Citation: Regeneron Pharmaceuticals Inc and Sanofi Biotechnology (Re), 2025 CACP 6
Commissioner's Decision #1687
Décision du commissaire nº 1687
Date: 2025-05-14

TOPIC: O00 Obviousness

SUJET: O00 Évidence

Application No. 2851751
Demande nº 2 851 751

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 2851751 having been rejected under subsection 199(1) of the *Patent Rules* (SOR/2019-251), has consequently been reviewed in accordance with paragraph 86(7)(c) of the *Patent Rules* (SOR/2019-251). The recommendation of the Patent Appeal Board and the decision of the Commissioner are to refuse the application.

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## INTRODUCTION

[1] This recommendation concerns the review of rejected patent application number 2851751, which is entitled “SARILUMAB AND METHOTREXATE COMPOSITIONS AND USE THEREOF FOR TREATMENT OF RHEUMATOID ARTHRITIS” and is owned by Regeneron Pharmaceuticals Inc and Sanofi Biotechnology. The Patent Appeal Board (the Board) reviewed the rejected application pursuant to paragraph 86(7)(c) of the *Patent Rules* (SOR/2019-251) (the *Patent Rules*).

[2] As explained below, we recommend that the Commissioner of Patents refuse the application.

## BACKGROUND

### The application

[3] The present application was filed under the provisions of the Patent Cooperation Treaty and has an effective filing date in Canada of October 10, 2012. It was laid open to public inspection on April 18, 2013.

[4] The claimed subject-matter relates to the use of an antibody comprising the antigen binding regions of sarilumab, a fully human anti-interleukin (IL)-6 receptor monoclonal antibody, alone or in combination with methotrexate (MTX) for treating rheumatoid arthritis (RA) in a subject that was previously ineffectively treated with a tumour necrosis factor alpha (TNF-α) antagonist or that was previously ineffectively treated with both methotrexate and a TNF-α antagonist.

[5] The application has 45 claims on file that were received at the Patent Office on April 4, 2022.

### Prosecution history

[6] On January 31, 2023, a Final Action was issued pursuant to subsection 86(5) of the *Patent Rules*. The Final Action indicated that the application is defective on the ground that all the claims 1 to 45 on file at the time of Final Action encompass

obvious subject-matter and therefore do not comply with section 28.3 of the *Patent Act,* RSC 1985, c P-4 (the *Patent Act*).

[7] The Applicants' Response to the Final Action dated May 31, 2023, disagreed with the obviousness assessment.

[8] On June 5, 2024, the application was forwarded to the Patent Appeal Board for review under paragraph 86(7)(c) of the *Patent Rules* along with a Summary of Reasons explaining that the Examiner's rejection is maintained as the arguments presented in response to the Final Action are not persuasive.

[9] In a letter dated June 5, 2024, the Patent Appeal Board forwarded a copy of the Summary of Reasons to the Applicants and requested that they confirm their continued interest in having the application reviewed.

[10] In a letter dated September 4, 2024, the Applicants confirmed their interest in having the review proceed.

[11] The instant Panel, comprising the undersigned members of the Board, was assigned to review the instant rejected application under paragraph 86(7)(c) of the *Patent Rules* and to make a recommendation to the Commissioner of Patents as to its disposition.

[12] In a Preliminary Review Letter sent on February 5, 2025, we set out our preliminary analysis of the obviousness issue with respect to the claims on file. The Panel was of the preliminary view that the claims on file encompass subject-matter that would have been obvious, contrary to section 28.3 of the *Patent Act*.

[13] The Preliminary Review Letter also provided the Applicants with an opportunity to make both written and oral submissions.

[14] In a letter dated February 14, 2025, the Applicants declined to participate in an oral hearing and indicated that written submissions would be provided.

[15] On March 6, 2025, the Applicants provided a written Response to the Preliminary Review Letter and a set of proposed claims (proposed claims).

## THE ISSUE

[16] The sole issue to be addressed by this review is whether the subject-matter of the claims on file is obvious contrary to section 28.3 of the *Patent Act*.

[17] After considering the claims on file, we reviewed the proposed claims to determine if they would be considered a necessary amendment under subsection 86(11) of the *Patent Rules*.

## PURPOSIVE CONSTRUCTION

### Legal principles and Office practice

[18] Purposive Construction is antecedent to any consideration of validity (*Free World Trust v Électro Santé Inc*, 2000 SCC 66 at para 19 [*Free World Trust*]).

[19] In accordance with *Free World Trust* and *Whirlpool Corp v Camco Inc*, 2000 SCC 67 [*Whirlpool*], purposive construction is performed from the point of view of the person of ordinary skill in the art (POSITA) in light of the relevant common general knowledge (CGK), considering the whole of the disclosure including the specification and drawings. In addition to interpreting the meaning of the terms of a claim, purposive construction distinguishes the essential elements of the claim from the non-essential elements. Whether or not an element is essential depends on the intent expressed in or inferred from the claim, and on whether it would have been obvious to the skilled person that a variant has a material effect upon the way the invention works.

[20] "Patentable Subject-Matter under the *Patent Act*" (CIPO, November 2020) [*PN2020–04*] also discusses the application of these principles, pointing out that all elements set out in a claim are presumed essential unless it is established otherwise, or such presumption is contrary to the claim language.

[21] Regarding the POSITA, several court decisions have provided additional context for their identification. In *Whirlpool* at para 53, the Supreme Court of Canada explained that although the POSITA is deemed to have no scintilla of inventiveness or imagination, a patent specification is addressed to "skilled

individuals sufficiently versed in the art to which the patent relates to enable them on a technical level to appreciate the nature and description of the invention". Moreover, "in the case of patents of a highly technical and scientific nature, that person may be someone possessing a high degree of expert scientific knowledge and skill in the particular branch of science to which the patent relates": *Consolboard v MacMillan Bloedel (Sask) Ltd*, [1981] 1 SCR 504 at page 525.

[22] In addition, the POSITA can represent a composite of scientists—highly skilled and trained persons who conduct scientific research to advance knowledge in an area of interest—and researchers: *Bayer Aktiengesellschaft v Apotex Inc* [1995] 60 CPR (3d) 58 at page 79:

> The notional skilled technician can be a composite of scientists, researchers and technicians bringing their combined expertise to bear on the problem at hand: "This is particularly true where the invention relates to a science or art that transcends several scientific disciplines." (*Per* Wetston J. in *Mobil Oil Corp. v. Hercules Canada Inc.* (unreported, September 21, 1994, F.C.T.D., at p. 5 [now reported 57 C.P.R. (3d) 488 at p. 494, 82 F.T.R. 211].)

[23] Regarding the identification of the CGK, it is well established that the CGK is limited to knowledge which is generally known by persons skilled in the field of art or science to which a patent relates: *Apotex Inc v Sanofi–Synthelabo Canada Inc*, 2008 SCC 61 at para 37 [*Sanofi*]; *Free World Trust* at para 31.

[24] More specifically, we consider that the assessment of CGK is governed by the principles stated in *Eli Lilly & Co v Apotex Inc*, 2009 FC 991 at para 97, upheld by 2010 FCA 240, citing *General Tire & Rubber Co v Firestone Tyre & Rubber Co Ltd*, [1972] RPC 457, [1971] FSR 417 (UKCA) at pages 482 and 483 (of RPC):

> The common general knowledge imputed to such an addressee must, of course, be carefully distinguished from what in the patent law is regarded as public knowledge. This distinction is well explained in Halsbury's Law of England, Vol. 29, para 63. As regards patent specifications, it is the somewhat artificial (see per Lord Reid in the Technograph case, [1971]

F.S.R. 188 at 193) concept of patent law that each and every specification, of the last 50 years, however unlikely to be looked at and in whatever language written, is part of the relevant public knowledge if it is resting anywhere in the shelves of the Patent Office. On the other hand, common general knowledge is a different concept derived from a common sense approach to the practical question of what would in fact be known to an appropriately skilled addressee—the sort of man, good at his job, that could be found in real life.

The two classes of documents which call for consideration in relation to common general knowledge in the instant case were individual patent specifications and “widely read publications”.

As to the former, it is clear that individual patent specifications and their contents do not normally form part of the relevant common general knowledge, though there may be specifications which are so well known amongst those versed in the art that upon evidence of that state of affairs they form part of such knowledge, and also there may occasionally be particular industries (such as that of colour photography) in which the evidence may show that all specifications form part of the relevant knowledge.

As regards scientific papers generally, it was said by Luxmoore, J. in British Acoustic Films (53 R.P.C. 221, at 250):

“In my judgment it is not sufficient to prove common general knowledge that a particular disclosure is made in an article, or series of articles, in a scientific journal, no matter how wide the circulation of that journal may be, in the absence of any evidence that the disclosure is accepted generally by those who are engaged in the art to which the disclosure relates. A piece of particular knowledge as disclosed in a scientific paper does not become common general knowledge merely because it is widely read, and still less because it is widely circulated. Such a piece of knowledge only becomes general knowledge when it is generally known and accepted without question by the bulk of those who are engaged in the particular art; in other

> words, when it becomes part of their common stock of knowledge relating to the art." And a little later, distinguishing between what has been written and what has been used, he said:
>
> "It is certainly difficult to appreciate how the use of something which has in fact never been used in a particular art can ever be held to be common general knowledge in the art."
>
> Those passages have often been quoted, and there has not been cited to us any case in which they have been criticised. We accept them as correctly stating in general the law on this point, though reserving for further consideration whether the words "accepted without question" may not be putting the position rather high: for the purposes of this case we are disposed, without wishing to put forward any full definition, to substitute the words "generally considered as a good basis for further action".

[25] Established reference works (such as textbooks, review articles, handbooks, etc.) or demonstrated commonality of certain knowledge in a number of disclosures in the field are relevant to the inquiry: Manual of Patent Office Practice (CIPO) at §12.02.02c, revised October 2019.

[26] Furthermore, information in a specification may also be evidence of the CGK as it could be reasonable to consider general or broadly worded assertions of conventional practice or knowledge as common general knowledge: *Corning Cable Systems LLC v Canada (Attorney General)*, 2019 FC 1065 and *Newco Tank Corp v Canada (Attorney General)*, 2015 FCA 47.

## Analysis

[27] Since both interpretation of term meaning and identification of the essential elements are done in light of the relevant CGK, one must first identify the POSITA to determine their CGK.

### *The POSITA and the relevant CGK*

[28] In the Preliminary Review Letter on pages 7 to 9 we set out a preliminary analysis in respect of the identification of the POSITA and their relevant CGK:

> The Final Action on page 3 defines the POSITA as "a team including a clinician, a molecular biologist, and an immunologist".
>
> The Response to the Final Action submits on page 2 that the above definition of the POSITA is unclear but does not explain how or why it is unclear and does not point to which aspect, if one in particular, lacks clarity.
>
> We preliminarily consider that defining the POSITA as a team including a clinician, a molecular biologist, and an immunologist is clear but is incomplete and overly broad when it comes to the fields of expertise relating to this application.
>
> Having reviewed the specification as a whole, it is our preliminary view that it generally relates to the technical field of therapeutic treatments of RA. Notably, the first paragraph of page 1 of the description states the following:
>
> > The present invention relates to the field of therapeutic treatment of rheumatoid arthritis. More specifically, the invention relates to the use of interleukin-6 receptor (ILSR) antagonists, such as anti-IL-6R antibodies combined with disease modifying antirheumatic drugs, to treat rheumatoid arthritis.
>
> Taking into account the above findings, we preliminarily consider that the POSITA is a multidisciplinary team comprising:
>
> - a researcher and clinician in the field of rheumatology who are specialized in RA diagnosis, treatment, and management, that are familiar with drug development and testing, and that are familiar with clinical efficacy and safety trials as well as their scoring metrics for RA;

- a molecular biologist who is familiar with designing and testing therapeutic humanized antibodies; and
- an immunologist who is familiar with the immune-related aspects of the pathogenesis of RA.

With regard to the CGK, the Final Action on page 3 states that the CGK includes “the use of therapeutic antibodies for the treatment of rheumatoid arthritis, including combination treatments. The use of methotrexate for treating rheumatoid arthritis was common general knowledge”.

The Response to the Final Action submits on page 2 that the Examiner’s assertion that combination treatments as part of the CGK is vague. Further, it is our understanding that the Applicant does not acknowledge that the teachings of the cited prior art documents support the Examiner’s characterisation of the POSITA and their CGK.

Our preliminary views expressed above with respect to the identity of the POSITA bear upon our preliminary assessment of the CGK expected from the POSITA that is detailed below.

In that regard, it is our preliminary view that the following pieces of knowledge were generally known at the relevant time and accepted without question by the bulk of those who are engaged in the particular fields of clinical and research rheumatology, and more particularly in the field of therapeutic treatments of RA:

- Therapeutic options for the treatment of RA. These options include combination therapies, conventional disease-modifying antirheumatic drugs (DMARDs), including MTX as the cornerstone of antirheumatic therapies, as well as biologic DMARDs, such as TNF-α antagonists (reviewed in Feely et al., “Therapeutic options for rheumatoid arthritis”, *Expert Opin. Pharmacother*., 10(13), pages 2095-2106, 2009 (*Feely*));
- Strategies after the failure of a TNF-α antagonist treatment of RA include the switch to an alternative class of biologics with a different mechanism of action as well as

combination therapies (reviewed in Papagoras et al., "Strategies after the failure of the first anti-tumor necrosis factor α agent in rheumatoid arthritis", *Autoimmunity Reviews*, vol. 9, pages 574–582, 2010 (*Papagoras*)); and

- Dose-ranging trials and dose selection constitute routine pharmaceutical work in the field of antirheumatic therapies to assess the safety and efficacy of potentially useful therapeutics.

[29] The Applicants did not contest or comment on our characterisations of the POSITA and their relevant CGK in the Response to the Preliminary Review Letter. We therefore adopt the above characterisations of the POSITA and their CGK for the purpose of our final analysis.

### *The claims on file*

[30] There are 45 claims on file. We consider that independent claims 1, 16 and 33 are representative of the claimed subject-matter and read as follows:

1. Use of an antibody that specifically binds to human IL-6 receptor and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises the three complementarity determining regions (CDRs) found within the sequence of SEQ ID NO:2 and wherein the VL comprises the three CDRs found within the sequence of SEQ ID NO:3, for treating rheumatoid arthritis in a subject that was previously ineffectively treated for rheumatoid arthritis with methotrexate and was previously ineffectively treated for rheumatoid arthritis with a TNF-α antagonist, wherein the antibody is for use in combination with methotrexate, and wherein the antibody is for subcutaneous use at a dosage between 100 mg and 200 mg once every two weeks, and wherein the subject achieves at least a 20% improvement in the American College of Rheumatology core set disease index after 12 weeks of treatment.

16. Use of an antibody that specifically binds to human IL-6 receptor and comprises a heavy chain variable region (VH) and a light chain variable

region (VL), wherein the VH comprises the three complementarity determining regions (CDRs) found within the sequence of SEQ ID NO:2 and wherein the VL comprises the three CDRs found within the sequence of SEQ ID NO:3, for treating rheumatoid arthritis in a subject that was previously ineffectively treated for rheumatoid arthritis with a TNF-α antagonist, wherein the antibody is for use in combination with methotrexate, wherein the antibody is for subcutaneous use at a dosage between 100 mg and 200 mg once every two weeks, and wherein the subject achieves at least a 20% improvement in the American College of Rheumatology core set disease index after 12 weeks of treatment.

33. Use of an antibody that specifically binds to human IL-6 receptor and comprises a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises the three complementarity determining regions (CDRs) found within the sequence of SEQ ID NO:2 and wherein the VL comprises the three CDRs found within the sequence of SEQ ID NO:3, for treating rheumatoid arthritis in a subject that was previously ineffectively treated for rheumatoid arthritis with a TNF-α antagonist, wherein the antibody is for subcutaneous use at a dosage between 100 mg and 200 mg once every two weeks, and wherein the subject achieves at least a 20% improvement in the American College of Rheumatology core set disease index after 12 weeks of treatment.

[31] Independent claims 3, 18 and 35 define the contemplated antibody with further references to the framework regions of the variable heavy and light chains.

[32] Dependent claims 2, 17 and 34 further specify the sequences of the heavy and/or light chain variable regions.

[33] Dependent claims 4, 5, 19, 20, 36 and 37 further specify that the antibody comprises a substitution in the VL framework region (claims 4, 19 and 36) or in the VH and VL framework regions (claims 5, 20 and 37).

[34] Dependent claims 6, 21 and 38 further specify that the antibody is sarilumab.

[35] Dependent claims 7, 8, 24 and 25 further specify that the antibody and methotrexate are for sequential use (claims 7, 8 and 24) or simultaneous use (claim 7, 24 and 25).

[36] Dependent claims 9, 10, 26, 27, 41 and 42 further specify the antibody dosing regimen (amount and frequency of administration).

[37] Dependent claims 11 and 28 further specify the MTX dose.

[38] Dependent claims 12, 13, 29, 30, 43 and 44 further specify a level of measured improvement achieved in the subject.

[39] Dependent claims 14, 15, 22, 23, 39 and 40 further specify the nature of the TNF-α antagonist.

[40] Dependent claims 31 and 45 further specify the length of the previous treatment of the subject with a TNF-α antagonist or that the subject was intolerant to at least one TNF-α antagonist.

[41] Dependent claim 32 further specifies that the subject was previously treated with MTX.

### *Essential elements*

[42] In the Preliminary Review Letter on page 13, we expressed the view that all of the elements in the claims on file are essential:

> As mentioned above, the elements set out in a claim are generally presumed essential unless it is established otherwise or such presumption is contrary to the claim language.
>
> In our view, the POSITA reading claims 1 to 45 in the context of the specification as a whole and the CGK would understand that there is no use of language in the claims indicating that any of the elements are intended as being non-essential.

> Although some of the claims express a list of alternatives, it is our view that the POSITA would understand that, when any one of these alternatives is chosen they are essential for that particular embodiment.
>
> Our preliminary view is therefore that all of the elements of claims 1 to 45 are essential.

[43] The Applicants did not contest or comment on the essentiality of the claimed elements and we therefore consider all of the elements of claims 1 to 45 to be essential for the purpose of this final analysis.

## OBVIOUSNESS

[44] For the reasons set out below, we consider claims 1 to 45 on file to define subject-matter that would have been obvious to the POSITA as of the claim date.

### Legal principles

[45] Section 28.3 of the *Patent Act* requires that the subject-matter of a claim not be obvious to the POSITA:

> The subject-matter defined by a claim in an application for a patent in Canada must be subject-matter that would not have been obvious on the claim date to a person skilled in the art or science to which it pertains, having regard to
>
> (a) information disclosed before the one-year period immediately preceding the filing date or, if the claim date is before that period, before the claim date by the applicant, or by a person who obtained knowledge, directly or indirectly, from the applicant in such a manner that the information became available to the public in Canada or elsewhere; and
>
> (b) information disclosed before the claim date by a person not mentioned in paragraph (a) in such a manner that the information became available to the public in Canada or elsewhere.

[46] In *Sanofi* at para 67, the Supreme Court of Canada states that it is useful in an obviousness inquiry to follow the following four-step approach:

> (1) (a) Identify the notional "person skilled in the art";
>
> (b) Identify the relevant common general knowledge of that person;
>
> (2) Identify the inventive concept of the claim in question or if that cannot readily be done, construe it;
>
> (3) Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed;
>
> (4) Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?

[47] In the context of the fourth step, the Court in *Sanofi* states that it may be appropriate in some cases to consider an "obvious to try" analysis and it identifies the following non-exhaustive factors to be considered in an obvious to try analysis [defined terms added]:

> Is it more or less self-evident that what is being tried ought to work? Are there a finite number of identifiable predictable solutions known to persons skilled in the art? [the Self-Evident Factor]
>
> What is the extent, nature and amount of effort required to achieve the invention? Are routine trials carried out or is the experimentation prolonged and arduous, such that the trials would not be considered routine? [the Extent and Effort Factor]
>
> Is there a motive provided in the prior art to find the solution the patent addresses? [the Motive Factor].

[48] For a finding that an invention was “obvious to try”, it must have been “more or less self-evident” to try to obtain the invention. Mere possibility that something might turn up is not enough” (*Sanofi* at para 66).

## Analysis

[49] As a preliminary matter, the following obviousness analysis will adopt the Applicants’ subject population designations that are used in their Response to the Preliminary Review Letter on page 2. More specifically:

- the subject population “previously ineffectively treated for rheumatoid arthritis with a TNF-α antagonist in combination with a methotrexate” is referred to herein as “the TNF-α antagonist + MTX non-responder population”; and
- the subject population “previously ineffectively treated for rheumatoid arthritis with a TNF-α antagonist” is referred to herein as “the TNF-α antagonist non-responder population”.

[50] On page 4 of the Response to the Preliminary Review Letter, the Applicants submitted that the TNF-α antagonist + MTX non-responder population and the TNF-α antagonist non-responder population are entirely different and distinct populations and further submitted that the Panel considered that they were the same.

[51] We agree that the TNF-α antagonist + MTX non-responder population and the TNF-α antagonist non-responder population are distinct populations. This distinction has been acknowledged and considered in the Preliminary Review Letter throughout the obviousness analysis, for example on pages 19 and 20 [newly designated populations added]:

> Within the context of the claimed subject-matter, we consider that the relevant questions here are whether it would have been more or less self-evident to the POSITA, based on the disclosures of [the cited prior art documents] and the relevant CGK, that the subcutaneous use of an

antibody comprising the antigen binding regions of sarilumab at a dosage between 100 mg and 200 mg once every two weeks for 12 weeks ought to be effective for the treatment of RA:

1) when used in combination with MTX in a subject that was previously ineffectively treated for RA with MTX and a TNF-α antagonist (claims 1 to 15 and 32) **[TNF-α antagonist + MTX non-responder population]**;

2) when used in combination with MTX in a subject that was previously ineffectively treated for RA with a TNF-α antagonist (claims 16 to 31) **[TNF-α antagonist non-responder population]**; and

3) when used in a subject that was previously ineffectively treated for RA with a TNF-α antagonist (claims 33 to 45) **[TNF-α antagonist non-responder population]**.

In our preliminary view, the POSITA (in view of their CGK) would consider that the scope of claims 16 to 31 and 33 to 45 encompasses a subject that was also previously ineffectively treated for RA with MTX and that the scope of claims 33 to 45 encompasses the use of MTX in combination with the recited antibody that specifically binds to human IL-6 receptor. In other words, all claims encompass the subcutaneous use of sarilumab at a dosage between 100 mg and 200 mg once every two weeks for 12 weeks in combination with MTX in a subject that was previously ineffectively treated for RA with MTX and a TNF-α antagonist.

…

Given the above considerations, it is our preliminary view that it would have been self-evident to the POSITA that the subcutaneous use of sarilumab at a dosage between 100 mg and 200 mg once every two weeks for 12 weeks in combination with MTX in a subject that was previously ineffectively treated for RA with MTX and a TNF-α antagonist **[TNF-α antagonist + MTX non-responder population]** ought to be effective for the treatment of RA.

> It is also our preliminary view that it would have been self-evident to the POSITA that the subcutaneous use of sarilumab at a dosage between 100 mg and 200 mg once every two weeks for 12 weeks alone or in combination with MTX in a subject that was previously ineffectively treated for RA solely with a TNF-α antagonist (i.e., not in combination with MTX) **[TNF-α antagonist non-responder population]** also ought to be effective for the treatment of RA.

[52] That being said, we also expressed in the quoted passage above our preliminary view that:

- the scope of claims 16 to 31 and 33 to 45 encompasses a subject that was also previously ineffectively treated for RA with MTX; and
- the scope of claims 33 to 45 encompasses the use of MTX in combination with the recited antibody that specifically binds to human IL-6 receptor.

[53] The Applicants did not contest or comment on those preliminary findings regarding the scope of claims 16 to 31 and 33 to 45 in their Response to the Preliminary Review Letter.

[54] We therefore remain of the view that the scope of claims 16 to 31 and 33 to 45 on file is broad enough to encompass both the TNF-α antagonist + MTX non-responder population and the TNF-α antagonist non-responder population because said claims do not explicitly exclude the TNF-α antagonist + MTX non-responder subpopulation and the POSITA would know, as part of their CGK, that TNF-α antagonists are used to treat patients who, in most cases, have previously failed to respond to MTX (as evidenced by *Papagoras* at page 575, left column and *Feely* on page 2102 section 10).

[55] Likewise, we remain of the view that the scope of claims 33 to 45 on file is broad enough to encompass the use of MTX in combination with the recited antibody that specifically binds to human IL-6 receptor as expressed in the quoted passage above because said claims do not explicitly exclude the use of MTX in combination with the recited antibody and the POSITA would know, as part of

their CGK, that TNF-α antagonists are generally used in combination with another DMARD, mainly MTX (as evidenced by *Papagoras* at page 575, right column, page 576 left column and by *Feely* in the background section as well as sections 5.2.1, 5.2.2, 5.2.3 and 11).

### *The POSITA and the relevant CGK*

[56] The POSITA and the relevant CGK have been identified above in the context of the purposive construction of the claims as of the publication date. It is our view that said CGK is also valid as of the claim date and is therefore relevant for assessing obviousness.

### *Identify the inventive concept of the claim in question or, if that cannot readily be done, construe it*

[57] The Preliminary Review Letter on pages 15 to 16 states the following about the inventive concepts of the claims on file:

> The Final Action on page 3 states the following with regard to an inventive concept for the claims on file:
>
> > The inventive concept of these claims pertains to the use of a particular antibody that specifically binds the human IL-6 receptor, which is sarilumab in some embodiments, for the treatment of rheumatoid arthritis in a subject that was previously ineffectively treated for rheumatoid arthritis with a TNF-α antagonist, wherein the antibody is for subcutaneous use. Claims 1-32 also include combination therapy with methotrexate. An additional embodiment includes the use of the antibody in a subject that was also ineffectively treated with methotrexate (claims 1-15).
>
> The Response to the Final Action submits on page 2 that the above assessment is incomplete as it omits claim features such as the doses and dosing regimen.

> As mentioned above, our preliminary view is that the POSITA would consider all of the elements in the claims to be essential, and so they should be reflected in the inventive concepts of the claims. Therefore, for the purposes of this assessment we take into account all of the essential elements of the claims. In our preliminary view, the combination of essential elements of independent claims 1, 3, 16, 18, 33 and 35 represents their inventive concepts as well.
>
> It is also our preliminary view is also that the elements of the dependent claims relating to the sequences of the heavy and/or light chain variable regions, the substitution in the VL framework region or in the VH and VL framework regions, the antibody identification, the type of use, the amount and frequency of administration, the MTX dosing regimen, the level of measured improvement, the nature of the TNF-α antagonist, the length of the previous treatment with a TNF-α antagonist or intolerance to at least one TNF-α antagonist, or a previous treatment with MTX, are part of the respective inventive concepts of the dependent claims.

[58] The Applicants did not contest or otherwise comment on the identification of the inventive concepts of the claims on file and we therefore consider that the combination of essential elements of independent claims 1, 3, 16, 18, 33 and 35 represents their inventive concepts and that the additional elements of the dependent claims are part of their respective inventive concepts.

### *Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed*

[59] The Preliminary Review Letter on pages 16 to 18 states the following about the differences that exist between the matter cited as forming part of the "state of the art" and the inventive concepts of the claims [newly designated populations added]:

> D1: Regeneron, "Sanofi and Regeneron Report Positive Phase 2b Trial Results with Sarilumab in Rheumatoid Arthritis", July 12,

2011. Retrieved from the internet from: https://investor.regeneron.com/news-releases/news-release-details/sanofi-and-regeneron-report-positive-phase-2b-trial-results.

D2: Emery et al., "IL-6 receptor inhibition with tocilizumab improves treatment outcomes in patients with rheumatoid arthritis refractory to anti-tumour necrosis factor biologicals: results from a 24-week multicentre randomised placebo-controlled trial", *Ann Rheum Dis*, 67**,** pages 1516-1523, 2008.

D3: Sanofi, "Effect of SAR153191 (REGN88) With Methotrexate in Patients With Active Rheumatoid Arthritis Who Failed TNF-α Blockers", Version 20 (September 27, 2011). Retrieved from the internet from: https://clinicaltrials.gov/study/NCT01217814.

D1 is a press release that discloses results from a phase 2b MOBILITY trial for combined use of sarilumab and MTX for treating patients with active RA who are inadequate responders to MTX therapy. The trial assessed sarilumab doses of 100 mg and 150 mg every week and 100 mg, 150 mg, and 200 mg administered subcutaneously every other week. An improvement of at least 20% in the American College of Rheumatology core disease set (ACR20) response after 12 weeks was seen in 49.0% of patients receiving the lowest sarilumab dose regimen and 72.0% of patients receiving the highest dose regimen compared to 46.2% of patients receiving placebo and MTX. Sarilumab also demonstrated significant benefit compared to placebo in ACR50 (at least 50% improvement) and ACR70 (at least 70% improvement) scores.

D2 discloses the use of a humanized anti-IL-6 receptor antibody, tocilizumab, in combination with MTX for treatment of RA refractory to TNF antagonist therapy. The patients previously had an inadequate response to one or more TNF antagonists, including etanercept, adalimumab, and infliximab. The baseline MTX dose was about 16 mg/week (Table 1). D2 teaches that 20-40% of RA patients show an inadequate response to

treatment with TNF inhibitors, alone or in combination with disease-modifying antirheumatic drugs (DMARDS) such as MTX (page 1516). D2 also teaches that tocilizumab in combination with MTX exhibits superior clinical efficacy compared with controls in several populations, including patients with an inadequate response to methotrexate (page 1516). In patients previously ineffectively treated for RA with a TNF antagonist, ACR20 was achieved at 24 weeks by 50.0%, 30.4% and 10.1% of patients in the 8 mg/kg, 4 mg/kg tocilizumab, and control groups, respectively (abstract, pages 1518-1519 and Figure 2A). At 12 weeks, ACR20 was achieved in about 44%, about 39%, and about 13% of patients in the 8 mg/kg, 4 mg/kg tocilizumab, and control groups, respectively (Figure 2A).

D3 discloses the study description of a Phase II clinical trial specifically investigating sarilumab in combination with MTX in RA patients that showed lack of adequate clinical response after at least 3 months of TNF-α blocker with MTX cotherapy.

In our preliminary view the main differences between the inventive concepts of independent claims 1, 3, 16, 18, 33 and 35 on file and the disclosures of D1, D2 and D3 are:

- D1 does not disclose that the previously treated subject was ineffectively treated with a TNF-α antagonist **[TNF-α antagonist + MTX non-responder population or TNF-α antagonist non-responder population]**;

- D2 does not disclose the use of sarilumab as the antibody that specifically binds to human IL-6 receptor and does not disclose subcutaneous administration of said antibody at a dosage between 100 mg and 200 mg once every two weeks; and

- D3 does not disclose the use of a dosage between 100 mg and 200 mg once every two weeks.

[60] The Response to the Preliminary Review Letter submits on pages 4 to 5 the following with regard to the relevant differences between the cited prior art documents and the claimed subject-matter:

> As the Board acknowledges, **D1** does not teach the claimed populations. **D1**, instead, reports treating a population that was inadequately treated with MTX.
>
> **D2** and **D3** do not teach treating the claimed populations with the claimed anti-IL-6R antibody and MTX at the presently claimed dose (i.e., a dose of 150 mg to 200 mg every two weeks).
>
> Instead, **D2** reports results from a Phase III clinical trial (RADIATE) that treated subjects that had an inadequate response to TNF inhibitors with tocilizumab, which is different from the claimed antibody, and MTX. Even *arguendo* **D2** discloses the claimed subject populations (which Applicants are not conceding), **D2** does not teach or suggest use of the claimed antibody, much less the claimed antibody at the specified dose and regimen for use in combination with MTX to treat the subject population as recited in the present claims.
>
> Similarly, **D3** fails to teach the claimed antibody at the specified dosing regimen for use in combination with MTX to treat a subject as recited in the present claims. In fact, **D3** is only a ***plan*** to study the efficacy and safety of sarilumab in participants with active rheumatoid arthritis who failed TNF-α blockers. **D3** does not provide ***any*** data. **D3** is completely silent on antibody doses or regimens for the subject population as recited in the present claims, much less. [emphasis in the original]

[61] It is our understanding that the Applicants' submissions are aligned with our characterisation of the differences that exist between D1 and the inventive concepts of the claims.

[62] Regarding D2, it is also our understanding that the Applicants' submissions are generally aligned with our characterisation of the differences with the exception

that the Applicants are not conceding that D2 discloses the claimed subject populations.

[63] We note that D2 discloses the following on page 1516 regarding the patients to be included in the phase III study:

> Patients 18 years of age and older with moderate to severe active RA and failure to respond or intolerance to one or more TNF antagonists within the past year were included. Patients had active RA for 6 months or more, swollen joint count (SJC) of 6 or more, tender joint count (TJC) of 8 or more, and C-reactive protein (CRP) greater than 1.0 mg/dl or erythrocyte sedimentation rate (ESR) greater than 28 mm/h at baseline. Patients discontinued etanercept (≥2 weeks), infliximab or adalimumab (≥8 weeks), leflunomide (≥12 weeks) and all DMARD other than methotrexate before receiving study medication. Patients had to be treated with methotrexate for 12 weeks or more before baseline (stable dose ≥8 weeks). [emphasis added]

[64] On the basis of that passage, we remain of the view that D2 discloses the treatment of a TNF-α antagonist + MTX non-responder population, a population encompassed explicitly by claims 1 to 15 and 32 on file. Further, and as explained at paras [52] and [55], we consider that the scope of claims 16 to 31 and 33 to 45 on file is broad enough to encompass the TNF-α antagonist + MTX non-responder population.

[65] Turning now to D3, we respectfully disagree that the study description found in D3 is limited to participants with active rheumatoid arthritis who only failed TNF-α blockers as suggested by the Applicants' submissions. The inclusion criteria section defines a participant considered as a Primary TNF-α blocker non-responder to be a patient with a "[l]ack of adequate clinical response after at least 3 months TNF-α blocker therapy (up to 2 agents) with MTX or other synthetic disease modifying anti-rheumatic drug (DMARD) co-therapy" [emphasis added].

[66] We therefore maintain the following characterisation of the differences that exist between the matter cited as forming part of the "state of the art" and the claimed subject-matter for our final analysis:

- D1 does not disclose that the previously treated subject was ineffectively treated with a TNF-α antagonist **[TNF-α antagonist + MTX non-responder population or TNF-α antagonist non-responder population]**;
- D2 does not disclose the use of sarilumab as the antibody that specifically binds to human IL-6 receptor and does not disclose subcutaneous administration of said antibody at a dosage between 100 mg and 200 mg once every two weeks; and
- D3 does not disclose the use of a dosage between 100 mg and 200 mg once every two weeks.

***Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?***

[67] In the Preliminary Review Letter on page 18 we explained why we considered that that an "obvious to try" analysis is appropriate in the instant case:

> Given that the subject-matter of the present claims relates to the field of therapeutic treatments of RA, a field which we consider an area of endeavor "where advances are often won by experimentation" (*Sanofi* at para 68), we are of the preliminary view that an "obvious to try" analysis is appropriate here. Accordingly, we will consider the three factors identified above in the "Legal principles" section.

[68] The Applicants did not contest or otherwise comment on the relevance of an "obvious to try" analysis and has presented arguments in response to our preliminary analysis that are aligned with the "obvious to try" approach taken. We therefore adopt the "obvious to try" analytical framework for our final analysis.

[69] The Preliminary Review Letter on pages 18 to 22 explains why it was our preliminary view that claims 1 to 45 on file encompass subject-matter that was obvious to try and thus would not have required any degree of invention from the POSITA in view of the cited prior art and the relevant CGK with regard to the differences that exist between the matter cited as forming part of the “state of the art” and the inventive concepts of the claims:

> Self-Evident Factor
>
> It is worth noting that a finding that it would have been more or less self-evident that what is being tried “ought to work” does not mean that certainty of success is required, otherwise there would be no point in describing it as something “to try”. Indeed, an “obvious to try” analysis is used precisely in areas where advances are won by experiment, so that success cannot be guaranteed before trying (*Les Laboratoires Servier v Apotex Inc*, 2019 FC 616 at para 269). Rather, what must be considered is whether it is more or less self-evident that the “try” ought to work in view of the CGK and the prior art; a mere possibility will not suffice but an amount of uncertainty is allowed in the obvious to try analysis: See *Janssen Inc v Apotex Inc*, 2021 FC 7 at para 135:
>
> > As to “ought to work”, it is clear that certainty of success is not required otherwise there would be no point in describing it as something “to try”. “Trying” implies the possibility of failure but with the expectation of success. While never easy to define on a spectrum of likely success, it is neither a Boston College Doug Flutie “Hail Mary” pass nor a Wayne Gretsky “open net shot”. Some limited experimentation is permitted in the context of the second factor. It is not to be arduous, inventive or unusual.
>
> Within the context of the claimed subject-matter, we consider that the relevant questions here are whether it would have been more or less self-evident to the POSITA, based on the disclosures of D1, D2, D3 and the relevant CGK, that the subcutaneous use of an antibody comprising the antigen binding regions of sarilumab at a dosage between 100 mg and 200

mg once every two weeks for 12 weeks ought to be effective for the treatment of RA:

1) when used in combination with MTX in a subject that was previously ineffectively treated for RA with MTX and a TNF-α antagonist (claims 1 to 15 and 32);

2) when used in combination with MTX in a subject that was previously ineffectively treated for RA with a TNF-α antagonist (claims 16 to 31); and

3) when used in a subject that was previously ineffectively treated for RA with a TNF-α antagonist (claims 33 to 45).

In our preliminary view, the POSITA (in view of their CGK) would consider that the scope of claims 16 to 31 and 33 to 45 encompasses a subject that was also previously ineffectively treated for RA with MTX and that the scope of claims 33 to 45 encompasses the use of MTX in combination with the recited antibody that specifically binds to human IL-6 receptor. In other words, all claims encompass the subcutaneous use of sarilumab at a dosage between 100 mg and 200 mg once every two weeks for 12 weeks in combination with MTX in a subject that was previously ineffectively treated for RA with MTX and a TNF-α antagonist.

The relevant considerations include:

- Switching to an alternative class of biologics with a different mechanism of action after the failure of a TNF-α antagonist treatment of RA was a commonly used strategy at the relevant date, as evidenced by *Papagoras*, or otherwise known from D2;

- D2 demonstrates that switching to an anti-IL-6 receptor monoclonal antibody in patients with RA who are responding inadequately to MTX or who are responding inadequately to both MTX and one or more TNF antagonists is effective;

- D3 specifically teaches to investigate the subcutaneous use of the anti-IL-6 receptor monoclonal antibody sarilumab (in combination with MTX) in RA patients that showed lack of adequate clinical response to a TNF-α blocker and MTX; and

- D1 discloses that sarilumab (in combination with MTX) shows efficacy in patients with active RA who are inadequate responders to MTX therapy and outlines dose ranging trials that include the subcutaneous use of a dosage between 100 mg and 200 mg once every two weeks for 12 weeks.

Given the above considerations, it is our preliminary view that it would have been self-evident to the POSITA that the subcutaneous use of sarilumab at a dosage between 100 mg and 200 mg once every two weeks for 12 weeks in combination with MTX in a subject that was previously ineffectively treated for RA with MTX and a TNF-α antagonist ought to be effective for the treatment of RA.

It is also our preliminary view that it would have been self-evident to the POSITA that the subcutaneous use of sarilumab at a dosage between 100 mg and 200 mg once every two weeks for 12 weeks alone or in combination with MTX in a subject that was previously ineffectively treated for RA solely with a TNF-α antagonist (i.e., not in combination with MTX) also ought to be effective for the treatment of RA.

The problem of treating RA in patients that were previously ineffectively treated for RA with MTX and a TNF-α antagonist was known (CGK, D2, and D3). After failure of a TNF-α antagonist treatment, the CGK (as evidenced by *Papagoras*) and the cited prior art (D2) teach switching to a biologic with a different mechanism of action, with an IL-6R antagonist being a prominent option. The number of available IL-6R antagonists was finite, and sarilumab was already under investigation for RA (D1 and D3).

Motive Factor

As explained above, the solutions to explore were limited and it is our preliminary view that the cited prior art documents D2 and D3 would

motivate the exploration of IL-6R antagonists (D2) and more specifically sarilumab (D3) as an alternative biologic for patients that were previously ineffectively treated for RA with MTX and a TNF-α antagonist.

With regard to a dosage regimen for sarilumab, it is our preliminary view that D1 would motivate the POSITA to try ranging trials that at least include, but are not limited to, the subcutaneous use of a dosage between 100 mg and 200 mg once every two weeks for 12 weeks.

Extent and Effort Factor

It is our preliminary view that the efforts required to achieve the claimed subject-matter are within the skills and capabilities of the POSITA and would not go beyond what is routine in the field. For example, dose-ranging trials for dose selection constitute routine pharmaceutical work in the field of antirheumatic therapies to assess the safety and efficacy of potentially useful therapeutics. In any case, dosage regimens encompassed by the independent claims are specifically disclosed in D1 within a relevant and related context of treating RA and therefore provided the POSITA a potential dosage regimen to try.

Therefore, in view of the above analyses of the relevant factors pertaining to an obvious to try analysis, we are of the preliminary view that it was obvious to try to obtain the subject-matter of independent claims 1, 3, 16, 18, 33 and 35.

As for the dependent claims 2, 4, 5, 6, 17, 19 to 21, 34, and 36 to 38 that further specify features as listed above on pages 12 to 13 in the “The claims on file” section, we are of the preliminary view that none of the features from the dependent claims would have required any degree of invention from the POSITA.

[70] Before addressing the arguments provided in the Response to the Preliminary Review Letter in details, we first note that the Applicants’ submissions focus on the proposed claims set rather than the claims on file. Even so, it is our view that the arguments and submissions presented on pages 3 to 6 of said Response to

the Preliminary Review Letter are also relevant to the claims on file and we will therefore consider those accordingly.

### *Self-evident factor*

[71] On pages 3 to 4 of the Response to the Preliminary Review Letter, the Applicants submitted that the potential “solution” of treatments for the claimed populations “problem” are not finite as the POSITA reviewing *Feely* and *Papagoras* would have numerous options for treating the TNF-α antagonist + MTX non-responder population or the TNF-α antagonist non-responder population. The Applicants also submitted that ignoring what the CGK (*Feely* and *Papagoras*) teaches as the available treatment options to a POSITA, and instead focusing on the solution of the inventors, is improper hindsight reconstruction.

[72] We note that whether it is more or less self-evident that what is being tried ought to work is the primary consideration of the self-evident factor. It is our view that whether there are a finite number of identifiable predictable solutions brings relevant information into the analysis to help determine how "self-evident" the claimed solution is to the POSITA. However, such a finding remains a non-determinative consideration within one of three non-exhaustive factors to be considered in an obvious to try analysis. In other words, it is our view that the existence of several possible solutions does not necessarily lead to the conclusion that a particular one is not self-evident to try (see *Eli Lilly Canada Inc v Apotex Inc*, 2018 FC 736, at para 120), especially if one solution is a prominent and predictable choice.

[73] That being said, we are of the view that the number of identifiable predictable solutions known to the POSITA for treating the TNF-α antagonist + MTX non-responder population or the TNF-α antagonist non-responder population were not infinite but limited with regard to treatment strategies. These few CGK treatment options are summarized in Table 1 of *Papagoras* on page 576:

**Table 1**
Treatment options after first anti-TNF-α failure.

| |
|---|
| 1. Optimize MTX/DMARDs |
| 2. Optimize anti-TNF-α dose/frequency |
| 3. Discontinue TNF-α blocker, treat with synthetic DMARDs only |
| 4. Add another biologic (not recommended) |
| 5. Switch to another TNF-α blocker |
| 6. Switch to another category of biologics |

[74] It is our view that those few strategies were predictable options commonly known in the art and they were well-defined as opposed to overly broad or not finite.

[75] In any case, it is our view that the analysis of the self-evident factor is contextual and includes the cited prior art disclosure, not only the CGK, as the cited prior art points directly at IL-6 inhibition as a strategy. In this narrower context, the universe of predictable solutions is no longer the few treatment options of Table 1 but instead becomes the use of an anti-IL-6 receptor monoclonal antibody after a TNF-α antagonist treatment failure as taught by D2 and D3. The number of available therapeutic IL-6R antagonists was finite, and sarilumab was already under investigation for treating RA (D1 and D3).

[76] The cited prior art documents D2 and D3 both specifically identify the use of an anti-IL-6 receptor monoclonal antibody among the few identifiable predictable solutions known for the treatment of a TNF-α antagonist + MTX non-responder population and D1 discloses effective dosing regimens for sarilumab + MTX in patients with active RA who are inadequate responders to MTX therapy, including the subcutaneous use of a dosage between 100 mg and 200 mg once every two weeks for 12 weeks. Further, it is our view that the POSITA, aware of the fact that sarilumab was selected in a clinical study for the treatment of a TNF-α antagonist + MTX non-responder population (D3), would reasonably expect success.

[77] Given the context of existing knowledge disclosed in D1, D2 and D3, was it more or less self-evident that the subcutaneous use of sarilumab, in combination with MTX, at a dosage between 100 mg and 200 mg once every two weeks for 12 weeks ought to be effective for the treatment of RA in a TNF-α antagonist + MTX

non-responder population or a TNF-α antagonist non-responder population? It is our view that it was.

[78] With regard to the submission that the analysis found in the Preliminary Review letter suffered from classic and improper hindsight reconstruction because it ignored the teachings of the CGK (e.g., *Feely* and *Papagoras*) about the available treatment options for the POSITA and instead focused on the solution of the inventors, we offer the following response.

[79] We were cognizant in the Preliminary Review Letter, and still are, of the caution against hindsight analysis that reconstructs an invention based on knowledge not found or suggested in the prior art. As mentioned above, the cited prior art directly points at the use of an anti-IL-6 receptor monoclonal antibody (D2 and D3), and more specifically at sarilumab + MTX (D3), after a TNF-α antagonist treatment failure. Our analysis was and is still focused on knowledge disclosed or suggested in the prior art.

### *Motivation factor*

[80] With regard to the motivation factor, the Applicants submitted on pages 4 to 5 of the Response to the Preliminary Review Letter that the POSITA would not be motivated by the cited prior art documents to select the claimed treatment, even less so the claimed dosage regimen and expect that the claimed treatment would be successful in treating the TNF-α antagonist + MTX non-responder population or the TNF-α antagonist non-responder population at the claimed doses:

> As the Board acknowledges, **D1** does not teach the claimed populations. **D1**, instead, reports treating a population that was inadequately treated with MTX.
>
> **D2** and **D3** do not teach treating the claimed populations with the claimed anti-IL-6R antibody and MTX at the presently claimed dose (i.e., a dose of 150 mg to 200 mg every two weeks).
>
> Instead, **D2** reports results from a Phase III clinical trial (RADIATE) that treated subjects that had an inadequate response to TNF inhibitors with

tocilizumab, which is different from the claimed antibody, and MTX. Even *arguendo* **D2** discloses the claimed subject populations (which Applicants are not conceding), **D2** does not teach or suggest use of the claimed antibody, much less the claimed antibody at the specified dose and regimen for use in combination with MTX to treat the subject population as recited in the present claims.

Similarly, **D3** fails to teach the claimed antibody at the specified dosing regimen for use in combination with MTX to treat a subject as recited in the present claims. In fact, **D3** is only a ***plan*** to study the efficacy and safety of sarilumab in participants with active rheumatoid arthritis who failed TNF-α blockers. **D3** does not provide ***any*** data. **D3** is completely silent on antibody doses or regimens for the subject population as recited in the present claims, much less.

In view of the above, one of skill in the art would not be taught how to select the claimed treatment from the numerous treatment choices less so the dose, dose regimen, and administration route, (and the Preliminary Report does not explain how one of skill in the art would select from the various antibodies, the dose options, and regimens) to arrive at the claimed invention much less have an expectation of success. For example, **D1**, which is the only document that reports doses for sarilumab, reports the doses in the context of treating a population previously effectively treated with MTX. **D1** reports five different dose regiments for the combination of sarilumab and MTX and showed that the highest percent of patients that achieved an ACR20 response were those that received the highest dose regimen (150 mg every week). In contrast, the presently claimed invention recites a lower dose regimen (i.e., 150 mg to 200 mg ***every two weeks***). **D3**, which is only a clinical study protocol does not report results let alone doses. And while **D2** reports doses, they are for an entirely different antibody administered with a different administration route and to a different population. One of skill in the art reviewing the cited documents would not be motived [sic] to combine the documents much less to expect that the

> claimed treatment would be successful in treating such a population at the claimed doses. [emphasis in the original]

[81] We respectfully disagree. It is our view that the cited prior art documents D2 and D3 provide a clear rationale and motivation for switching the TNF-α antagonist + MTX non-responder population from TNF-α antagonists to IL-6R antagonists (D2) and more specifically to sarilumab (D3) as an alternative biologic using a different mechanism of action. Notably, D3 provides very specific motivation as it proposes sarilumab trials in a TNF-α antagonist + MTX non-responder population.

[82] With regard to the dosing regimen, it is our view that the POSITA would have been generally motivated to determine a therapeutically effective route, dose and timing of administration for sarilumab. In that regard, although the POSITA would know that the patient population of D1 is not a TNF-α antagonist + MTX non-responder population or a TNF-α antagonist non-responder population, it is our view that the POSITA would be nonetheless motivated to try dosage regimens of sarilumab that were known to be therapeutically effective in RA patients and thus D1 would motivate the POSITA to try ranging trials that at least include, but are not limited to, the subcutaneous use of a dosage between 100 mg and 200 mg once every two weeks for 12 weeks.

[83] The Applicants also submitted that the underlying pathogenesis resulting in two RA populations would be different and thus the POSITA would not be motivated to try the same treatment for a population with RA but with an inadequate response to MTX or TNF-α antagonist and in a population with an inadequate response to both MTX and TNF-α antagonist.

[84] We respectfully disagree. The POSITA would know that MTX, TNF-α antagonists and sarilumab have different mechanisms of action and would know that switching from a therapeutic that failed to another therapeutic with a different mechanism of action is a common strategy. As stated above, D3 proposes sarilumab + MTX trials in a TNF-α antagonist + MTX non-responder population and D1 discloses that sarilumab + MTX is effective in an MTX non-responder population. It is therefore our view that the POSITA would have been generally

motivated to try the sarilumab + MTX, in any RA patient population that is non-responsive to either MTX (increase adenosine, decrease pyrimidine synthesis), a TNF-α antagonist (TNF-α inhibition) or both as sarilumab (IL-6 inhibition) does not act through the same mechanism of action.

[85] In any case, and as explained above at paras [52] and [55], it is our view that: i) the scope of claims 16 to 31 and 33 to 45 on file is broad enough to encompass both the TNF-α antagonist + MTX non-responder population and the TNF-α antagonist non-responder population; and ii) the scope of claims 33 to 45 on file is broad enough to encompass the use of MTX in combination with the recited antibody that specifically binds to human IL-6 receptor.

### *Extent and effort factor*

[86] With regard to the extent and effort factor, the Applicants submitted on page 5 of the Response to the Preliminary Review Letter that the Panel's preliminary finding that the effort required to achieve the claimed invention would not go beyond what is routine is not the relevant consideration.

[87] According to the Applicants, "[t]he proper question is not whether an invention is the result of routine pharmaceutical development, but rather whether a person of ordinary skill in the art would have viewed the outcome of the process—here, arriving at the treatments for the claimed populations—as one of a finite number of identified, predictable solutions". On that basis, the Applicants conclude that "[b]ecause the Board has not established that the solutions are finite, their obvious to try analysis fails".

[88] We respectfully disagree. *Sanofi* at para 69 describes the extent and effort factor as follows:

> What is the extent, nature and amount of effort required to achieve the invention? Are routine trials carried out or is the experimentation prolonged and arduous, such that the trials would not be considered routine?

[89] It is therefore our view that considering whether the efforts required to achieve the claimed subject-matter are within the skills and capabilities of the POSITA

and would not go beyond what is routine in the field, as we did in the Preliminary Review Letter, is a proper consideration in the context of the extent and effort factor analysis.

[90] The Applicants appear to conflate the self-evident and extent and effort factors in an “obvious to try” analysis. We have already acknowledged and considered the argument regarding whether there is a finite number of identifiable predictable solutions within our analysis of the self-evident factor above because it is our view that such considerations bring relevant information into the analysis to help determine how "self-evident" the claimed solution is to the POSITA.

[91] In any case, we reiterate our view here that the number of identifiable predictable solutions known to the POSITA for treating the TNF-α antagonist + MTX non-responder population or the TNF-α antagonist non-responder population were not infinite but limited with regard to treatment strategies and that taking into account the cited prior art disclosures that point directly at IL-6 inhibition as a strategy, the predictable solutions taught by the state of the art are finite and focused on the use of an anti-IL-6 receptor monoclonal antibody + MTX after a TNF-α antagonist treatment failure as taught by D2 and D3.

[92] Further, the Federal Court of Appeal in *Apotex Inc v Janssen Inc*, 2021 FCA 45, at paras 30 to 36, clarified that the consideration of whether it is “more or less self-evident that what is being tried ought to work” is simply one factor among several, which is not in itself determinative and does not constitute a requirement. We consider that the same applies to the consideration of whether there is a finite number of identifiable predictable solutions known to the POSITA; it is not in itself determinative and does not constitute a requirement. It is therefore our view, independent of our conclusion above regarding how finite and predictable were the identifiable solutions, that any finding in that regard would not have been dispositive of the question of whether it was obvious to try to obtain the claimed subject-matter as implied by the Applicants’ submissions.

[93] The Response to the Preliminary Review Letter did not contest or otherwise comment on our preliminary view regarding the efforts required to achieve the claimed subject-matter. We therefore remain of the opinion that the efforts

required to achieve the claimed subject-matter are within the skills and capabilities of the POSITA and would not go beyond what is routine in the field. Notably, we consider that dose-ranging trials for dose selection constitute routine pharmaceutical work in the field of antirheumatic therapies to assess the safety and efficacy of potentially useful therapeutics. Notwithstanding this view, it is also our opinion that the POSITA, in trying to identify a therapeutically effective dosing regimen for the use of sarilumab in a TNF-α antagonist + MTX non-responder population or a TNF-α antagonist non-responder population, would use available information from D1.

### *Was it obvious to try to obtain the invention?*

[94] Taking into account all the above assessments of the relevant factors pertaining to an obvious to try analysis as well as the submissions and arguments presented in the Applicants' Response to the Preliminary Review Letter, we are of the view that it was obvious to try to obtain the subject-matter of independent claims 1, 3, 16, 18, 33 and 35 on file.

[95] With regard to the dependent claims 2, 4 to 15, 17, 19 to 32, 34 and 36 to 45 on file that further specify features as listed above at paras [31] to [41] in the "The claims on file" section, the Response to the Preliminary Review Letter did not offer specific submissions on those features and we therefore remain of the view that none of the features from the dependent claims would have required any degree of invention from the POSITA.

## Conclusion on obviousness

[96] In light of the above considerations, it is our view that the claims on file encompass subject-matter that would have been obvious to the POSITA, as of the relevant date, having regard to D1, D2 and D3 in view of their CGK, contrary to section 28.3 of the *Patent Act*.

## PROPOSED CLAIMS

[97] As mentioned in the “Prosecution history” section above, the Applicants submitted a set of claims comprising claims 1 to 45 with the Response to the Preliminary Review Letter (proposed claims).

[98] For the reasons that follow, we do not consider that the proposed claims overcome the defect explained above with respect to section 28.3 of the *Patent Act*.

[99] Proposed independent claims 1, 3, 15, 18, 33 and 35 recite a dose of 150 mg to 200 mg every two weeks whereas the independent claims on file recite a dose of 100 mg to 200 mg every two weeks.

[100] Proposed independent claims 1 and 3 recite “treating rheumatoid arthritis in a subject that was previously ineffectively treated for rheumatoid arthritis with a TNF-α antagonist in combination with methotrexate” whereas claims 1 and 3 on file recite “treating rheumatoid arthritis in a subject that was previously ineffectively treated for rheumatoid arthritis with methotrexate and was previously ineffectively treated for rheumatoid arthritis with a TNF-α antagonist”. We consider that both phrases encompass a TNF-α antagonist + MTX non-responder population.

[101] Proposed claims 11 and 28 further specify that MTX is for use “in combination with the antibody”.

[102] Proposed claims 15, 23 and 40 are amended to delete the phrase “the group consisting of”.

[103] We have already expressed above our view as to why the subject-matter of the claims on file is obvious and does not comply with section 28.3 of the *Patent Act*. We consider that our obviousness analysis of the claims on file equally applies to proposed claims 1 to 45 as the subject-matter of those claims is encompassed by one or more of the claims on file and thus has already been considered within our obviousness analysis above.

[104] In that regard, we already considered a patient population comprising a “subject that was previously ineffectively treated for rheumatoid arthritis with a TNF-α antagonist in combination with methotrexate” when we considered a TNF-α antagonist + MTX non-responder population and we already considered a dose of 150 mg to 200 mg every two weeks when we considered a dose of 100 mg to 200 mg every two weeks.

[105] We therefore conclude that the proposed claims encompass subject-matter that would have been obvious to the POSITA, as of the relevant date, having regard to D1, D2 and D3 in view of their CGK, contrary to section 28.3 of the *Patent Act*.

[106] Since the proposed claims would not overcome the defect identified for the claims on file, they are not considered “necessary” amendments for compliance with the *Patent Act* and *Patent Rules* as required by subsection 86(11) of the *Patent Rules*.

## RECOMMENDATION OF THE BOARD

[107] In view of the above, we recommend that the application be refused on the basis that the subject-matter of claims 1 to 45 is obvious, contrary to section 28.3 of the *Patent Act*.

| | | |
|---|---|---|
| Marcel Brisebois | Lewis Robart | Christine Teixeira |
| Member | Member | Member |

## DECISION OF THE COMMISSIONER

[108] I concur with the conclusions and recommendation of the Board that the application be refused on the basis that the subject-matter of claims 1 to 45 is obvious, contrary to section 28.3 of the *Patent Act*.

[109] Therefore, in accordance with section 40 of the *Patent Act*, I refuse to grant a patent on this application. Under section 41 of the *Patent Act*, the Applicants have six months within which to appeal my decision to the Federal Court of Canada.

Konstantinos Georgaras

Commissioner of Patents
Dated at Gatineau, Quebec
this 14th day of May, 2025.