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

Reserved on: 5th February, 2024
Pronounced on: 14th May, 2024

\+ **C.A.(COMM.IPD-PAT) 458/2022**

ALIMENTARY HEALTH LIMITED ..... Appellant

Through: Mr. Hari Subramanium and Mr. Sanuj Das, Advocates.

versus

CONTROLLER OF PATENTS AND DESIGN ..... Respondent

Through: Mr. Harish Vaidyanathan Shankar, CGSC with Mr. Srish Kumar Mishra, Mr. Alexander Mathai Paikaday and Mr. Krishnan V., Advocates.

CORAM:
HON'BLE MR. JUSTICE SANJEEV NARULA

JUDGMENT

SANJEEV NARULA, J.:

1. This judgment addresses the issue of refusal of the Indian Patent Application No. 3989/DELNP/2012 [hereinafter '*subject patent application*'], which involves formulation of a probiotic bacterium, specifically the strain of *Bifidobacterium longum* designated as NCIMB 41676 (AH1714).[1] The subject patent application has been refused by the Assistant Controller of Patents and Designs [hereinafter '*Controller*'] under Section 15 of the Patent Act, 1970 [hereinafter '*the Act*'] by the impugned order dated 27th November, 2018.

[1] Hereafter, the strain from the '*Bifidobacterium longum'* species of the subject application is interchangeably referred to as NCIMB 41676 or AH1714.

2. The subject patent application details a formulation where this strain is utilized at concentrations exceeding 10^6 colony-forming units (cfu) per gram, combined with an ingestible carrier. These carriers range from pharmaceutically acceptable forms like capsules, tablets, or powders to various food products such as acidified milk, yogurt, frozen yogurt, and other dairy derivatives. The core of the dispute revolves around the patentability of this formulation, specifically its inventive step. Key issues under scrutiny include whether the properties attributed to this formulation of specific strain of *Bifidobacterium longum* are sufficiently distinct from prior art to merit patent protection and whether the claimed synergistic effects of the formulation demonstrate a significant technical advancement.

PROCEEDINGS LEADING TO THE PRESENT APPEAL:

3. The subject application was filed as a national phase entry of PCT application. The First Examination Report (FER) issued on 27th March, 2017, *inter alia*, held that the claims lacked inventive step under section 2(1)(ja) and were non-patentable under Section 3(c), 3(d) and 3(i) of the Act.

4. The Appellant filed a response to the FER on 31st August, 2017. The claims were amended and limited to a total of 13 claims from the original set of 38 claims. Subsequently, Respondent issued a notice of hearing with the following observations and objections under Section 2(1)(ja) over cited prior art Documents D1 to D5, and the subject matter of claims 1-13 as not inventions under section 3 (c), (d) and (e) of the Act :

> "*D1: US20040265279 D2: WO2009127566 D3: W02006SE01117 D4: Medina M, Izquierdo E, Ennahar S, SanzY. Differential immunomodulatory properties of Bifidobacterium logum strains: relevance to probiotic selection and clinical applications. Clinical &*

Experimental immunology. 2007 Dec 1; 150(3):531-8. D5: Imaoka A, Shima T, Kato K, Mizuno S, Uehara T, Matsumoto S, Setoyama H, Hara T, Umesaki Y. Anti-inflammatory activity of probiotic Bifidobacterium: enhancement of IL-10 production in peripheral blood mononuclear cells from ulcerative colitis patients and inhibition of IL-8 secretion in HT29 cells. World journal of gastroenterology. 2008 Apr 28;14(16):2511. D1 discloses t a probiotic bacterium. Bifidobacterium infantis 35624. Serum cytokine levels were examined pre- and post-consumption. Soluble IL-6 receptor (siL-6R) and IL-8 levels were significantly decreased following probiotic feeding. SIL-6R is required for IL-6 signalling while IL-8 is a pro-inflammatory chemokine. D2 discloses edible compositions comprising probiotics. Composition comprising Bifidobacterium longum ATCC BAA-999. This composition can be used to attenuate reductions in hippocampal BDNF expression and/or to treat or prevent anxiety and related disorders. A particular suitable daily dose of Bifidobacterium Iongum ATCC BAA-999 is from 105 to 1011 cfu. D3 discloses use of probiotic bacteria for the manufacture of a food product having probiotic bacteria is at least one of Lactobacillus casei F19 (LMG P-17806), Lactobacillus acidophilus NCFB 1748 ox Bifidobacterium lactis Bb 12. D4 discloses the ability of different strains of Bifidobacterium longum to induce cytokine production by peripheral blood mononuclear cells (PBMCs) has been evaluated. Live cells of all B. longum strains greatly stimulated regulatory cytokine interleukin (IL)-IO and pro-inflammatory cytokine tumour necrosis factor (TNF) - production. Strains of the same species also induced specific cytokine patterns, suggesting that they could drive immune responses in different directions. The probiotic strain B. longum W11 stimulated strongly the production of T helper 1 (Thi) cytokines while B. Iongum NCIMB 8809 and BIF53 induced low levels of Thi cytokines and high levels of iL-10. D5 discloses the anti-inflammatory activity of probiotic Bifidobacteria in Bifidobacteria-fermented milk (BFM) which is effective against active ulcerative colitis (UC) and exacerbations of UC, and to explore the immunoregulatory mechanisms. Peripheral blood mononuclear cells (PBMNC) from DC patients or l-rT-29 cells were co-cultured with heat-killed probiotic bacteria or culture supernatant of Bifidobacterium breve strain Yakult (BbrY) or Bifidobacterium bifidum strain Yakult (BbiY) to estimate the amount of IL-10 or iL-8 secreted. Probiotic Bifidobacterium strains in BFM enhance IL-10 production in PBMNC and inhibit IL-8 secretion in intestinal epithelial cells, suggesting that BFM has anti-inflammatory effects against ulcerative colitis. The document D1 regarded as being the closest prior art to the subject-matter of present application and discloses a probiotic bacterium. Bifidobacterium infantis 35624. D2 discloses edible compositions comprising Bifidobacterium Iongum ATCC BAA-999. D4 discloses the

ability of different strains of Bifidobacterium longum to induce cytokine production by peripheral blood mononuclear cells (PBMCs) has been evaluated. Live ceils of all B. Iongum strains greatly stimulated regulatory cytokine interleukin (IL)-IO and pro-inflammatory cytokine tumour necrosis factor (TNF) - production. D5 discloses Probiotic Bifidobacterium strains in BFM enhance L-IO production in PBMNC and inhibit IL-8 secretion in intestinal epithelial cells, suggesting that BFM has anti-inflammatory effects against ulcerative colitis. The strain of Bifidobacterium is already disclosed and known and its use in probiotic is also disclosed. So the isolated strain of Bifidobacterium and its formulation as probiotic can be produced by the teaching, suggestion and motivation of document D1 to D5. Any person skilled in art can isolate the different strain of microorganism and produce the formulation of probiotic containing Bifidobacterium and carrier molecule selection is obvious to person skilled in art. Therefore, an inventive step for the subject matter of claims 1-13 cannot be acknowledged as per requirement u/s 2(1)(ja) of the Patents Act, 1970 in view of the disclosure in prior art documents D1 to D5.

Non-Patentability u/s 3

1. The subject matter of claim 1-13 is not patentable u/s 3 (c) of the Act as it claims for naturally occurring substance or cell. The subject matter of these claims directed towards the isolated strain of Bifidobacterium which is a naturally occurring microorganism. The independent claim no. 1 discloses the formulation, while the formulation contain only bacteria or microorganism which is naturally occurring microorganism or isolated from a biopsy specimen. Thereby the subject matter defines and attempts to claim naturally occurring microorganism or just mere discovery of living substance occurring in nature. So it meets the criteria of section 3 (c) of The Indian Patents Act, 1970. 2. The subject matter of claim 1-13 is not patentable u/s 3(d) of the Act as it claims the mere discovery of any new property or new use for a known microorganism, it cannot be treated patentable invention as per the Act 1970. The strain of Bifidobacterium is already disclosed in D1 and D4 and its use as probiotic bacteria is also known. The concentration claimed in present application is also known in prior art and disclosed in D3. The carrier molecule or substance does not make any technical feature for the present invention; hence the microorganism in the formulation is the only technical feature, which is already known and disclosed in prior arts. So the strain of Bifidobacterium is known and its use in composition of probiotic is also known in prior art. So, the present set of claims are just mere use or new use of known microorganism by using the isolated form of microorganism in probiotic which does not result in the enhancement of the known efficacy so it comes under sec. 3 (d) of Indian Patent Act, 1970. 3. Amended claims 1-13 attract section 3(e) and needs to show

synergy data"

5. During the hearing, the Appellant provided thorough responses to the objections noted in the hearing notice and further supplemented these responses with written submissions submitted post-hearing. In an effort to address the concerns raised, the Appellant revised the principal claim by incorporating elements from claims 6 and 10 into claim 1, aiming to clarify and strengthen the patentability of the invention. Despite these efforts, the Assistant Controller of Patents and Designs was not persuaded by the amendments and the arguments presented. Consequently, the application was denied pursuant to Section 15 of the Act. The decision of the Assistant Controller, is as follows:

> *"Objection A:*
> *Applicant agent filed 10 amended claims online on 24/09/2018 making reference to a formulation of Bifidobacterium longum strain NCIMB 41676.*
> *Prior art also disclose similar probiotic formulations comprising Bifidobacterium. D1 discloses method of treating depression using probiotic bacterium selected from the group consisting of Lactobacillus strain. Bifidobacterium strain, Lactobacillus salivarius, Lactobacillus casei, Bifidobacterium longum/infantis, Lactobacillus salivarius strain UCC 118, Lactobacillus caseistrain AH113, and Bifidobacterium infantis strain 35624. They also disclose pharmaceutical compositions comprising a probiotic, or an active derivative, fragment or mutant thereof, for administration in a food substance, a tablet, capsule or other formulation for enteral or parenteral administration. D1 discloses the use of Bifidobacterium longum as probiotic in composition for treating depression.*
>
> *D2 discloses edible compositions comprising Bifidobacterium longum in the range of 10^4-10^{10} wherein the composition is a food composition, a pet food composition, a dietary supplement, a drink, and/or medical composition. Additionally with at least one other kind of other food grade bacteria, wherein the food grade bacteria are preferably selected from the group consisting of lactic acid bacteria, Bifidobacteria, Propionibacteria or mixtures thereof and at least one prebiotic. The formulation was intended to increase hippocampal BDNF expression, treat or prevent anxiety and/or anxiety related disorders,*

neurodegenerative diseases.

D3 discloses composition comprising a probiotic bacteria selected from the group consisting of Lactobacillus casei F19 (LMG P-17806), Lactobacillus acidophilus NCFB 1748 and Bifidobacterium lactis Bb12 and combinations thereof comprising at least one of milk, a cereal, a fruit.

D4 discloses the ability of different strains of Bifidobacterium longum to induce cytokine production by peripheral blood mononuclear cells (PBMCs) has been evaluated. Live cells of all B. longum strains greatly stimulated regulatory cytokine interleukin (IL)-IO and pro-inflammatory cytokine tumour necrosis factor (TNF) – production

D5 discloses the anti-inflammatory activity of probiotic Bifidobacteria in Bifidobacteria fermented milk (BFM) which is effective against active ulcerative colitis (UC) and exacerbations of UC, and to explore the immunoregulatory mechanisms.

Applicant agents arguments and annexures have been considered but not found persuasive as prior art advocates and discloses that probiotics such as Bifidobacterium, Lactobacillus strains have excellent health benefits and could be explored as formulation for various health benefits. Based on prior art for a skilled person to explore known probiotics such as Bifidobacteium Longam and isolate a strain which shows beneficial activity and make and claim a formulation for therapeutic application to obtain predictable results is obvious. The disclosures of prior art D1-D5 provide sufficient information and motivation to a skilled artisan to explore and apply the same to an extended embodiment of choice based on desirability and intended result. Thereby inventive step is not acknowledged u/s 2(l)(ja) of the Patent s Act 1970

Objection B (1-3):
In view of applicant agent submissions to the hearing notice, the amendments, deletions in claims, annexure A, objection B is met.

Order: In view of the above, the requirements of objection A of hearing notice is not met and hence the application 3989/DELNP/2012 is refused u/s 15 of Patents Act."

APPELLANT'S CONTENTIONS:

6. Mr. Hari Subramanium, counsel for the Appellant, presents the following case:

6.1 The Respondent has merely quoted paragraphs related to different strains of Bifidobacterium from cited documents from D1 to D5 without actually analysing and interpreting the cited documents in entirety.

6.2 None of the cited documents provide any teaching or suggestion to arrive at a novel strain of *Bifidobacterium longum* NCIMB 41676 (AH 1714) which works synergistically. Therefore, the application ought not to have been refused.

6.3 The Respondent overlooked the corresponding patent applications, for instance, in Europe and United States, the Appellant has been granted patent despite similar prior art citations. Reliance is placed on the decisions of the Intellectual Property Appellate Board dated 11th January, 2021 in OA/16/2016/PT/KOL in the matter of ***Arthritis Relief Plus Ltd. v. Controller of Patents and Designs***.[2]

6.4 The Respondent has disregarded the experimental data in the specification which establishes the technical advancement of *Bifidobacterium longum* NCIMB 41676 (AH 1714) over other strains.

6.5 The Respondent has made a critical error in the appreciation of facts. While acknowledging the novelty of both the strain and the formulation comprising this strain, and further recognizing that neither the strain itself falls under the ambit of Section 3(c) nor do the strain and its formulation fall under Sections 3(d) or 3(e) of the Act, they have nonetheless overlooked a crucial aspect. The Respondent failed to acknowledge that the formulation comprising the said strain possesses inventiveness, which sets it apart from the prior art cited in the proceedings.

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[2] Decision dated 11th January, 2021, in *OA/16/2016/PT/KOL* titled *Arthritis Relied Plus Ltd v. Controller of Patents and Designs*

6.6 The Respondent has presented a contradictory stance in their evaluation. On one hand, they have acknowledged that the formulation claimed in Claim 1 is patentable under Section 3(e) — a section that typically excludes 'inventions' from patentability. On the other hand, they have denied the patent application on the grounds of lacking an inventive step. Given that the Respondent has already recognized the formulation as patentable, it logically follows that an acknowledgement of the inventive step is implicit. To hold otherwise would be inconsistent with the initial finding of patentability under Section 3(e).

6.7 The claimed formulation of the subject patent application, contains a non-obvious strain of *Bifidobacterium longum* which is neither present in any of the prior arts, nor are there sufficient teachings which can be found in prior arts D1- D5.

RESPONDENT'S CONTENTIONS:

7. *Per contra*, Mr. Harish Vaidyanathan Shankar, CGSC for Respondent, strongly defends the impugned order and argues that the claims in the patent application are obvious to a person skilled in the art and therefore since the prior arts disclosed the claim invention, the application has been right refused on the ground of lack of inventive step.

7.1 The prior art discloses methods of treating depression using probiotic bacterium (Abstract) selected from the group consisting of Lactobacillus strain, Bifidobacterium strain, Lactobacillus salivarius, Lactobacillus casei, *Bifidobacterium longum*/infantis, Lactobacillus salivarius strain UCC 118, Lactobacillus casei strain AH113, and Bifidobacterium infantis strain 35624. They also disclose pharmaceutical compositions comprising a probiotic, or

an active derivative, fragment or mutant thereof, for administration in a food substance, a tablet, capsule or other formulation for enteral or parenteral administration. D1 discloses the use of *Bifidobacterium longum* as a probiotic in composition for treating depression.

7.2 D2 discloses edible compositions that include *Bifidobacterium longum*, ranging from 10^4 to 10^{10} CFUs. Claim 8 specifically outlines that these compositions may take the form of a food product, a pet food, a dietary supplement, a beverage, and/or a medical formulation. Additionally, these compositions are characterized by the inclusion of at least one other type of food-grade bacteria. The preferred bacteria are selected from a group that includes lactic acid bacteria, *Bifidobacteria*, *Propionibacteria*, or their mixtures, coupled with at least one prebiotic. The primary intent of the formulation, as specified, is to enhance hippocampal BDNF expression and to treat or prevent anxiety, anxiety-related disorders, and neurodegenerative diseases.

7.3 D3 discloses a composition comprising a probiotic bacteria selected from the group consisting of Lactobacillus casei F19 (LMG P-17806), Lactobacillus acidophilus NCFB 1748 and *Bifidobacterium* lactis Bb12, and combinations thereof comprising at least one of milk, a cereal, a fruit.

7.4 D4 discloses the ability of different strains of *Bifidobacterium longum* to induce cytokine production by peripheral blood mononuclear cells (PBMCs) has been evaluated. Live cells of all B. longum strains greatly stimulated regulatory cytokine interleukin (IL)-10 and pro-inflammatory cytokine tumor necrosis factor (TNF) – production, the most commonly proposed benefits of the consumption of probiotics. *Lactobacillus* and *Bifidobacterium* strains used as probiotics have been acknowledged for their

role in preventing and treating acute gastrointestinal infections, allergy and atopic diseases and inflammatory bowel diseases [12–14]. The beneficial effects of these strains are based partly on their ability to regulate differentially the production of anti- and pro-inflammatory cytokines and the T helper 1 (Th1)/Th2 balance. D4 suggested that B. longum strains have shown to divert immune responses into different directions in vitro, either towards a pro-inflammatory or a regulatory profile. This suggests that different strains may have different functional roles and applications in diverse pathological conditions.

7.5 D5 discloses the anti-inflammatory activity of probiotic *Bifidobacteria* in Bifidobacteria-fermented milk (BFM) which is effective against active ulcerative colitis (UC) and exacerbations of UC, and explores the immunoregulatory mechanisms.

7.6 The Appellant's oral as well as written arguments and documents were considered, but not found persuasive. The prior art clearly advocates for and discloses the significant health benefits associated with probiotics, such as strains of *Bifidobacterium* and *Lactobacillus*. It suggests these probiotics can be formulated for various health benefits. Consequently, for a person skilled in the art, it would be a routine undertaking to explore well-known probiotics like *Bifidobacterium longum*, isolate a strain demonstrating beneficial activity, and then develop and claim a formulation for therapeutic applications. The ability to achieve predictable results from such an exploration renders the claim obvious and lacks the requisite inventiveness as stipulated by patent law.

7.7 Prior arts disclose that probiotics such as *Bifidobacterium*, *Lactobacillus* strains have excellent health benefits and could be explored as

a formulation for various health benefits. Further prior art also discloses edible compositions comprising probiotic *Bifidobacterium* strains.

7.8 The instant formulation contains only 1 active ingredient *Bifidobacterium longum* NCIMB 41676 (AH1714) in the amount of more than 10^6 cfu per gram.

7.9 It is further submitted that the instant application is not inventive as the application of edible probiotic formulations of *Bifidobacterium* strains, in the claimed amount, having excellent health benefits (including depression, cytokine interleukin (IL)-10 and pro-inflammatory cytokine tumour necrosis factor (TNF) – production) is already known and explored herein without any inventive merit. There is "no surprising element" in the instant formulation when seen in the light of prior arts. Whatever is emphasised in the instant application is obvious in light of prior arts as referred hereinabove.

ANALYSIS AND FINDINGS:

8. The Controller of Patents referenced prior art documents, D1: US 20040265279; D2: WO 2009127566; D3: WO 2006SE01117; D4: Medina et al.; and D5: Imaoka et al., to conclude that the subject application lacks an inventive step. On the basis of the said prior art documents, the Controller has held that the strain of *Bifidobacterium* claimed in the subject patent application is known and its use as a probiotic has already been disclosed. Accordingly, the Controller concluded that the isolated strain of *Bifidobacterium* and its subsequent formulation as a probiotic could be derived by applying the teachings, suggestions, and motivations provided in documents D1 to D5.

9. Indeed, D1 to D5 outline various strains of *Bifidobacterium*, particularly *Bifidobacterium longum*, and their probiotic effects, influencing cytokine levels to confer health benefits like anti-inflammatory, anti-depressant, and anti-obesity effects. However, the Appellant argues that *Bifidobacterium* constitutes a broad genus, within which *Bifidobacterium longum* is a specific species known to exhibit a wide range of strain-specific behaviours and characteristics. The Appellant claims that the inventive step in the subject patent application focuses on the formulation of *Bifidobacterium longum* (NCIMB 41676), which is unique because of its distinct immunomodulatory effects, distinguishing it from the prior art.

10. It is well established within the scientific community—as evident from the prior art documents—that significant diversity exists within species. Different strains within these species distinctly influence immune responses, which can be directed toward either pro-inflammatory or regulatory outcomes. These variations play a crucial role in impacting human health, either positively or negatively. Thus, given the vast potential for variation among these strains, the key issue is whether the characteristics and benefits of the NCIMB 41676 strain represent a substantial improvement in therapeutic efficacy over these existing solutions satisfying the criteria of inventive step beyond the known properties of other *Bifidobacterium* strains.

11. This evaluation requires an assessment of microbial genetics and the specific bioactive properties claimed, with the aim to discern whether these represent mere variations of known strains or constitute innovative therapeutic advancements deserving of patent protection.

Jurisprudence on the legal and technical standards for objective assessment

12. For our analysis on inventive steps, the decision of the Supreme Court in ***Biswanath Prasad Radhey Shyam v. Hindustan Metal Industries Ltd.***[3] ***and Hoffmann-La Roche Ltd & Anr. v Cipla Ltd***.,[4] serve as the foundation. These rulings underscore the necessity for an objective assessment of obviousness and inventive step, which should be firmly anchored in the technical knowledge and capabilities of a person skilled in the art as of the priority date. A pertinent framework from the ***Hoffmann-La Roche*** (supra) outlines the required inquiries to assess inventive step as follows:

Step 1: Identify an ordinary person skilled in the relevant art.

Step 2: Determine the inventive concept embodied in the patent.

Step 3: Attribute to a skilled but unimaginative ordinary person what was common general knowledge in the art at the priority date.

Step 4: Identify the differences between the prior art and the alleged invention to ascertain whether these differences are merely ordinary applications of law or entail various complex steps involving both theoretical and practical applications.

Step 5: Assess whether these differences, viewed in the context of the known invention, constituted steps that would have been obvious to the skilled person, while avoiding a hindsight approach.

13. The concept of '*Person Skilled in the Art*' *(PSITA)* has been explained in ***F.Hoffmann-La Roche Ltd & Anr. v Cipla Ltd.***.[5] and further elaborated in ***Enercon India Ltd. v. Aloys Wobben***.[6] The PSITA in the context of the

[3] (1979) 2 SCC 511
[4] 2015: DHC:9674-DB
[5] 2015: DHC:9674-DB
[6] ORA/41/2009/PT/CH (MANU/IC/0057/2013)

present case is not only proficient in the general practices of microbiology but is also up-to-date with the latest developments, particularly those related to the isolation and application of bacterial strains for health benefits.

14. In evaluation of the inventive step in patent law, the jurisprudential guidelines established through judicial precedents emphasize the importance of avoiding hindsight bias. This is crucial to ensure that the inventive step is assessed based solely on the information that was available to the public before the priority date of the patent application.

15. The objective analysis of inventive step helps to foster genuine innovation and discourage the monopolization of trivial enhancements that do not substantially enrich the technical field. By doing so, it ensures that only those advancements that provide a substantial benefit to the technical field are protected by patents. It also helps prevent the patenting of mere incremental advancements or "workshop improvements" that a skilled craftsman could likely achieve without exerting an inventive effort. (see: ***Biswanath Prasad Radhey Shyam (supra)***.

Objective Analysis of Inventive Step:

16. Having established the legal and technical standards for assessment of inventive step, we now proceed to consider whether the use of *Bifidobacterium longum* NCIMB 41676 in the subject patent application represents a significant advancement beyond the ordinary capabilities of a person skilled in the art (PSITA) and constitutes a substantial improvement in the existing knowledge, rather than being a mere application of routine techniques. In this context, the first claim of the subject patent application, which is the only independent claim, is relevant for understanding the

invention and its inventive contribution. The independent claim is set out as follows:

> *"1. A formulation* ***comprising a strain of Bifidobacterium longum NCIMB 41676 (AH1714)****, wherein the Bifidobacterium longum NCIMB 41676 strain is present in an amount of more than 10^6 cfu per gram of the formulation; and* ***an ingestible carrier*** *wherein the ingestible carrier is a pharmaceutically acceptable carrier such as a capsule, tablet or powder or is a food product such as acidified milk, yoghurt, frozen yoghurt, milk powder, milk concentrate, cheese spreads, dressings or beverages."*

17. The Claim No. 1 describes a formulation comprising a strain of Bifidobacterium longum NCIMB 41676 (AH1714). In this formulation, the strain is present in an amount of more than 10^6 cfu per gram of the formulation, combined with an ingestible carrier. The ingestible carrier can be a pharmaceutically acceptable form, such as a capsule, tablet, or powder, or a food product, such as acidified milk, yogurt, frozen yogurt, or other dairy derivatives, including milk powder, milk concentrate, cheese spreads, dressings, or beverages. The description of the invention provides background information and supports the claim No. 1, which is directed towards a formulation by emphasizing the unique characteristics of the strain, its biotherapeutic properties and its significant immunomodulatory properties. Further, the description of the invention also discloses various health-promoting benefits of the strain, particularly through various dairy and pharmaceutically acceptable carriers.

Key Distinctions from Prior Arts

18. Now, we proceed to analyse each of the cited prior art documents. The Appellant has claimed that the strain NCIMB 41676, provides significant therapeutic advancements over the prior arts cited by the

Controller, particularly in terms of cytokine modulation and gastrointestinal health benefits. Its unique immunomodulatory properties offer improved efficacy and safety in treating various inflammatory and mental health conditions. To highlight the distinction and ascertain the advantages, if any, a comparison with prior art documents is presented below:

(a) D1: US 2004/0265279 A1, identifies *Bifidobacterium infantis* 35624 and its regulatory immune responses effective in treating depression. However, we note that this prior art reveals a different secretion pattern for cytokines such as IL-12, IFNγ, and IL-6 compared to the appellant's invention. In the Appellant's invention, Example 5 provides a comparison of the immunomodulatory activity of Bif 1714 (NCIMB 41676) with *Bifidobacterium* strain 35624 (D1). It is seen that while both cultures of strain 35624 and 1714 gave a similar pattern for many of the cytokines measures, 1714 gave a different, advantageous secretion pattern for IL-12, IFNγ and IL-6. Appellant's strain demonstrates significantly lower levels of these cytokines, which are detailed in Tables 5 and 6 of the specification, indicating improved efficacy in the *in vivo* ulcerative colitis model. IL-6, in particular, is crucial in various diseases, and the appellant's strain's ability to modulate its secretion presents a significant therapeutic advantage. The Appellant has demonstrated that while *Bifidobacterium longum* infantis strain UCC35624 and NCIMB 41676 exhibit similar patterns for many cytokines, NCIMB 41676 uniquely shows significantly lower levels of IL-12, IFNγ, and IL-6, suggesting an improved profile for treating inflammatory conditions without the risks associated with higher cytokine levels. These differences, as exemplified in the studies conducted by the appellant are as follows:

(i) IL-6: Incubation with NCIMB 41676 results in a substantially lower IL-6 level compared to UCC35624, making it a promising candidate for conditions exacerbated by IL-6.

(ii) IL-12 and INF-γ: Shows markedly lower levels when treated with NCIMB 41676, reinforcing its potential in immune modulation and therapeutic applications.

(iii) These results, alongside the specific *in vivo* efficacy demonstrated in ulcerative colitis models, strongly suggest that NCIMB 41676 possesses advantageous properties over the strains described in the prior art, thus supporting the claim of technical advancement.

(b) D2: WO 2009/127566 A1: This prior art discloses *Bifidobacterium longum* ATCC BAA-999 and its use to attenuate reductions in hippocampal BDNF expression and/or to treat or prevent anxiety and related disorders. There is no motivation or suggestion that would lead a skilled artisan to the claimed strain NCIMB 41676, as this document focuses on reducing BDNF expression.

(c) D3: WO 2007/043933: This document does not disclose or suggest the use of any *Bifidobacterium longum* strains and instead focuses on applications of *Bifidobacterium lactis*. Further, the use of *Bifidobacterium lactis* is also directed towards treatment of obesity and improving metabolism. Therefore, the said prior art would not be a relevant prior art.

(d) D4: M. Medina et al.: This prior art discloses a number of different B. longum strains for possible use as probiotics. These include BB536, NCC2705, W11, NCIMB 8809, ATCC15707, BIR 324 and BIF53. D4 acknowledges the critical aspect of probiotic research— each strain of

Bifidobacterium possesses unique and distinct properties, making it improper to extrapolate the probiotic effects of one strain to another. Specifically, D4 states (at page 532) that the probiotic effects of a specific strain must not be assumed applicable to other strains, emphasizing that observing characteristics in one strain does not create an expectation of similar benefits in another. Further elaboration in D4 (page 535) demonstrates that different strains of the same species can elicit immune responses in opposite directions due to their unique cytokine stimulation effects. This variability extends to their ability to modulate cytokine production, as discussed on page 536, where it is noted that there are significant variations among strains of the same *Bifidobacterium* species in their capacity to influence cytokine levels. Moreover, the discussion continues (bridging pages 536-537) to explain that strains of *Bifidobacterium longum* can diverge greatly in their immune responses in vitro, ranging from pro-inflammatory to regulatory profiles. This variability underscores the necessity for careful selection and testing to identify strains with specific therapeutic functionalities. The scientific consensus, as reflected in D4, advises against generalizations concerning the probiotic effects of *Bifidobacterium* strains, highlighting the complexity and specificity required in developing therapeutically functional probiotics. In conclusion, D4 illustrates that developing new, therapeutically useful strains of *Bifidobacterium longum* involves overcoming significant scientific challenges. It is not merely a matter of identifying a new strain but ensuring that the selected strain meets specific therapeutic criteria, a process that lacks any guarantee of success and involves extensive empirical testing.

(e) D5: Akemi Imaoka et al.: D5 studies *Bifidobacterium bifidum* strain

Yakult (BbiY) and *Bifidobacterium breve* strain Yakult (BbrY), which are distinct from the strain discussed in the Appellant's patent application, *Bifidobacterium longum* NCIMB 41676. Further, in comparison, the complete specification of the subject patent invention provides detailed empirical evidence highlighting the unique therapeutic benefits of *B. longum* NCIMB 41676, not mentioned in any of the prior art, including:

i) Anti-inflammatory Benefits: NCIMB 41676 has demonstrated efficacy in reducing undesirable inflammatory activity, as detailed in Examples 3, 4, 5, and 6 of the specification (pages 155 to 162).

ii) Gastrointestinal Health**:** It is effective in the treatment and prevention of ulcerative colitis and irritable bowel syndrome, detailed in Example 5 (page 161, lines 10-18).

iii) Cytokine Modulation**:** This strain modifies the levels of IL-10 and reduces pro-inflammatory cytokines, as shown in Examples 3 and 4.

iv) Mental Health Applications**:** NCIMB 41676 has been found effective in the treatment or prevention of depression, mood disorders, and anxiety disorders, with specific findings presented in the description of the invention (pages 161 and 164) and reinforced by Example 7.

Evaluation of Obviousness in Light of Prior Art and Technical advancement:

19. None of the cited prior art documents D1 to D5 either alone or in combination motivate PSITA to arrive at a formulation comprising a strain

of *Bifidobacterium longum* NCIMB 41676 wherein the strain is present in an amount of more than 10^6 cfu per gram of the formulation. Nevertheless, we must also deliberate whether the features of the subject invention that differ from the prior art would have been obvious to a person skilled in the art, employing a strict avoidance of hindsight bias. The term "obvious" is not explicitly defined within the Indian Patent Act, nonetheless, the concept has been extensively interpreted through multiple judicial decisions across various jurisdictions, including the US, UK, and India. There are various tests deployed by courts to determine obviousness, such as the 'Obvious to try approach', 'Problem/solution approach', 'Could-Would approach' and the 'Teaching Suggestion Motivation Test'. These tests were thoroughly analysed in the judgment by the Coordinate Bench of this Court in ***Avery Dennison Corporation v. Controller of Patents and Designs.*** [7] Each of these methodologies emphasizes a different aspect of how to assess the innovation in question against prior art.

20. Therefore, consistent with established jurisprudence on this matter, the mere presence of individual elements of an invention in prior art documents does not, in itself, conclusively establish obviousness. To determine obviousness, there must be a clear coherent thread from the prior art(s) to the invention, and this path should be straightforward. The coherent thread should lead from the prior art to the invention, suggesting a logical and foreseeable progression of technology or methodology. An inventive step requires more than just assembling known elements; it involves a non-obvious conceptual leap that would not be readily deduced by someone with ordinary skills in the field without the benefit of hindsight. The inventive

[7] 2022/DHC/004697

step should not simply be an obvious next step based on prior art but should involve a significant, non-obvious advancement that could not be easily deduced by a skilled practitioner at the time of the invention. It is essential to discern whether the invention represents "a simple substitution of one known element for another to obtain predictable results" or if it constitutes an "obvious to try" scenario—choosing from a finite number of identified, predictable solutions with a reasonable expectation of success. The core principle is thus: whether the invention is actually obvious or merely appears obvious in hindsight due to our current knowledge. If it is the latter, it is hindsight bias and is unacceptable. However, if the coherent thread is evident, the subject patent shall not be denied on account of obviousness.

Distinctive Features and Therapeutic Efficacy of the Subject Invention:

21. Applying these standards to the case of NCIMB 41676, it becomes imperative to scrutinize whether the unique properties of this strain, and the methods of its application, represent a clear departure from established knowledge and practices. The core distinction of the instant invention lies in the formulation demonstrating synergistic and enhanced therapeutic efficacy in comparison with the closest prior art, D1. The critical question thus is, whether the formulation of *Bifidobacterium longum* NCIMB 41676 demonstrating this synergism or enhanced efficacy would have been obvious to a person skilled in the art.

Evaluating Obviousness in Light of Prior Art and Judicial Decisions:

22. The prior arts do not refer to a formulation involving *Bifidobacterium longum* 1714, and whereas the closest prior art, D1, discloses a different strain, *Bifidobacterium infantis* 35624. The data presented by the Appellant

shows that the invention significantly reduces cytokine levels—nearly 50% compared to D1— thereby enhancing its anti-inflammatory efficacy. This marked reduction underscores not merely an incremental adjustment but a substantial improvement in clinical outcomes.

23. The prior art D4 emphasizes that various strains of *Bifidobacterium longum* can result in differing cytokine profiles, which may adopt either pro-inflammatory or regulatory roles. This variability among strains illustrates the challenge in generalizing the anti-inflammatory properties across all strains of *Bifidobacterium longum*. The potential subspecies strains of *Bifidobacterium longum* are virtually infinite, and prior art D4 underscores that these strains can exhibit widely divergent effects, negating any reasonable expectation of success. The significant differentiation in immune response capabilities between strains, highlighted by the reduction in cytokine levels as demonstrated by strain 1714, supports Appellant's contention that the subject invention "lies so much out of the track of what was known before".[8]

24. Thus, while commonality in prior arts and the subject invention might be traced to the species *Bifidobacterium longum* and its general therapeutic properties, this broad similarity does not justify a generalization of effects across all strains. In fact, prior art D4 explicitly states that each strain may possess unique and sometimes entirely opposite properties, emphasizing the individuality of each strain's therapeutic potential. Therefore, considering the infinite potential for variation within strains of the species, the collection of prior arts D1 through D5, at best provide broad information on different strains of *Bifidobacterium longum* and their diverse medical applications.

However, the formulation with its unique cytokine modulation profile claimed in the subject patent application, has shown enhanced efficacy, deviating significantly from what was previously known. Consequently, it would be reasonable to infer that the invention did not follow a predictable path but represented a significant and non-obvious leap in the application of probiotic science. This marked departure from existing knowledge is an indication that the subject patent application was not obvious to those skilled in the art, on the priority date of the invention and thereby meets the requirements for patentability.

Lack of reasoning or analysis in the impugned order:

25. The impugned order, while briefly acknowledging the arguments and annexures submitted by the applicant's agents, fails to provide a persuasive and detailed analysis as required by law. The controller's decision superficially notes that prior art discloses the health benefits of probiotic strains such as *Bifidobacterium* and *Lactobacillus*, and suggests that exploring these known probiotics for various health benefits is within the reach of a skilled person. However, the order lacks a substantive examination of how the specific *Bifidobacterium longum* NCIMB 41676 strain presented in the patent application is obvious or lacks an inventive step in light of the detailed disclosures from prior art documents D1 to D5. The decision simply concludes that the information provided in these documents would lead a person skilled in the art to predictably achieve the claimed therapeutic benefits, without considering the prior art document D4 as a whole and misses out a thorough analysis of the distinct characteristics

[8] *Biswanath Prasad Radhey Shyam v. Hindustan Metal Industries Ltd, (1979) 2 SCC 511*

or enhanced efficacy of the NCIMB 41676 strain-based formulation.

26. This Court has time and again held that the Patent Office must issue a 'speaking order,' with detailed comparative analysis of the existing knowledge and the claimed invention while deciding the objection of section 2(1)(ja) of the Act. The decision in ***Agriboard International*** (supra) reiterates this requirement, drawing upon the Supreme Court's ruling ***in Manohar v. State of Maharashtra & Ors***.[9] which underlines the necessity of application of mind and recording of reasons as fundamental elements of natural justice, particularly while rejecting patent applications. The court has emphasised that, the controller must specifically address three crucial aspects:

- the disclosures of the prior art;
- the invention claimed in the current application;
- the reasoning why the claimed invention would be obvious to a person skilled in the art in light of the prior art.

27. The shortcomings in the present case become stark against the backdrop of Section 2(1)(ja) of the Patent Act 1970, which defines an 'inventive step' as a feature that not only marks a technical advance over the existing knowledge or bears economic significance, but also is non-obvious to a person skilled in the field. The controller ought to have analysed the existing knowledge and articulate how a skilled person could logically and predictably progress from this knowledge to the invention claimed. Without such analysis, the rejection of a patent application on the grounds of lacking an inventive step is untenable, unless the absence of

[9] AIR 2013 SC 681

inventiveness is unequivocally evident. In this instance, such clarity is not present, rendering the decision to reject the application untenable.

28. In light of this detailed analysis, the ground of refusal—specifically, the lack of an inventive step—cannot be sustained as it is clearly met, and thus the appeal should be allowed to this extent. However, the Court has identified several other inadequacies in the impugned order. Consequently, there is a necessity for a fresh examination to decide on the grant or refusal of the subject patent application. This further examination must be precisely focused to evaluate issues that were not addressed in the impugned order but are crucial for the determination of the patent application.

29. It is pertinent to note that, initially the Appellant filed the subject patent application for the strain itself and later the same was amended to claim a specific formulation of the strain. This aspect has not been thoroughly examined by the Controller, particularly concerning how the formulation claim relates to the original strain. The Appellant's decision to narrow the claims from the strain to its formulation raises questions about the novelty of the formulation itself, suggesting it might simply be another manifestation of the strain. Given these circumstances, the Court deems it necessary to direct a limited revaluation of 'novelty' of the subject patent application, specifically in the context of the formulation being claimed by the Appellant. This re-evaluation would ascertain whether the formulation, as claimed, genuinely introduces a novel aspect distinct from the strain itself or if it merely repackages existing knowledge. At this juncture, we must also observe that Appellant has relied upon the grant of corresponding patent applications in the US and the European Patent Office (EPO). While taking those into consideration, the prosecution histories in these jurisdictions must

also be examined for reassessing the subject patent application in light of the provisions of the Patent Act. This comparative analysis is essential to ensure that specific issues, which might have been overlooked or misinterpreted in the initial assessment by the Controller, are thoroughly addressed.

30. Accordingly, the appeal is disposed of with the following directions:

(i) The impugned order dated 27th November, 2018 is set aside and the matter is remanded to the Respondents for a fresh consideration.

(ii) The patent application for the subject patent is restored to its original number.

(iii) Prior to deciding the matter afresh, Appellant shall be granted a hearing, and the notice of such hearing must clearly delineate the objection(s). In addition to any outstanding objections, the Controller shall address the following questions in the final order, after giving the Appellant an opportunity to respond to the said question. The set of questions are as follows:

a. Is the strain of *Bifidobacterium longum* designated as NCIMB 41676 (AH1714) and also the specific formulation claimed in Claim 1, novel or not? For the said analysis, the Controller shall consider whether the patent publication WO2010055499 (and its priority documents), and specifically Claim 15 of the publication, constitutes prior art, given that the earliest priority date of said Claim is 11th November, 2008, and the priority date of the subject patent application is 11th November, 2009.

b. Does the claimed formulation pertain to a specific dosage or method of administration for using the strain, and is the same responsible for the technical advancement of the subject patent application? If yes,

whether such a patent can be granted under the Act?

c. Whether the Claims in the subject patent application are directed towards the second medical use of Bifidobacterium longum NCIMB 41676 (AH1714). If so, are claims concerning second medical use permissible under the relevant guidelines of the Patent Office and the Act?

(iv) The Controller is directed to render the final decision within a period of four months from the date of conclusion of the hearing.

31. With the above directions, the appeal stands disposed of.

32. The Registry is directed to supply a copy of this judgment to the office of the Controller General of Patents, Designs and Trademarks of India on email llc-ipo@gov.in for compliance of the directions in the judgment. In addition, let ld. CGSC also communicate the said directions to the office of the CGPDTM.

SANJEEV NARULA, J

MAY 14, 2024
as