and PI3K inhibitor not PI3K-α inhibitor namely, *alpelisib,* on the other.

PRIOR ART D4

23. Prior art D4 (WO 2011/029082) relates to the following compound of formula (I), which includes some provided substituents, to compositions and use of the compounds in the treatment of diseases ameliorated by inhibition of phosphatidylinositol 3-kinase.



24. Document D4 discloses (page10) PI3K-α inhibitors of the invention for treating proliferative diseases, including color. Page 30 of D4, discloses the combination of EGFR and PI3K/Akt in the following language:

> *"....Furthermore, in an in vitro model of breast cancer with a cell line that harbors a PTEN mutation and over-expresses EGFR inhibition of both the PI3K/Akt pathway and EGFR produced a synergistic effect (She et al., Cancer Cell 8:287-297(2005)). These results indicate that the combination of gefitinib and PI3K/Akt pathway inhibitors would be an attractive therapeutic strategy in cancer."*

It is significant to note that, the above mentioned para of D4 does not specify the EGFR inhibitor as claimed in the subject application. Further, this combination also fails to specify the PI3K-α inhibitor as claimed in Claim 1 of the claimed invention.

25. Predicated on the aforesaid observations in prior arts D1 to D4, in conclusion it can be inferred that the combination of two compounds, that is Compound A and Compound B, as specified in Claim 1 of subject application is not disclosed in any of the prior arts D1 to D4. Though, D1 discloses B Raf inhibitor of formula 1 as claimed in the present invention apart from also disclosing the combination of B Raf and PI3K inhibitor, yet, this combination under D1, does not specify the PI3K-α inhibitor as claimed in the present invention.

26. As observed and noted above, though, the prior art D2, under para 71 discloses Erlotinib/Cetuximab and B-Raf inhibitors, however, the inhibitor Encorafenib is not disclosed. It is relevant to note that the invention

claimed under D3 is a combination of B-Raf inhibitor - dabrafenib and not Encorafenib on one hand and inhibitor PI3K and not PI3K-α, on the other. However, it must be accepted that page 4 of prior art D3 discloses the inhibitor PI3K-α and its use for the treatment of cancer. At page 30, the D4, discloses the combination of EGFR and PI3K/Akt, however, does not specify either the EGFR inhibitor or PI3Kα inhibitor as claimed in the subject application.

27. As cited earlier, para 69 of D2 discusses the method for subjects/patients unresponsive to B-raf inhibitors. The para further discloses 3 other methods which are (i) administering an effective amount of an ERK inhibitor, (ii) administering an effective amount of an inhibitor of EGFR signaling, and (iii) administering an effective amount of an inhibitor of EGFR signaling in combination with a B-Raf inhibitor. Thereafter, para 70 of D2 discusses the methods for inhibiting EGFR signalling. The methods under this para are inhibiting EGFR kinase activity, binding to the extracellular domain of EGFR to inhibit activation or by inhibiting the activity and signaling of EGF ligand. Under para 71, D2 discloses the Inhibitors of EGFR signaling including Erlotinib and Cetuximab. Reading para 70 and 71 together, it is clear that Erlotinib and Cetuximab are mentioned in terms of the methods for inhibiting EGFR signalling.

28. As discussed in earlier, the title and field of the invention of D2 states that the said invention particularly relates to the detection of mutations or RTK overexpression that are diagnostic and/or prognostic and correlating the detection with cancer treatment. In such a case, it becomes crucial to discuss such motivation/teaching to choose the specific compounds of the combination claimed under claim 1 of the present

invention. The impugned order completely failed to discuss that how the Person Skilled in the Art would be motivated to choose the claimed compounds, i.e., Compound-A (Encorafenib) and Erlotinib / Cetuximab (from D2 or any other cited prior arts) to apply it to the combination mentioned under para 19 of D2.

29. Similarly, D4 at page 30 para 14 discusses the synergy between EGFR and PI3K/Atk pathway, without specifying the claimed compounds of present invention. Therefore, the submission of the respondent as mentioned under para 4.4.3 above that D4 discloses all the 3 compounds as claimed in claim 1 of the present invention, cannot be accepted. Thus it can be safely inferred that none of the cited prior art D1 to D4 specify the combination of compound A (B-Raf Inhibitor), Encorafenib, and Erlotinib/Cetuximab (EGFR inhibitor). Further, the prior arts D1 to D4 also fail to disclose the combination of compound A (B-Raf Inhibitor), Encorafenib, and EGFR inhibitors Erlotinib or Cetuximab and optionally, Compound B, i.e. PI3K-α inhibitor (alpelisib).

30. Having reached the aforesaid conclusion in respect of the prior arts D1 to D4, this Court would now examine the other limb of the impugned order in respect of technical advancement. While discussing the technical advancement of the subject application, the impugned order notes the following Table cited by the appellant in the CS of the present invention:

Grp	n	Treatment Regimen				Mean Volume, mm^3			T/C or T/T_0	Statistical Significance					Regressions		Mean BW Nadir	Deaths	
		Agent	mg/kg	Route	Schedule	Day 1	Day 29	Change		vs G1	vs G2	vs G3	vs G4	vs G8	PR	CR		T R	N T R
1	10	Vehicle 1 Vehicle 2	--- ---	po po	bid x 28 qd x 28	122	1065	943	---	---	---	---	---	---	0	0	-0.6% Day 8	0	0
2	10	Cpd. A	20	po	bid x 28	122	1016	894	95%	ns	---	---	---	---	0	0	-0.1% Day 8	0	0
3	10	Cpd B	25	po	qd x 28	122	660	538	57%	ns	---	---	---	---	0	0	-2.5% Day 8	0	0
4	10	Cetuximab	20	ip	biwk x 4	125	955	830	88%	ns	---	---	---	---	0	0	-1.2% Day 8	0	0
5	10	Cpd. A Cpd. B	20 25	po po	bid x 28 qd x 28	125	491	366	39%	ns	ns	ns	---	***	0	0	-0.7% Day 4	0	0
6	10	Cpd.A Cetuximab	20 20	po ip	bid x 28 biwk x 4	125	239	114	12%	**	**	---	**	ns	0	0	---	0	0
7	10	Cpd B Cetuximab	25 20	po ip	qd x 28 biwk x 4	125	584	459	49%	ns	---	ns	ns	***	0	0	-1.4% Day 4	0	0
8	10	Cpd A Cpd. B Cetuximab	20 25 20	po po ip	bid x 28 qd x 28 biwk x 4	123	120	-3	-2%	***	***	**	***	---	0	0	---	0	0
9	10	Paclitaxel	30	iv	qod x 5	122	229	107	11%	**	---	---	---	---	0	0	-10.1% Day 11	0	0

31. Examples 2 and 3 of the claimed invention provide the data from the clinical studies which, according to the appellant, indicate that the tumor growth from day 1 to day 29 was reduced in group 6 and there was regression in group 8. The dual combination of Compound A with Cetuximab when administered on Group 6, slowed down the tumour progression to 12% and significant inhibition. The table shows the improvement in combination upon Compound A monotherapy in Group 2 (95%) and Cetuximab monotherapy in Group 4 (88%). Similarly, the triple combination of Compound A, Compound B, and Cetuximab when administered on Group 8, resulted in tumor regression by -2%. This treatment shows improvement upon Compound A monotherapy in Group 2 (95%), Compound B monotherapy in Group 3 (57%), and Cetuximab monotherapy in Group 4 (88%).

32. Based on the above-mentioned data, the impugned order notes that the cited prior arts also disclose similar combinations relying upon the data cited in the documents D2 and D3. The impugned order also relied on the data contained in Tables 2, 3 and 4 from D3.

33. It may be relevant at this stage to also examine Table 2 of D3 which discloses the synergy and cytotoxicity data of the combined dosing of

Compounds A & B for colon cancer cell lines. Table 2 contains the combination of the PI3K inhibitor (Compound B) and the BRAF inhibitor (Compound A). As per the page 21 of D3, Compound A is "N-{3-[5-(2-amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol -4-yl]-2-fluorophenyl}-2,6-difluorobenzenesulfon amide", which is not Encorafenib, the inhibitor as claimed under claim 1 of the subject invention of the subject application. Similarly, Compound B used under Table 2 of D3 is "2,4-difluoro-N- {2-(methyloxy) -5-[4- (4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide", which is Omipalisib and not Cetuximab/Erlotinib, the EGFR as claimed in claim 1 of the subject invention. Similarly, the combination in the prior art is the same as noted above and the results under Table 3 and 4 on pages 30 and 34 respectively of D3, are also the same.

34. In order to analyse and conclude that the claimed invention has not been able to demonstrate enhanced efficacy in comparison to the prior arts, the respondent also relied upon Figure 34B of D2, noting thereby that an increased efficacy was observed when both compounds were administered in combination. However, as discussed above, under prior art D2, as per para [0041], the RAF inhibitor used in para 51 is "*RAF inh a*" {2,6-difluoro-N-(3-methoxy-IH-pyrazolo[3,4-b]pyridin-5-yl)-3-(propylsulf-onamido)benzamide)} which is different from Encorafenib as claimed under claim 1 of the present invention of the subject application. The data shown in Figures 34A and 34B is based on the result of the same experiment.

35. The impugned order, based on the abovementioned data from D2 and D3, rejects the enhanced efficacy provided under examples 2 and 3 of the CS of subject application however, fatally, does not discuss that the

compounds used are BRAF and PI3K-α inhibitors which are not the same as disclosed in prior arts D1 to D4. Similarly, the submission of the respondent that D1, D2/IPD2 and D4 read together would teach PSITA to come to the claimed triple combination, is without any explanation as to what para/part of D1, D2 and D4 teaches to combine the 3 claimed compounds.

36. Therefore, based on the above discussion, this Court is not satisfied with the reasoning given under the objection of lack of inventive step in the impugned order.

Objection under Section 3 (d) of the Act:

37. As noted above, Claim 1 of the present invention claims a pharmaceutical combination which comprises a B-Raf inhibitor of Compound A (or a pharmaceutically acceptable salt) and an EGFR inhibitor (Cetuximab or Erlotinib) and optionally a PI3K-α inhibitor (Compound B).

38. The impugned order states that the claimed compound is derivative of the known compounds and therefore not allowable under Section 3(d) of the Act. For clarity, Section 3 (d) of the Act is reproduced hereunder:

> *"(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 they differ significantly in properties with regard to efficacy;"*

39. In regard to the above, it would be apposite to consider the following reasoning provided in the impugned order on non-patentability under Section 3 (d) of the Act:

> *"5.3. Section 3(d) of Patents Act, 1970:*
> *Claims 1-4 refer to a pharmaceutical combination comprising (a) a 8-Raf inhibitor of the formula or a pharmaceutically acceptable salt thereof, (b) an EGFR inhibitor, wherein me EGFR inhibitor is cetuximab or erlotinib, and, optionally (c) a PI3K-a inhibitor, wherein the PI3K-a inhibitor is a compound of Formula (1).*
> *It is observed that the submission of the agents for the applicants have focused on the efficacy of the combination as per table 1 at page 32 of the specification. However, it has been shown in the subsequent sections, (especially lack of inventive step) that such combinations are known from the prior art arts. In view of the same, the claims of the invention fall u/s 3(d) of Patents Act, 1970.*
>
> *A5.8. Non- patentability u/s 3(d) of Patents Act, 1970: The claimed invention refers to a pharmaceutical combination comprising (a) a B - Raf inhibitor of the formula or a pharmaceutically acceptable salt thereof, (b) an EGFR inhibitor, wherein the EGFR inhibitor is cetuximab or erlotinib, and, optionally (c) a PI3K-a inhibitor, wherein the PI3K-a inhibitor is a compound of Formula (I). The agents for the applicant has shown table 1 at page 32 of the specification to show efficacy of the claimed combination, however, such combinations and the results are known from the prior art (see para on lack of inventive step u/ s 2(1)(ja) of Patents Act, 1970. Hence, the pharmaceutical combination of the present application falls u/ s 3(d) of the Patents Act, 1970."*

40. Contrary to the reasoning of the learned Controller, the appellant submitted that the present invention does not fall under Section 3(d) of the Act as it is a claimed combination of two or three pharmacologically active specific agents, that is, a B-Raf inhibitor, an EGFR inhibitor, and an optional PI3K-α inhibitor and that none which is a new form, salt, ester, ether, polymorph, metabolite, isomer, or derivative of any known substance referred to in the prior art. As per the appellant, the present invention is a combination of distinct, independent active pharmaceutical agents. The impugned order states that such combinations are disclosed under the cited

prior art, without specifying the known compounds.

41. Further, assuming that the learned Controller is considering the individual compound of the combination as a known derivative, such consideration has been rejected by the Calcutta High Court in ***Topotarget UK Limited v. Controller General of Patents and Designs, Mumbai & Ors. (IPDPTA/50/2023)***. The Calcutta High Court emphasised that under Section 3(d) of the Act, a combination of two separate active drugs cannot be treated as derivatives of each other and therefore fall outside the scope of Section 3(d) entirely. The relevant para is reproduced as follows:

> *"Para 13: Section 3(d) is only applicable when the invention is a new form of a single known substance and is put to the test of "therapeutic efficacy". Section 3(d) is also applicable to combinations involving derivatives of a known substance whether alone or with the known substance itself. A combination of two separate active drugs cannot be treated as derivatives of each other and therefore do not fall within the scope of section 3(d) of the Act. In the present case, the appellant had claimed that the invention is directed towards a composition and not a salt of PXD-101. Arginine and meglumine are inactive ingredients and not derivatives of PXD-101. In such circumstances, the invention was claimed to be a multi-component composition and fell outside the scope and ambit of section 3(d) of the Act. This aspect of the matter has not even been dealt with in the impugned order and vitiates the finding under section 3(d) of the Act."*

42. Applying the aforesaid proposition it is clear that the learned Controller has erroneously presumed the known compound from the compounds disclosed under the cited prior art, which was neither specified nor identified in the impugned order.

43. Learned controller, so far as efficacy and combinations are concerned, has relied on the reasoning given under the objection of lack of inventive step. However, it is significant to note that even the reasons furnished for sustaining objections under section 2 (1) (ja) of the Act, also do not identify the known compound. Additionally, this Court has already rejected the objections raised under section 2(1)(ja) of the Act in the

preceding paragraphs. Therefore, it can be inferred that the "known compound" in the cited prior art is not identified by the learned Controller.

44. Thus, this Court is unable to agree with the reasoning provided by the learned Controller under the objection of non-patentability under Section 3(d) of the Act.

Objection under Section 3 (i) of the Act:

45. The reasoning provided under the objection of non-patentability under Section 3 (i) of the Act in the impugned order is as follows:

> *"Section 3(i) of Patents Act, 1970: I •*
> *Since no amendment to the claims have been carried-out, I refer to the objection raised in the hearing letter and reiterate the same:*
> *The amended claims relate to therapy and method of treatment and falls u/ s 3(i) of Patents Act, 1970. The amended claims filed in response to the submission by the agents for the applicant reads as follows :*
> *"A pharmaceutical combination comprising: (a) a B-Raf inhibitor of the formula· (Compound A) or a pharmaceutically acceptable salt thereof, (b) an EGFR inhibitor, wherein the EGFR inhibitor is cetuximab or erlotinib and, optionally, (c) a PI3K-a inhibitor, wherein the PI3K-a inhibitor is a compound B of Formula (Compound B) or a pharmaceutically acceptable salt thereof for simultaneous , separate or sequential administration. Claims fall u/ s 3(i) of the Patents Act, 1970 since the invention relates to a- ,"combination therapy" . The specification also clearly mentions on page 22; the dose and treatment schedule which clearly shows that the triple combination is a method of treatment and falls within the ambit of combinational therapy. The contents on this page is provided for ready reference:*
> *"Compound A Capsule for oral use as assigned once or twice daily Compound B Tablet for oral use as assigned once or twice daily Cetuximab Intravenous infusion 400 mg/m2 initial infusion/ 250 mg/m2 subsequent infusions". The inventive aspect lies in the · therapy and treatment and thus falls u/ s 3(i) of Patents Act, 1970.*
> *• It is noted that the agents for the applicants have provided the following in the response regarding this objection:* "Section 3(i) is not applicable to the present application as claims of the present application are directed to pharmaceutical combination. The ultimate use in treatment of cancer is only its industrial application and therefore Section 3(i) by no stretch of imagination is attracted".
> *• The response provided by the agents for the applicant is not sufficient to overcome this objection since the submission does not provide any evidence which proves contrary to the objection raised in the hearing letter.*

It maybe noted that since this objection is still not met and is maintained, the application can be refused solely on this basis.
Notwithstanding the above, I provide my analysis and interpretation on the other objections raised in the hearing letter."

46. Contrary to the reasoning of the learned Controller, the appellant submits that the claims of the subject application are product claims directed to a "pharmaceutical combination" and not to a method of treatment of human beings. Learned counsel for the appellant would submit that the independent claim 1 is for a pharmaceutical combination and unambiguously is a product claim.

47. For clarity, Section 3 (i) of the Act is reproduced as follows:

(i) any process for the medicinal, surgical, curative, prophylactic diagnostic, therapeutic or other treatment of human beings or any process for a similar treatment of animals to render them free of disease or to increase their economic value or that of their products."

48. While reading the expression "*for simultaneous, separate or sequential administration*" under Claim 1 of the subject application in the light of its CS, it is clear that same is a functional descriptor of the claimed pharmaceutical combination and not a method step. It describes the range of ways in which the constituent actives, as a defined combination, may be administered without transforming the product into a method. This phrase does not impose or claim any particular therapeutic protocol, physician intervention, or sequential step.

49. The learned controller relied on the paragraph taken from example 1 of CS of the subject application, which describes the treatment schedule of the study as under:

"Compound A Capsule for oral use as assigned once or twice daily Compound B Tablet for oral use as assigned once or twice daily Cetuximab Intravenous infusion 400 mg/m2 initial infusion/ 250 mg/m2 subsequent infusions". The inventive aspect lies in the · therapy and treatment and thus falls u/ s 3(i) of Patents Act, 1970."

50. It is trite that working examples are provided by the patentee to demonstrate the workability and practical implementation of the claimed invention. For any invention to be patented, it is imperative for such invention to be demonstrated to be not only theoretical but also practical. Thus the mere providing of examples does not describe the scope of the patent. The aforesaid view is fortified by the judgement of this Court in ***Bayer Pharma Aktiengesellschaft vs. The Controller of Patents and Design, Neutral Citation: 2024:DHC:2395***, wherein, it was emphasised that the working examples are essential for demonstrating the feasibility and workability of an invention, and do not define the patent's scope. The relevant para is reproduced as follows:

> *"8. Regarding the objection under Section 3(i) of the Act, the Court observes that the impugned order lacks a substantive basis for dismissing the subject application on this specific ground. Moreover, under Section 10(4)(c) of the Act, to consider the invention as articulated by the Applicant, it is imperative to interpret the scope of the claims. Claim 1, as delineated, clearly indicates to the Court that it pertains exclusively to a product rather than a process. Consequently, based on the claim's composition and its representation within the application, the Court determines that Section 3(i) of the Act, which pertains to methods of treatment, does not apply to the case at hand.*
>
> *9.* ***Therefore, the Court finds merit in the contention of Mr. Banerjee that mere recitations of the unit numbers of the components in claim 1 cannot render it ineligible for patent protection under Section 3(i) of the Act.*** *Notably, in the said claim, as defined, there is neither any reference to a particular disease/ treatment, nor any reference regarding the modes/ manner of administration of the composition. In patent law, the claims of a patent define the boundaries of the patent protection. That is, they set out the legal limits of what the patent covers. The claims must be clear, specific, and supported by the description within the patent application. They are the most critical part of a patent application because they determine the extent of protection granted by the patent.* ***Working examples, on the other hand, are provided in the subject application to demonstrate the practical implementation of the invention. These examples are intended to show that the invention is feasible and workable and how it can be carried out in practice. They provide support and understanding for the claimed invention, showing that it is not just a theoretical concept, but has practical applicability. Thus, while working examples are essential for***

> ***demonstrating the feasibility and workability of an invention, they do not define the patent's scope. The scope is determined by the claims, which must be interpreted in light of the description and any examples provided.*** *The reasoning for applying Section 3(i) of the Act to the subject application is therefore, misplaced. Mr Banerjee also relies on the decision of this Court in Societe Des Produits Nestle SA v. The Controller of Patents and Design and Anr.,2 where, in a similar situation, the Court referenced the Manual of Patent Office, Practice and Procedure, which gives the guidance for examination with respect to exclusion of medical, surgical, curative, prophylactic, diagnostic, therapeutic or other treatment, and held that the claims in respect of the composition are patentable, and not hit by Section 3(i) of the Act. In the present case as well, the claim 1, as defined, in the opinion of the Court, does not render the application to be non- patentable."*

51. It is clear that claim 1 of the subject application is not framed as a process/ a protocol/ a dosing schedule, or a treatment regimen. Therefore, the subject matter of the present invention is excluded by Section 3(i) of the Act as the said provision bars a process, not a product and a combination.

Objections under Section 10(5) & 10(4) (c) of The Act:

52. The impugned order notes that this objection is not met since the claims are not clear and sufficiently definitive to the scope of the invention in the absence of mention of any significant technological contribution over the prior art cited documents. It may be apposite to reproduce the relevant paragraph from the impugned order, which reads thus:

> *"5.4. Claims [u/ s 10(5) & 10(4) (c)]:*
>
> *This objection is not met since the claims are not clear and sufficiently definitive to the scope of the invention in the absence of mention of any significant technological contribution over the prior art cited documents. Thus, these claims are not allowable u/s 10(5)."*

53. The paragraph extracted hereinabove sadly lacks in providing any reason whatsoever. In view of the rejection by this Court of the reasons furnished by the learned Controller on the objections in respect of technical advancement as analysed in the preceding paragraphs, this Court is of the considered opinion that this objection too, needs reconsideration.

CONCLUSIONS:-

54. In view of the aforesaid analysis, the subject matter patent application is remanded back to the learned Controller for denovo reconsideration of the objections raised. The learned Controller is directed to dispose of the subject patent application within a period of six months from date of receipt of this Order.

55. Needless to state that the respondent shall grant an opportunity of hearing to the appellant before deciding the matter.

56. It is made clear that the learned Controller shall decide the subject patent application on its own merits without being influenced by the observations made above.

57. The appeal is disposed of in the aforesaid terms.

TUSHAR RAO GEDELA
(JUDGE)

JULY 23, 2026
rl/sumit/kct