



IN THE HIGH COURT OF JUDICATURE AT MADRAS

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Judgment reserved on	15.12.2023
Judgment pronounced on	06.03.2024

CORAM

The Hon'ble Mr. Justice **SENTHILKUMAR RAMAMOORTHY**

(T) CMA (PT) No.118 of 2023
(OA/22/2018/PT/CHN)

Immunas Pharma, Inc.
Kanagawa Science Park R&D D11F, 3-2-1, Sakado, Takatsu-ku
Kawasaki-shi, Kanagawa 213-00123, Japan
National Center for Geriatrics and Gerontology
36-3, Gengo, Morioko-machi, Obu-shi
Aichi 4748511, Japan ... Appellant

v.

Assistant Controller of Patents and Designs,
Government of India, Patent Office,
Intellectual Property Building,
G.S.T. Road, Guindy,
Chennai – 600 032.
...Respondent

PRAYER: This Civil Miscellaneous Appeal is filed under Section 117-A of the Patents Act, 1970, praying to set aside the order dated 31 January 2018 and issued by the Respondent in Indian Patent Application No.6334/CHENP/2009 for patent be allowed to proceed to grant.

For Appellant: Mr.P.V. Balasubramaniam, Senior Advocate
for De Penning & De Penning

For Respondent: Mr.N.Vijayaraman, SPC



JUDGMENT

Background

The appellant assails an order dated 29 December 2017 by which Indian Patent Application No.5542/CHENP/2010, which is the national phase application derived from PCT Application No. PCT/JP09/052039 dated 06 February 2009, was rejected.

2. The appellant filed the above mentioned application dated 03 September 2010 for grant of patent in respect of an invention titled “Antibody Capable of Binding Specifically to A-beta Oligomer and Use Thereof” by claiming its priority date from JP Application No.2008-028386 dated 08 February 2008, JP 2008-201058 dated 04 August 2008 and US Application No.61/085, 545 dated 01 August 2008. Upon a request being made, the respondent issued the first examination report (FER) on 22 September 2014. In the FER, objections were raised *inter alia* on the grounds of lack of unity; lack of inventive step in view of prior art documents D1-D4; claims 1-8 not being patent-eligible under Section 3 (c) of the Patents Act, 1970 (the Patents Act); claims 9-17 not being patent-eligible under Section 3(e) of the Patents Act; and claims 18-22 not being patent-eligible under Section 3(i) of the Patents Act . On 27 October 2014,



the appellant filed a response to the FER. By such response, the claims were amended and the claim was restricted to a single antibody labelled as 6E4.

3. A further examination report was issued on 10 August 2015 raising objections *inter alia* that: the claimed invention lacks an inventive step in view of prior arts D1-D4; claims 1-8 are not patent eligible under Section 3(c); claims 9-17 are not patent eligible under Section 3(e); claims 18-22 are not patent eligible under Section 3(i); and claims 23-24 do not comply with Section 10(4)(c). A response was filed thereto on 22 September 2015 along with amended claims 1-4. It was stated that the claimed invention was not obvious from cited prior art documents because it is specific to A-beta oligomers. The objection under Section 3(c) was refuted by contending that the 6E4 antibody is not naturally occurring and that even the antigen is not found in nature. Claims 9-22 were deleted in response to the objections under Sections 3(e) and (i). Claims 23-24 were also deleted to meet the objection under Section 10(4)(c). By hearing notice dated 29 March 2017, objections were raised in respect of unity of invention; under Section 3(c) in respect of amended claims 1-3 and under both Section 10(4)(c) and 3(e) in respect of amended claim 4. In the written submissions filed after the hearing on 13 July 2017, claim 4 was deleted. Claims 1-2

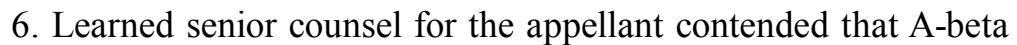


were amended and limited to a single antibody 6E4 to meet the unity of invention objection, and the objection under Section 3(c) was dealt with by pointing out that the sequence under numerical identifier [400] should be the determining factor and not the organism from which the sequence is derived, i.e. sequence identifier [213].

4. By impugned order dated 29 December 2017, the respondent confirmed the Section 3(c) objection by holding that the claimed antibody with specific amino acid H or L sequence is an inherent feature and does not distinguish it from those that occur in nature. It was further held that the antibody 6E4, which is the subject of the patent claim, was discovered and, hence, not patent-eligible. The present appeal arises in the above facts and circumstances.

Counsel and their contentions

5. Oral arguments on behalf of the appellant were advanced by Mr.P.V.Balsubramaniam, learned senior counsel, assisted by Mr. Vijay Anand of De Penning and De Penning. The respondent was represented by Mr.N.Vijayaraman.



7. On the interpretation of Section 3(c) of the Patents Act, learned

senior counsel relied on the judgment of the Intellectual Property Appellate Board(the IPAB) in *The University of British Columbia v. Controller of Patents, order dated 31 December 2020*, particularly paragraph 9 thereof, for the principle that a non-human monoclonal antibody does not attract



Section 3(c) of the Patents Act. He also relied on clause 09.03.05.03 of the

Manual of Patent Office Practice and Procedure dated 26 November 2019

and paragraph 11 of the Guidelines for Examination of Biotechnology

Applications for Patent, issued in March 2013, to contend that the Patent

Office's position therein is that anything freely occurring in and isolated

from nature is not patent-eligible. He also placed for consideration a list of

patents granted in respect of antibodies by the Indian Patent Office.

8. Since the respondent did not make submissions, the stand of the respondent can only be gleaned from the impugned order. The operative portion of the order is as under:

“In the reply the applicant has stated that the claimed 6E4 which is a mouse anti-human A-beta oligomer antibody is an antibody that can be produced only when mice are immunized with a sufficient amount of human A-beta oligomer prepared by copolymerizing the the modified A-beta and the synthetic A-beta, but cannot be present in the body of a mouse without immunization at all. Here, the claimed antibody with specific amino acid H or L chain sequence are the inherent features and do not distinguish



the claimed antibody, H chain or L chain from those which occur in nature. Hence the antibodies produced are natural nonliving substance which is not patentable u/s 3(c) of the Patents Act 1970.

The affidavit filed by the applicant is considered, but the technical advancement for 6E4 antibody to substantiate the instant invention was not provided in the specification (ie) the improving A-beta oligomer specific antibody 6E4 was not exemplified in the specification. It is also stated in page 3 of the specification the inventor has discovered 6 types of antibodies 4a5,5A9, 4H5, 6E4 and 64H and hence the claimed antibody targeting the same antigen is considered as an alternative and which has been selected among possible antibodies.”

In effect, the above paragraphs indicate that the claimed invention was rejected on the ground that antibody 6E4 is naturally occurring and was merely discovered. In sum, the rejection is under Section 3(c) of the Patents Act.



Discussion, analysis and conclusions

9. Before grappling with the legal and factual issues that the determination of this dispute entails, it is necessary to summarize the scientific terms, concepts and principles that are germane for an understanding of the dispute. Since antibodies are naturally or synthetically produced to defend the organism (such as human beings) against antigens, a good place to start is with antigens. An antigen is a molecule that an antibody binds to and attacks. Typical examples of antigens are bacteria, viruses, fungi, toxins or even allergens. The antigenic site to which the antibody binds is called an epitope. Antibodies are immunoglobulin(Ig) molecules. Naturally occurring antibodies are produced in the human body by B cells, which are specialized white blood cells. Antibodies are proteins consisting of about four polypeptides.

10. Most, if not all, naturally occurring antibodies are polyclonal, i.e. they are produced by many distinct B cells/lymphocytes and each polyclonal antibody typically has different specificity. Therefore, different polyclonal antibodies for the same antigen may bind to different epitopes of the antigen. Polyclonal antibodies are, consequently, polyvalent and their affinity to a particular epitope, i.e. the extent to which an antibody is drawn



to and binds to an epitope, is low. There could also be variation in avidity, which is a measure of the strength of interaction between antibody and antigen, as between monoclonal and polyclonal antibodies. Monoclonal antibodies have monovalent affinity, i.e. they bind to the same epitope of the antigen. Monoclonal antibodies are broadly of four categories: non-human, i.e. produced in a non-human host such as a mouse; chimeric, i.e. containing parts or regions from different organisms; humanized, i.e. derived from non-human species and, thereafter, grafted into a human framework so as to minimize risk of immunological reactions; or human, i.e. produced in transgenic animals based on human germline sequences. Each antibody molecule comprises two heavy chains and two light chains, which roughly form a structure like the alphabet 'Y'. Each heavy (H) and light (L) chain has a variable (V) region and a constant (C) region. The constant regions form the trunk of the Y and do not come into contact with the epitope of the antigen. Each antibody has six chains: three in the heavy and three in the light chain. The amino acids constituting the tips of the variable regions form loops while folding, which are referred to as complementarity determining regions (CDRs). The claim of inventiveness generally centres around the sequences relating to the CDRs.



11. Against this backdrop, the first issue that requires determination pertains to the interpretation of clause (c) of Section 3. The said provision is set out below:

“What are not inventions – The following are not inventions within the meaning of this Act, –

*“(c)the **mere** discovery of a scientific principle or the formulation of an abstract theory or **discovery of any living thing or non-living substance occurring in nature**”(emphasis added).*

Prior to its amendment by Act 38 of 2002, the provision was as under:

“(c) the mere discovery of a scientific principle or the formulation of an abstract theory”

The Patents Act was enacted pursuant to a report of the Iyyengar Committee. In the said report, at paragraph 328 thereof, the Committee was of the view that discoveries are universally not patentable. The rationale appears to be that a discovery is a process by which something already in existence is found, whereas an invention is the creation of something that was not in existence previously. Given that the Patents Act was intended to foster inventiveness and not to reward discovery of things that already exist, the basis for the exclusion is clearly discernible.



12. As is evident from the pre-amended text, this provision was originally limited to the mere discovery of scientific principles or the formulation of abstract theories. The first limb dealt with discovery and the second with the intellectual exercise of formulating an abstract theory. The qualifier “mere”, which is an adjective, was added before the noun “discovery” in the first limb to underscore that something more than a discovery of a scientific principle, such as the production of a novel device that operates on such scientific principle, may fall outside the scope of patent exclusion. Because the second limb does not deal with discovery but to the formulation of a abstract theory, if the intention were to apply the adjective “mere” to the second limb, it should have been placed before the noun “formulation” in such limb. What about the third limb: “discovery of any living thing or non-living substance occurring in nature”? To begin with, it would be a strained construction to conclude that the adjective “mere” does not reach and qualify the second limb but qualifies the third. The ordinary rule of grammar and, therefore, one of the principles of statutory construction is that a modifier, such as the word “mere”, would qualify the entire series of nouns or verbs if such series is a straightforward parallel construction, whereas, it would be restricted to the nearest reasonable referent otherwise. For instance, if the second limb did not exist and Section



3(c) had been framed as follows: *the mere discovery of a scientific principle or of any living thing or non-living substance occurring in nature*, both the adjective “mere” and the noun “discovery” would have applied to both limbs as the phrase would not make sense otherwise. Reference may be made to *Reading Law, The Interpretation of Legal Texts, Antonin Scalia and Bryan Garner, 2012 Edition, Thomson/West*, for an illuminating discussion on these principles of interpretation.

13. Another aspect to be noticed, in this regard, is that the noun “discovery” in the third limb is intended to apply both to living things and non-living substances occurring in nature. This is a pointer, albeit not conclusive, that the adjective “mere” does not extend to this limb as otherwise even a “living thing” could fall outside the scope of patent exclusion if there is something more than mere discovery. As discussed earlier, the amendment to this clause was effected by Act 38 of 2002, which was enacted pursuant to the Patents (Second Amendment) Bill 1999 (Bill No.49). In the Statement of Objects and Reasons, in relevant part, it is stated as under with regard to the amendment of Section 3:

“(b) to modify section 3 of the present act to include exclusions permitted by TRIPS Agreement



and also subject matters like discovery of any living or non-living substances occurring in nature in the list of exclusions which in general do not constitute patentable invention”

Clause 4 of the bill provides as under:

“sub-clause (b) seeks to amend clause (c) of Section 3 so as to include discoveries of any living thing or non-living substance occurring in nature as not inventions patentable.”

It is noticeable that the qualifier “mere” was not used in the Statement of Objects and Reasons for Bill No.49 or in clause 4. If Parliament intended to apply the qualifier, it is likely that the word “mere” would have found place before the word “discovery”. It should also be noticed that clause (d) of Section 3, which also uses the qualifier “mere” uses it in each limb of the provision. Hence, the text, interpreted as per the ordinary rules of grammar, the immediate statutory context, and the legislative history of amended clause (c) of section 3 point to the same conclusion, i.e. that the qualifier “mere” is confined to the nearest reasonable referent “discovery of a scientific principle” and does not extend to “the discovery of any living thing or non-living substance occurring in nature.” For reasons set out above, I deviate from the interpretation of the Delhi High Court, in this regard, in



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Diamond Star Global Sdn. Bhd. v. Joint Controller of Patents and Designs, 2023 SCC OnLine Del 1879.

14. The next aspect to which I turn my attention is the impact of the phrase “occurring in nature”. Does it also apply to the expression “living thing”? The ordinary rules of syntax would indicate the following structure if the intention were to extend “occurring in nature” to “living thing”: *'the discovery of any living or non-living thing occurring in nature'*. Even otherwise, given the current state of science, the extension of “occurring in nature” to “living thing” would create a redundancy that cannot ordinarily be imputed to Parliament. Thus, I conclude that the expression “occurring in nature” in the third limb of Section 3(c) only qualifies the nearest reasonable referent “non-living substance”.

15. Before answering questions relating to the scope of Section 3(c) in the Indian statutory context, it is instructive to examine judgments of the US Supreme Court in this regard, and I discuss the same next. Section 101 of the US Patent Act prescribes as under:

“Whoever invents or discovers any new and useful process, machine, manufacture, or composition of



matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.”

Two aspects are conspicuous: no express patent exclusions are prescribed; and even discovery appears to fall literally within the scope of patent protection. In this statutory context, in paragraph 14 of the SCC OnLine Report, the US Supreme Court in *Sidney A. Diamond v. Ananda M. Chakrabarty*(*Chakrabarty*), 1980 SCC OnLine US SC 128, held, in relevant part, as under:

“This is not to suggest that Section 101 has no limits or that it embraces every discovery. The laws of nature, physical phenomena, and abstract ideas have been held not patentable....Thus a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that $E=mc^2$; nor could Newton have patented the law of gravity. Such discoveries are “manifestations of nature, free to all men and reserved exclusively to none...”

On noticing that the bacterium, in that case, was man-made, the US Supreme Court held in *Chakrabarty* that it was patent-eligible.



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16. In *Mayo Collaborative Services, dba Mayo Medical Laboratories v. Prometheus Laboratories Inc.(Mayo)*, 2012 SCC OnLine

US SC 28, in the context of process claims regarding the dosage level of thioprine drugs, it was held that the claims apply natural laws describing the relationships between the concentration in the blood of certain thioprine metabolites and the likelihood that the drug dosage would be ineffective or induce harmful side effects. Therefore, the claims were held to be patent-ineligible. In *Association for Molecular Pathology et al v. Myriad Genetics et al*, 133 S.Ct. 2107 (2013), the US Supreme Court concluded that a claimed invention for discovery of the precise location and sequence of two human genes was patent-ineligible, whereas a synthetically created complementary deoxyribonucleic acid (cDNA) was held to be patent eligible.

17. Reverting to Indian law, as noticed earlier, Section 3(c) uses the expression “occurring in nature” to qualify “discovery of a non-living substance.” While it could be argued that this qualifier is only intended to underscore that the exclusion would not apply to a non-living substance that is man-made, in my view, said explanation does not withstand close scrutiny because such non-living substance, if man-made and novel, would not be



discovered; it would be created or invented. If man-made but not novel, it would be produced and not discovered. It would also not surmount the Section 2(1)(j) hurdle and the Section 3(c) exclusion is clearly not intended for such non-living substances. What is the sequitur of the use of the expression “occurring in nature”: would a synthetic version of a substance that rarely occurs in nature but is required to be produced in large quantities for the treatment of serious illnesses qualify for or be excluded from patent protection? Should a patent applicant establish that such non-living substance never occurs in nature? The text of clause (c) of Section 3 contains guidance.

18. The statutory prescription is “discovery of any ... non-living substance occurring in nature”. Both the use of the noun “discovery”- which implies finding something which already exists and not producing, engineering or making something - and the use of the present continuous form “occurring in nature” indicate that the exclusion will only apply to the process of finding a hitherto undiscovered non-living substance by identifying and isolating it from nature. While reaching this conclusion, I take on board the presumption in statutory construction that redundancy should not be imputed to Parliament, and that the expression “occurring in



nature” should not be robbed off all meaning and purpose. Ultimately, it should not be lost sight of that Section 3(c) is confined to patent exclusions or ineligibility and passing through such filter does not guarantee the grant of patent.

19. The real challenge with regard to a patent application in respect of a synthesized non-living substance, especially a monoclonal antibody, is establishing novelty, technical advance and not patent eligibility. For such purpose, the sequence of the antibody, especially the CDRs, may need to be compared with known antibody sequences. The patent applicant may also be required to establish that it does not fall within other exclusions in Section 3, such as sub-section (d) thereof, and further satisfy the requirements of Section 2(1)(j) of the Patents Act. The judgments of the IPAB, such as *Biogaia*, *The University of British Columbia* and *Health Protection Agency* record substantially similar conclusions. Although not a concern in this case because of the nature of claims, the other legitimate concern from the Indian Patent Office perspective, in the context of monoclonal antibodies, could be to closely examine the width of claims so as to ensure that very broad claims focused entirely or largely on functionality



are not allowed because that could impede instead of fostering inventiveness in future.

20. The conclusion of the respondent that the antibodies claimed in the appellant's invention occur in nature was strongly refuted by learned counsel for the appellant on the basis that the antibody was engineered by an elaborate process. In order to substantiate such contention, the appellant relied on internal page 16 of the complete specification, which, in relevant part, is set out below:

“The monoclonal antibodies of the present invention can be produced as follows:

Synthetic A-beta 1-42 (Peptide Institute Inc., Osaka) is dissolved in distilled deionized water or a 10 mM phosphatic buffer solution, and this is incubated at 37°C for 18 hours. Then the peptides are separated by 4-12% SDS-PAGE, and visualized by CBB staining, and the portion of the A-beta 1-42 tetramer alone which is not contaminated with the A-beta 1-42 monomer is cut out and used as an antigen. On the other hand, a preparation containing a large amount of the A-beta 1-40 oligomer is prepared by mixing (i) a modified A-beta 1-40 prepared by chemically linking 6-carboxytetramethylrhodamine (6-Tamra) (SIGMA) to



the N terminus of a synthetic A-beta 1-40 peptide using a conventional method with (ii) synthetic A-beta 1-40 (Peptide Institute, Inc., Osaka) at a ratio of 5:100, 10:100, 20:100, 30:100, 40:100, 50:100, 60:100, 70:100, or 80:100, preferably 90:100, or more preferably 100:100, and carrying out polymerization reaction for three hours, preferably six hours, or more preferably 20 hours. Next, Balb-c mice are immunized with 2.5 ug of either the A-beta 1-42 oligomer emulsified using complete Freund's adjuvant by injecting the antigen into their foot pad. Subsequently, booster immunizations are carried out six times. Hybridomas are produced from the inguinal lymph node by fusion with Sp2/O-Ag14 cells using polyethylene Glycol 1500”

21. The response of the respondent was that hybridoma technology is well known and that the use of such process cannot be construed as inventive. As stated earlier, it was also held that antibody 6E4 is naturally occurring and was merely discovered. The appellant does not, however, assert inventiveness in the use of hybridoma technology. Inventiveness is asserted with regard to the production of a monoclonal antibody, which targets a specific epitope. From the description set out in the complete



specification, the conclusion that follows is that the antibody of the claimed invention was undoubtedly not isolated from a human being, but was engineered in the manner described in internal page 16 of the complete specification.

22. The respondent also relied on the fact that the description of the organism in the sequence listing is *homo sapiens*. Some explanation is necessary for the appreciation of this contention and to put it in perspective. Every patent application in respect of substances such as antibodies is required to be accompanied by a sequence listing. The World Intellectual Property Organisation (WIPO) has formulated standards in relation to. The currently applicable standard is Standard 26(St.26). At the relevant point of time, Standard 25 was applicable. Standard 25 prescribes the mandatory and optional information that should be provided in the sequence listing. Such mandatory information includes information relating to the organism from which the nucleotide or amino acid sequence originates and setting out the sequence. Standard 25 also prescribes that such information is required to be provided against the numerical identifier [213] and [400], respectively.



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23. The appellant does not dispute the respondent's contention that the organism of origin was listed as *homo sapiens* in the sequence listing, including the SEQ IDs in respect of which claims were made. The appellant contended, however, that a sequence listing should be most categorically identified by the numeric identifier [400], which depicts the sequence. Specifically, the appellant contended that the organism of origin, i.e numeric identifier [213], is merely indicative of the origin of the protein, even if such protein is recombinant or synthetically obtained, and does not lead to the extrapolated conclusion that the antibody is naturally occurring. In light of the conclusions drawn on the interpretation of Section 3(c) of the Patents Act, the contention of the respondent that the claims are in respect of the discovery of an antibody/non-living substance occurring in nature cannot be countenanced merely because the organism specified in the sequence listing is *homo sapiens*. As discussed earlier, such conclusion would be justified only if the appellant had discovered/found a hitherto unknown antibody and isolated it from nature.

24. In light of the disclosures in the complete specification, the conclusion that follows is that the antibody was generated by injecting an engineered antigen into the mice. After doing so, material extracted from the



inguinal lymph of the mice was fused with myeloma cells by the hybridoma process. This resulted in the antibody over which the patent claim is made.

When all these facts and circumstances are considered cumulatively, in the context of my conclusions on the scope and ambit of Section 3(c) of the Patents Act, I conclude that the claimed invention is not excluded from patent protection under clause (c) of section 3. Consequently, the impugned order cannot be sustained and is hereby set aside.

25.As regards other objections in the FER, it was recorded as under in the impugned order:

“Regarding objection no.1, of the hearing notice the amended claims 1-3 are now related to a single antibody only...”

“Regarding objections no.3-5 of the hearing notice the claim 4 is deleted to overcome this objection.”

Since all the other objections in the FER were subsequently dropped pursuant to the deletion of corresponding claims, in view of the above conclusion that the Section 3(c) rejection is untenable, I direct that the claimed invention proceed to grant on the basis of the current claims, which were submitted in course of hearings before the respondent. For the avoidance of doubt, the said claims are set out below:



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“We claim:

- 1. An antibody that binds A-beta oligomer, of any one of (1) to (2) below:*
 - (1) an antibody that comprises an H chain having the amino acid sequence SEQ ID No.89 as CDR1, the amino acid sequence of SEQ ID No:91 as CDR2, and the amino acid of SEQ ID No:93 as CDR3; and an L chain having the amino acid sequence of SEQ ID No:95 as CDR1, the amino acid sequence of SEQ ID NO:97 as CDR2; and the amino acid sequence of SEQ ID NO:99 as CDR3;*
 - (2) an antibody that comprises an H chain having the amino acid sequence of SEQ ID NO:85 as VH; and an L chain having the amino acid sequence of SEQ ID NO:87 as VL.*
- 2. The antibody as claimed in claim 1, comprising an H chain having the amino acid sequence of SEQ ID NO:81 and an L chain having the amino acid sequence of SEQ ID NO:83.*
- 3. The antibody as claimed in claims 1, wherein the antibody is a chimeric antibody or a human antibody.”*



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26.(T)CMA(PT)No.118 of 2023 is allowed on the above terms

without any order as to costs.

06.03.2024

Index : Yes/No

Internet : Yes/No

Neutral Citation : Yes/No

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To

Assistant Controller of Patents and Designs,
Government of India, Patent Office,
Intellectual Property Building,
G.S.T. Road, Guindy,
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SENTHILKUMAR RAMAMOORTHY J.

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Pre-Delivery Judgment in
(T) CMA (PT) No.118 of 2023
(OA/22/2018/PT/CHN)

06.03.2024