Citation: Adama Makhteshim Ltd, 2022 CACP 10

Commissioner's Decision #1617
Décision du commissaire nº 1617
Date: 2022-03-29

TOPIC: O00 Obviousness

SUJET: O00 Évidence

Application No. : 2,677,058

Demande nº 2 677 058

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 2,677,058 having been rejected under subsection 30(3) of the *Patent Rules* (SOR/96-423) as they read immediately before October 30, 2019 (the former *Patent Rules*), has consequently been reviewed in accordance with paragraph 199(3)(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 Canadian patent application number 2,677,058, which is entitled “Polymorphs of 3-(E)-2-{2-[6-(2-Cyanophenoxy)Pyrimidin-4-yloxy]Phenyl}-3-Methoxyacrylate”. Adama Makhteshim Ltd is the sole Applicant. A review of the rejected application has been conducted by a Panel of the Patent Appeal Board pursuant to paragraph 199(3)(c) of the *Patent Rules*.

[2] As explained in more detail below, our recommendation is that the Commissioner of Patents refuse the application.

BACKGROUND

The Application

[3] The application was filed under the *Patent Cooperation Treaty* and has an effective filing date in Canada of January 16, 2008. It was laid open to public inspection on August 7, 2008.

[4] The rejected application relates to amorphous and crystalline forms of azoxystrobin, and processes for their preparation and use a fungicide. Azoxystrobin was first marketed in 1998 as a broad spectrum fungicide for use on agricultural and horticultural crops.

[5] The claims are directed to a crystalline polymorphic form of azoxystrobin designated Form B, as well as mixtures comprising Form A, a known polymorph of azoxystrobin, and Form B. A polymorph is a specific crystalline form of a compound that can crystallize in different forms. Different crystalline forms may have different physicochemical properties, for example, dissolution rate, solubility, bioavailability and manufacturability. The description does not disclose any such properties for Form B or mixtures comprising Form A and Form B of azoxystrobin.

[6] The application has 30 claims on file that were received at the Patent Office on February 14, 2014.

Prosecution History

[7] On October 30, 2018, a Final Action was written under subsection 30(4) of the former *Patent Rules*. The Final Action states that the present application is defective on the ground that:

- claims 1 to 30 are obvious and do not comply with section 28.3 of the *Patent Act*

[8] In the response to the Final Action dated April 29, 2019, the Applicant argues that the subject-matter of the claims should not be considered obvious.

[9] On July 17, 2019, the application was forwarded to the Patent Appeal Board for review under paragraph 30(6)(c) of the former *Patent Rules* along with a Summary of Reasons explaining that the Applicant's arguments presented in the response to the Final Action are not persuasive and the rejection is maintained.

[10] In a letter dated July 19, 2019, the Patent Appeal Board forwarded a copy of the Summary of Reasons to the Applicant and requested that they confirm their continued interest in having the application reviewed.

[11] In a letter dated October 17, 2019, the Applicant confirmed their interest in having the review proceed.

[12] The present Panel was formed to review the rejected application under paragraph 199(3)(c) of the *Patent Rules*. On December 13, 2021, the Panel sent a Preliminary Review letter detailing our preliminary analysis and opinion that all the claims on file are obvious and do not comply with section 28.3 of the *Patent Act*. The Preliminary Review letter also provided the Applicant with an opportunity to make oral and/or written submissions.

[13] The Applicant declined the opportunity for an oral hearing but submitted a written response to Preliminary Review letter on February 17, 2022 arguing for the patentability of the claims on file.

Issue

[14] In view of the above, the following issue is considered in this review:

- Are claims 1 to 30 on file obvious and therefore non-compliant with section 28.3 of the *Patent Act*?

LEGAL PRINCIPLES AND PATENT OFFICE PRACTICE

Purposive construction

[15] According to *Free World Trust v Électro Santé Inc*, 2000 SCC 66 and *Whirlpool Corp v Camco Inc*, 2000 SCC 67, a purposive construction of the claims is performed from the point of view of the person skilled in the art in light of the relevant common general knowledge and considers 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 person skilled in the art that a variant has a material effect upon the way the invention works.

[16] "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.

Obviousness

[17] Section 28.3 of the *Patent Act* requires that the subject-matter of a claim not be obvious to the person skilled in the art:

> 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 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.

[18] In *Apotex Inc v Sanofi-Synthelabo Canada Inc*, 2008 SCC 61 at para 67 [Sanofi], 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?

[19] With respect to the second step of the obviousness analysis, Sanofi recognizes at paras 76 to 78 that the inventive concept of a claim can differ from its construction where the inventive concept of a patent is not clear from the claims themselves. For example, as may be the case with a bare chemical formula. Under these circumstances it is acceptable to read the specification to determine the inventive concept of the claims.

[20] Although Sanofi dealt with a selection patent, subsequent decisions from the lower courts have considered that, outside of the context of a selection patent, the inventive concept can consider the special properties of a compound, along with any alleged advantages that are supported by the description. For example, in *Apotex v Shire*, 2021 FCA 52, the Federal Court of Appeal states at para 84:

> In sum, the judge committed no error in having regard to these properties and beneficial features of LDX in determining the inventive concept of the claims in issue. I am also satisfied that the description was sufficient to allow the judge to construe these properties as features of the compound as claimed in the independent claims, such that they should form part of the inventive concept. Unlike the situation seen in *Bristol-Myers*, these beneficial properties were the "solution taught by the patent" claim. They explain the source of the motivation to pursue the solution (*Bristol-Myers* at para 75).

[21] 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. For a finding that an alleged invention is obvious to try, it must be more or less self-evident to try to obtain the alleged invention in advance of routine testing. The mere possibility that something might work is not sufficient.

[22] The Court in Sanofi 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]

ANALYSIS OF THE CLAIMS ON FILE

Purposive construction

The claims on file

[23] There are 30 claims on file. The Preliminary Review letter, on pages 5 to 6, expresses the preliminary view that claims 1, 10, 16 and 22 are representative of the independent claims for the purpose of the analysis. Claims 1, 10, 16 and 22 are as follows:

1. Crystalline polymorph Form B of methyl (*E*)-2-{2-[6-(2- cyanophenoxy) pyrimidin-4-yloxy] phenyl}-3-methoxyacrylate, wherein the polymorph exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2θ (+/-0.2°θ) at about 7.5, 11.75, 13.20 and 19.65.

10. A process for the preparation of a crystalline polymorph Form B of methyl (*E*)-2-{2-[6-(2- cyanophenoxy) pyrimidin-4-yloxy] phenyl}-3-methoxyacrylate, the process comprising crystallizing said compound from a solvent mixture

comprising water and an organic solvent selected from the group consisting of an alcohol, and an amide.

16. A mixture of crystalline polymorphic Form A and Form B of methyl (*E*)-2-{2-[6-(2-cyanophenoxy) pyrimidin-4-yloxy] phenyl}-3-methoxyacrylate, wherein Form A exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2θ (+/-0.2°θ) at about 6.25, 13.8, 17.65, 19.05, 26.4 and 28.5, and Form B is as defined according to any one of Claims 1 to 9.

22. A process for the preparation of a mixture of a crystalline polymorph Form A and Form B of methyl (*E*)-2-{2-[6-(2- cyanophenoxy) pyrimidin-4-yloxy] phenyl}-3-methoxyacrylate, according to any one of Claims 16 to 21, the process comprising

    (a) crystallizing said compound from a solvent mixture comprising an alcohol and an anti-solvent selected from aliphatic and aromatic hydrocarbon; and

    (b) isolating the resulting crystals.

component is derived from at least one bio-based material.

[24] Independent claims 13 to 15 relate to a composition comprising the polymorph of claim 1 and its use in combating fungus in a plant. Likewise, independent claims 28 to 30 relate to a composition comprising the mixture of polymorphs of claim 16 and its use as a fungicide. Independent claims 25 and 26 define alternative processes for preparing the mixture of polymorphs of claim 16.

[25] Dependent claims 2 to 9, 11, 12, 17 to 21, 23, 24 and 27 define additional limitations with regard to the further spectral characterization of Form B (claims 2 to 9), Form A (claims 17 to 20) or the mixture of polymorphs (claim 21), type of solvent (claim 11), specific process steps (claim 12), type of alcohol (claims 23 and 27) and type of anti-solvent (claim 24).

[26] The response to the Preliminary Review letter did not contest or comment on the Panel's consideration of claims 11, 10, 16 and 22 as being representative of the independent claims. Likewise, the response to the Preliminary Review letter did not contest the characterization of dependent claims 2 to 9, 11, 12, 17 to 21, 23, 24 and 27 as providing further limitations with regard to: the further spectral

characterization of Form B, Form A or the mixture of polymorphs, the type of solvent, the specific process steps, the type of alcohol and the type of anti-solvent.

The person skilled in the art

[27] The Preliminary Review letter, on pages 6 to 7, adopts the following characterization of the person skilled in the art used in the Final Action, which is not disputed in the response to the Final Action:

> The POSITA (which may include a team of persons having varying expertise) is considered to at least include an organic chemist in product development having experience with, or knowledge of, polymorphs, and their impact on product performance.

[28] The response to the Preliminary Review letter did not contest the Panel's characterization of the person skilled in the art. Therefore, we adopt the above characterization for this analysis.

The relevant common general knowledge

[29] The Preliminary Review letter, on pages 7 to 8, adopts the characterization of the common general knowledge used in the Final Action. The Preliminary Review letter indicates that the response to the Final Action did not contest or comment on this characterization and after reviewing the specification and the reference documents listed in the Final Action considers the common general knowledge identified in the Final Action is reasonable:

> [Emphasis in original] This POSITA would have knowledge of the methods of screening for polymorphs by preparing new forms using standard crystallization techniques (see for example, **D3, D4** and **D5**). Furthermore, the POSITA would expect that any solid form of a molecule with an established fungicidal activity, such as azoxystrobin, would also have that same activity to some degree, since biological activity is an effect of the molecule, and the molecules are chemically identical. Screening is generally carried out using standard crystallisation techniques to crystallise the products from solution from a number of different solvents of various polarities. Crystallisation is usually attempted from **solvents used in the final steps of the synthesis, formulation and processing**. The following are also indicated as common recrystallisation solvents: water, methanol, ethanol, propanol, isopropanol, and mixtures thereof, if appropriate. Standard crystallisation

> techniques such as agitation, heating, cooling, changing the pH, and partial evaporation or concentration of clear saturated solutions are all indicated. Furthermore, the POSITA would be aware from the CGK document **D5** that an array of solvents (e.g. from 96 to 413 solvents), can be rationally screened taking into account different solvent properties. This array of solvents, as well as other typical conditions mentioned above (such as temperature, evaporation, etc.), can be rationally screened using established high-throughput screening techniques.
>
> …
>
> With regard to the CGK of the POSITA, the FA identified that prior art documents **D3**, **D4** and **D5** would form part of the CGK of the POSITA:
>
> D3: Byrn *et al.*, "Pharmaceutical Solids: A Strategic Approach to Regulatory Considerations", Pharma. Res., Vol. 12, No. 7, pages 945–954, 1995.
>
> D4: Caira, "Crystalline Polymorphism of Organic Compounds", Topics in Curr. Chem., Vol. 198, pages 163–208, January 1998.
>
> D5: Hilfker *et al.*, "Approaches to Polymorphism Screening", Polymorphism: in the Pharmaceutical Industry, Chapter 11, pages 287–308, 2006.
>
> Having reviewed the instant specification, as well as D3, D4 and D5, we are of the preliminary view that the above characterization of the CGK is reasonable. D3 and D4 are review articles and D5 is a book chapter, all of which discuss methods of preparing and characterizing polymorphs that were generally known and accepted without question by the bulk of those who are engaged in the particular arts of organic chemistry and agrochemical compositions at the claim date. Although the role of serendipity in the discovery of polymorphs is known, routine experimental screening to investigate solid-state polymorphism is encountered in all areas of research involving solid substances with the goal of finding the most optimal form of a compound.

[30] The response to the Preliminary Review letter submits that the Preliminary Review did not provide fair consideration to the many references referred to in their previous submissions and lists five previously identified references that are now said to frame the common general knowledge in a contrary manner:

> Previous submissions by the Applicant have pointed to at least as many references that frame the common general knowledge in a contrary manner. Yet, the references that form part of the prosecution history were not discussed or considered in the Preliminary Review. Many of the references quoted by the Applicant are much more recent than the D3-D5 references, and if anything, should

> be give more weight as they more accurately reflect the common general knowledge at the time of the invention. Although D3-D5 may allegedly imply that identifying polymorphs is a simple task, over a decade later, the references discussed below clarify that the process itself is much more difficult, and highly unpredictable. D3-D5 substantially oversimplify the practical aspect of what is necessary to identify a novel polymorph.

[31] We respectfully disagree with the submission that the references that form part of the prosecution history were not discussed or considered in the Preliminary Review. The Preliminary Review letter, on pages 12 to 13, explicitly acknowledges these references in the context of the obvious to try analysis. Their consideration at step four of the obviousness analysis is consistent with the Applicant's previous submissions. For example, the response to the Final Action cites these references in the obvious to try assessment to emphasize the unpredictable nature of crystallization.

[32] Further, although four of the five references were published after the filing date of the present application, they confirm that the unpredictably associated with crystallization and the screening of polymorphs using standard methodology were well known at the relevant date. In fact, the unpredictability of polymorphism is one of the reasons why polymorph screens are necessary. Therefore, we do not agree that the references frame the common general knowledge in a contrary manner to what was identified in the Preliminary Review letter. For example, Lee et al., "Crystal Polymorphism in Chemical Process Development" Annual Review of Chemical and Biomolecular Engineering, Volume 2, pages 259 to 280, 2011 [Lee et al.] identifies screening as an essential activity and discusses the diverse range of approaches involved in a polymorph screen on pages 268 to 269:

> Given the significance of polymorphism, solid form screening is an essential activity and it is initially caried out at the drug discovery-development interface. The intent of the screen is to uncover all possible crystalline phases and to identify an optimal solid form suitable for development.
>
> …
>
> Generally polymorph screening involves a diverse range of approaches including recrystallizing the drug substance from solution via antisolvent addition, cooling, and evaporation; crystallization from the melt or amorphous phase; slurrying (and slurry bridging); grinding (neat and liquid assisted); spray drying; sublimation; vapor diffusion; thermal desolvation of solvates; and subjecting the drug to various

> process-induced stresses (heat, pressure, and shear). Figure 4 illustrates the classical methods; slow crystallization processes favor thermodynamically stable phases, and kinetic forms are more likely to nucleate in processes in which crystallization occurs immediately. Most of the traditional methods are amenable to automated high-throughput technology. As a result, large sets of crystallization experiments can be performed using small amounts of APIs in a short period of time using robotic platforms for sample generation and analysis. The different methods to derive multiple solid forms have been extensively reviewed. It is necessary to exploit different approaches, as one method may produce a specific polymorph exclusively.
>
> Solvent-based approaches, in particular solution crystallization methods and slurry experiments, should incorporate a diverse set of solvents and solvent mixtures covering a wide range of properties (e.g., hydrogen bond acceptors/donors, polarity, dipole moment, dielectric constant, viscosity). […] Solvents commonly used for the development of a crystallization process or in processing should be included as part of the screen.

[33] The response to the Preliminary Review letter further contends that one of the cited references rebuts D3 to D5:

> Laird states:
>
> > [Emphasis in original] "A statement in recent paper "Serendipity often plays a key role in the discovery of new forms, because no general methodology exists for producing new forms of a given compound", will ring true to many process chemists, who may have seen a new crystalline form appear late in the development of a new drug substance. … **Prediction of crystal structure from a given chemical substance, and hence its polymorphism, is a desired goal which has not been routinely achieved, despite one or two successes with specific molecules.**"
>
> This reference rebuts D3-D5, as it effectively states that although it is desirable to obtain polymorphs, such a task has not been routinely achieved. The lack of routinely achieving a crystal structure of chemical substances speaks to how although the art provides some general guidance, the act of actually identifying a polymorph remains elusive.

[34] We do not agree with the interpretation in the response to the Preliminary Review letter that Laird effectively states that the task of obtaining polymorphs was something that was not routinely achieved at the relevant date. In our view, the quoted excerpt refers to the prediction of specific crystal structures as being something that has not been routinely achieved, as evidenced by the subsequent sentence in Laird:

> Periodically, blind tests are organised where scientists are challenged to predict crystal structures of specific molecules, and the results are compared to the actual experimental results.

[35] We also note that the cited excerpts in the response to the Preliminary Review letter confirm the prevalence of polymorphism and their serendipitous discovery was well known at the relevant date. Further, Lee et al. explain on page 262 that the strong interest in crystal polymorphism can be attributed to its frequent occurrence and the fact that significant differences in chemical and physical characteristics may arise with changes in the solid-state form that can affect the manufacturability, performance and/or quality of a molecule. In other words, at the relevant date, it was common general knowledge that standard polymorph screening was routinely used to achieve serendipitously produced polymorphs.

[36] Finally, the response to the Preliminary Review letter notes that a number of recent Canadian Court decisions that pertain to the general understanding in the art regarding polymorphs are also relevant as they contradict the generalized assertions of D3 to D5:

> [Emphasis in original] For example, in Pfizer Canada Inc. v. Apotex Inc., 2017 FC 774 at paragraph [232] the accepted testimony from experts in the field resulted in the Judge characterizing the common general knowledge as:
>
> > [232] The Skilled person would know generally of the existence of crystalline and polymorph screening, and as Apotex's expert put it, that crystal and polymorph screening was "specialized work that had to be done. As Dr. Park deposed, polymorph screening was not rote work, was difficult and in her experience required skill and judgment. <u>It was not possible to predict at the outset of a polymorph screen how many solid forms would identified, what they would be, or what solid forms would result from any particular method or set of conditions.</u> Therefor, as Dr. Park deposed from her experience, and Dr. Myerson deposed as an expert on the subject, <u>this process often required numerous experiments and analyses, and strategy and judgment had to be employed to make decisions about how to proceed based on the results that we obtained such that the number of potential experiments that can be conducted is extremely large.</u>
>
> Contrary to the very generalized assertions of D3-D5, based on expert testimony, the Judge has concluded that irrespective of whether general methods and techniques are known, the actual process itself is not routine, and it would not be

> possible to predict what forms, if any, will be identified. Strategy and judgement is necessary to make decisions about how to proceed.

[37] We do not agree that the characterization of the common general knowledge in the art regarding polymorphs and corresponding conclusions as found in recent Canadian Court decisions is relevant to the present case. As explained in *Apotex Inc v Pfizer Canada Inc*, 2019 FCA 16 at para 41 [ODV FCA], "[h]owever trite, each case is to be decided on the basis of the specific evidentiary record put before a judge." Consistent with this guidance, the Appeals Judge, at para 42, also affirms the Federal Court's understanding that the jurisprudence does not establish any "hard and fast rules" on obviousness when it comes to evaluating whether or not a salt screen or any other form of experimentation is obvious or not.

[38] We also note that the cited decision concerns a case with a relevant date for assessing obviousness that predates the relevant date of the present case by six years. Importantly, the common general knowledge concerning polymorph screening evolved significantly during this time to include the use of automated high-throughput screening technology as evidenced by D5 and Lee et al.

[39] Further, concerning the expert testimony cited above, we have already acknowledged the unpredictably associated with crystallization and that the screening of polymorphs using standard methodology was well known at the relevant date. Moreover, the expert testimony does not contradict that the person skilled in the art would generally know about methods of crystalline and polymorph screening. Rather, it recognizes that sometimes it is necessary to go beyond the routine aspects of a polymorph screen and employ strategy and judgment to make decisions about how to proceed. For example, the course of experimentation required to identify a particular polymorph that could be safely stored, formulated into a drug, and effectively delivered to patients may be in the nature of a research program, as was the evidence in the cited decision.

[40] In light of the above, we conclude that the relevant common general knowledge identified in the Preliminary Review letter is appropriate and reasonable in the context of the facts of the present case and we therefore adopt it for this analysis.

Essential elements

[41] The Preliminary Review letter, on page 8, expresses the preliminary view that the person skilled in the art would consider all of the elements in the claims to be essential:

> As stated above, all of the elements set out in a claim are presumed essential unless it is established otherwise or where such a presumption is contrary to the claim language: *PN2020-04*. Further, a claim element is essential when it would have been obvious to the skilled person that its omission or substitution would have a material effect on the way the invention works: *Free World Trust* at para 55; *PN2020-04*.
>
> With respect to claim language, our preliminary view is that the POSITA reading claims 1–30 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 optional, preferred or were otherwise intended to be non-essential. Although claims 10 and 11 list a group of organic solvents, where one is selected, those solvents are considered essential elements of the claims. Likewise, in claim 23 which lists a group of alcohols as alternatives, where one is selected, those alcohols are also considered essential elements of the claim. Therefore, our preliminary view is that the POSITA would consider all of the elements in the claims to be essential.

[42] The response to the Preliminary Review letter did not contest or comment on this preliminary identification of the essential elements. Therefore, we adopt the above identification of the essential elements for this analysis.

Obviousness

[43] All 30 claims on file were rejected in the Final Action for obviousness.

The person skilled in the art and the relevant common general knowledge

[44] The person skilled in the art and the relevant common general knowledge have been identified as part of the purposive construction of the claims. Although in this context the information forming the relevant common general knowledge is identified using the publication date, this information is also considered common general knowledge at 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

[45] The Preliminary Review letter, on pages 9 to 10, indicates that the inventive concepts identified in the Final Action are generally consistent with the language of the process, composition and method for use claims. The Preliminary Review letter also indicates that the person skilled in the art would construe the inventive concepts of compound claims 1 and 16 to include their fungicidal activity:

> [Emphasis in original] The FA, on page 5, identifies the inventive concepts of the claims on file as follows:
>
> > The inventive concepts of claims 1 and 16 are not readily discernable from the claims themselves. A bare chemical name and peaks from an XRPD pattern, as well as IR, DSC or Raman data are not sufficient to determine inventiveness. In cases such as this, it is acceptable to read the specification to determine the inventive concept (*Sanofi*, para. 77).
> >
> > The inventive concepts of claims 1 and 13–15 are crystalline polymorph **Form B** of azoxystrobin, fungicidal compositions thereof, and methods for use as fungicides.
> >
> > The inventive concept of independent claim 10 is a process for the preparation of crystalline polymorph **Form B** comprising in solvent mixtures of water and an organic solvent which is either an alcohol or an amide.
> >
> > The inventive concepts of claims 16 and 28–30 are a *mixture* of crystalline polymorph **Form A** with instant crystalline polymorph **Form B** of azoxystrobin, fungicidal compositions thereof, and methods for use as fungicides
> >
> > The inventive concept of independent claims 22, 25 and 26 is processes for the preparation of mixtures of crystalline polymorph **Form A** and **Form B** comprising crystallising in solvent mixtures of an alcohol and an anti-solvent or either an aliphatic or aromatic hydrocarbon
> >
> > The inventive concepts of the dependent claims 2-9, 11-12, 17-21, 23-24 and 27 are the same as the inventive concepts of the corresponding independent claims. The additional limitations (e.g. XRPD peaks, IR, DSC, or Raman data, or solvents used) in these dependent claims are considered at step 4.
>
> The RFA did not contest or comment on these inventive concepts. In our preliminary view these inventive concepts are generally consistent with the language of the process, composition and method for use claims, but do not appear to take into account any special properties that may form part of the inventive concept of the

compound claims. As noted above in the FA, the inventive concepts of claims 1 and 16 are not readily discernable from the claims themselves—the reference to the polymorph Form B of azoxystrobin in claim 1 is limited to a bare chemical formula and an x-ray diffraction pattern and in claim 16 the reference to the mixture of polymorph Form A and Form B of azoxystrobin is similarly limited. Therefore, we consider it appropriate to read the specification as a whole to determine whether additional characteristics, associated with the polymorph Form B or mixture of polymorph Form A and Form B of azoxystrobin, may be construed as being part of the inventive concept of these claims.

In this regard, the description discloses that azoxystrobin "is a systemic, broad-spectrum fungicide with activity against the four major groups of plant pathogenic fungi" (page 1). Further, we are of the preliminary view that the POSITA would reasonably expect that the polymorph Form B of claim 1 and mixture of polymorph Form A and Form B of claim 16, would also be useful as a broad-spectrum fungicide. As such, it is our preliminary view that the POSITA would consider the fungicidal activity to be part of the inventive concept of claims 1 and 16.

With respect to dependent claims 2-9, 11-12, 17-21, 23-24 and 27 which define additional limitations with regard to further characterization of Form B (claims 2–9), Form A (claims 17–20) or the mixture of polymorphs (claim 21), type of solvent (claim 11), specific process steps (claim 12), type of alcohol (claims 23 and 27) and type of anti-solvent (claim 24), in our view, the POSITA would consider these limitations as part of the inventive concepts of these claims.

[46] The response to the Preliminary Review letter did not contest or comment on this preliminary identification of the inventive concepts. Therefore, we adopt the above identification of the inventive concepts of the claims for this analysis.

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

[47] The Preliminary Review letter, on pages 10 to 11, applies the following two documents against the claims on file:

D1:	WO 98/07707	Berry, I.G., *et al*.	26 February 1998 (26-02-1998)
D2:	EP 0 382 375	Clough, J.M., *et al.*	16 August 1990 (16-08-1990)

[48] D1 discloses the preparation of crude (*E*) methyl-2-[2-(6-(2-cyanophenoxy) pyrimidin-4-yloxy) phenyl]-3-methoxypropenoate (azoxystrobin) and subsequent purification by crystallization from methanol (see Examples 1 and 2).

[49] D2 discloses the preparation of various derivatives of propenoic acid useful as fungicides. Example 3 specifically discloses the preparation of (*E*) methyl-2-[2-(6-(2-cyanophenoxy) pyrimidin-4-yloxy) phenyl]-3-methoxypropenoate (azoxystrobin). "Recrystallization from ether/dichloromethane/n-hexane gave [azoxystrobin] as a pale yellow powder (1.20g, 64% yield), mp 110–111°C; 1H NMR delta: 3.63(3H,s); 3.74(3H,s); 6.42(1H,s); 7.19–7.47(6H,m); 7.50– (1H,s); 7.62–7.75(2H,m); 8.40(1H,s)ppm. In a subsequent preparation of [azoxystrobin], recrystallisation gave a white crystalline solid, mp 118–119°C."

[50] The Preliminary Review letter, on page 11, identifies the following differences between the cited prior art and the inventive concepts of the claims:

> We are of the preliminary view that the POSITA would consider that the main difference between the teachings of either D1 or D2 and the inventive concept of the claims related to polymorph Form B of azoxystrobin is that the "state of the art" does not disclose:
>
> - The polymorphic Form B of azoxystrobin (i.e. the spectral and thermal parameters of claims 1–9);
>
> With respect to the related process of claims 10–12, the POSITA would consider that an additional difference is:
>
> - Neither D1 nor D2 disclose crystallising the polymorph Form B of azoxystrobin from a solvent mixture comprising water and an organic solvent that is an alcohol or an amide.
>
> Likewise, in our preliminary view, the POSITA would consider that the main difference between the teachings of either D1 or D2 and the inventive concept of the claims related to a mixture of polymorph Form A and Form B of azoxystrobin is that the "state of the art" does not disclose:
>
> - A mixture comprising the polymorphic Form A (i.e. the spectral and thermal parameters of claims 16–21) and Form B of azoxystrobin (i.e. the spectral and thermal parameters of claims 1–9);
>
> With respect to the process for preparing the mixture of claims 22–27, the POSITA would consider that an additional difference is:
>
> - Neither D1 nor D2 disclose crystallising a mixture of polymorph Form A and Form B of azoxystrobin from a solvent mixture as claimed.

[51] The response to the Preliminary Review letter did not dispute this identification of

the differences. Therefore, we adopt the above differences between the cited prior art and the claims on file for this analysis.

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?

[52] At this stage it must be determined whether the nature of the invention is such as to warrant an obvious to try test. At para 68, Sanofi explains that an obvious to try test may be appropriate in "areas of endeavor where advances are often won by experimentation" and that "[i]n such areas, there may be numerous interrelated variables with which to experiment." The Preliminary Review letter, on page 12, acknowledges the submissions made in the response to the Final Action relate to the obvious to try analysis described in Sanofi and considers that an obvious to try analysis is warranted in the present case. The response to the Preliminary Review letter did not comment or contest this approach, therefore, we will use this framework for the purposes of this analysis.

Self-Evident Factor

[53] This factor considers whether it would have been more or less self-evident that what is being tried ought to work in advance of routine testing. The Preliminary Review letter, on pages 12 to 14, considers the submissions in the response to the Final Action concerning the unpredictable nature of crystallization and why screening for polymorphs does not meet the test as outlined in Sanofi. It also notes that the response to the Final Action compares the present case to several court decisions to explain why screening for polymorphs can only be considered "worth a try", with only a mere possibility that something might turn up.

[54] The Preliminary Review letter, on pages 14 to 15, also considers the analysis in the Summary of Reasons which disagrees with these conclusions. The Summary of Reasons refers to the guidance in ODV FCA to explain that prior decisions cannot be used to force a given conclusion on obviousness based on broad factual similarities to the detriment of otherwise significant differences in a given case: See ODV FCA at paras 41 to 44.

[55] In this view, the Preliminary Review letter agrees with the assessment in the Summary of Reasons that there are specific factual differences between the decisions cited in the response to the Final Action and the present case:

> We agree with the assessment in the SOR that there are specific factual differences between the decisions cited in the RFA and the present case. We are also mindful of the guidance in *ODV FCA* not to force a given conclusion on obviousness based on broad factual similarities to the detriment of otherwise significant differences in a given case. In this regard, it is noted that in both cases cited in the RFA there was evidence the invention was not self-evident from the prior art and the common general knowledge on the facts of those cases. As indicated in the SOR, for *ODV FC*, that evidence included the prior art teaching that ODV fumarate, another salt of ODV, did not work. In *Abbott,* there was evidence that it is standard procedure to dry the solvate before analyzing it. In this view, "the inventive portion of Abbott's discovery was to seal the wet Clarithromycin to prevent drying and analyse it" (para 76).

[56] The response to the Preliminary Review letter submits that the Summary of Reasons and Preliminary Review letter misinterpret the finding of non-obviousness in ODV FCA and argues that in ODV FCA the finding of non-obviousness did not turn on the evidence that there no motivation that ODV succinate would work but rather that it is based on the inability of the skilled person to predict that Form I ODV succinate could be made or that it existed. The response to the Preliminary Review letter concludes that the particulars of ODV FCA are substantially similar the present case and support a finding of non-obviousness:

> [Emphasis in original] In the Summary of Reasons, which appears to have been adopted by the Board, the Examiner implies that <u>the only reason</u> the claims were found to be inventive in this case is that there was no motivation that ODV succinate would work, as ODV fumarate, another salt of ODV, had not worked. In other words, it appears that the implication is that in this decision, in the absence of the poor bioavailability of the related salt ODV fumarate, the ODV succinate salt would have been obvious. The conclusion was that in the present application, there is no evidence that Form B was problematic, nor is there any evidence that Form B provides a solution to a problem in the art.
>
> That is not a correct understanding of the finding of the Federal Court Judge, nor of the finding of the Appeal Judge. The Court of Appeal found that it was clear from the reasons that the finding of non-obviousness had been based on the inability of the skilled person to predict that Form I ODV succinate itself could be made or that it even existed (see paragraph [38]).

> …
>
> From the comments of the trial Judge, it is clear that the conclusion that the claims are inventive was based upon the simple fact that the skilled worker would have had no knowledge or been able to predict what forms existed, nor how they could be formed. This conclusion was reached even though there were known methods of crystallization and polymorph screens, and while it was acknowledged that it is desirable to search for new and improved compounds.
>
> Absent the main conclusion of the trial Judge is any reference to the ODV fumarate salt, or the difficulties it may have encountered. While the evidence respecting the fumarate salt may have played a secondary role in the conclusion of the Judge, as discussed at paragraph [306], the case did not turn on this aspect. This may have contributed to the conclusion that the Judge had already made, but there is no evidence that this was directly responsible for the finding. In other words, contrary to the assertion of the Examiner and the Board, this case does not speak to the requirement that a challenge needs to be overcome during the discovery of the molecule, that the art must lead away from the molecule, or that the molecule must solve a problem in the art, in order for a salt or polymorph to be patentable.

[57] We disagree that the Summary of Reasons and Preliminary Review letter imply that the finding of non-obviousness in ODV FCA is only because there was no motivation that ODV succinate would work. As noted in the Preliminary Review letter, in ODV FCA the evidence that the invention was not self-evident from the prior art and the common general knowledge included the prior art teaching that the fumarate salt had already been shown not work. The reference to the fumarate salt was to highlight that there are specific factual differences between the cited decision and the present case and not to suggest that this was the only reason for the finding of non-obviousness in ODV FCA.

[58] We also disagree that the particulars of ODV FCA are substantially similar to the present case. The background knowledge that led to the search for a new ODV drug as well as the experimentation that went into the discovery of ODV succinate Form I are unique to that case. For example, as explained in *Pfizer Canada Inc v Apotex Inc*, 2017 FC 774 at paras 21 to 25 [ODV FC] the background knowledge that led to the search for a new ODV drug included the fact that there was no solid-state form of ODV itself that could be safely stored, formulated into a drug, and effectively delivered to patients. In fact, ODV was only known to exist as the active metabolite of the prodrug venlafaxine which is metabolized to ODV in the body.

[59] Further, the searched for new ODV drug required several key characteristics: stability, solubility, permeability and bioavailability. It had to be a stable, that is, a drug that could be stored safely throughout the manufacturing and distribution processes. It further had to be soluble such that it would be able to dissolve in the gastrointestinal tract. Finally, the drug had to be permeable and bioavailable, and thus able to cross over from the gastrointestinal tract into the bloodstream where it could do its work in the body's systems. In particular, the drug had to be able to penetrate the blood-brain barrier in order to act on the brain.

[60] In addition to having stability, solubility, permeability and bioavailability, the searched for new ODV drug needed to have these qualities without unacceptable adverse side effects such as nausea and vomiting which were known issues with ODV.

[61] The evidence of the invention story behind ODV succinate Form I is that it required more than a routine polymorphic screen: ODV FC paras 36 to 41

> [36] Initially, Wyeth worked with ODV fumarate, a known salt form of ODV, but without success.
>
> [37] Wyeth also attempted to make a pro-drug of ODV, again without success.
>
> [38] In addition, and previously, Wyeth had also worked with a number of other salt forms of ODV, but without success.
>
> [39] Wyeth then set out to determine if it could identify a more appropriate salt form, a route in respect of which there was internal and science-based skepticism, a point Apotex challenged and which I will address shortly. Eventually Wyeth found the ODV succinate salt form, which it then with further research and experimentation, developed into a crystalline form then known as Form "A", which subsequently became known as Form I ODV succinate. Having identified positive properties of this new crystal Form I ODV succinate in terms of solubility and stability, it engaged SSCI to test the crystalline Form I ODV succinate and identify and test for other crystalline forms; SSCI did so and identified three other crystalline forms of ODV succinate plus one amorphous form of ODV succinate.
>
> [40] Wyeth conducted studies *in vivo* (in the body) in mice, and in cells *in vitro* (outside the body), together with *in vivo* tests on rats, beagle dogs and ultimately with human volunteers.
>
> [41] Wyeth determined that the crystalline Form I ODV succinate had the requisite stability, together with solubility in addition to both suitable permeability and

> bioavailability. Wyeth then performed additional studies to develop sustained release formulations of Form I ODV succinate.

[62] To paraphrase the Appeals Judge at para 41 of ODV FCA: contrary to what the response to the Preliminary Review appears to urge, ODV FCA cannot be used to force a given conclusion on obviousness based on broad factual similarities to the detriment of otherwise significant differences in the present case.

[63] We also note that at paras 50 to 51 of ODV FCA the Appeals Judge rejected the assertion that the trial Judge should have only considered the salt and crystal experiments that directly led to the initial preparation of Form I ODV succinate and made it clear that the whole of the invention story behind ODV succinate Form I was relevant:

> [50] The reality, however, is that identifying a stable crystal form was not the end of the process for Wyeth. Indeed, although Wyeth's objective was to develop the compound as a drug, the new crystal form still needed to be characterized. Moreover, Wyeth was unaware of whether other forms of ODV succinate could be made and whether their stability was sufficient to be used as a drug. In other words, Wyeth did not know "what they had". Wyeth thus considered it necessary to undertake a complete polymorph screen for ODV succinate and retained the specialized laboratory SSCI to conduct further analysis on the crystal sample. SSCI's testing occurred under a variety of conditions in order to attempt to identify as many different solid state forms as possible. The evidence accepted by the Federal Court Judge in this regard demonstrates that the creation and the analysis of a new solid state form flows from a detailed investigation. The Federal Court Judge concluded on the basis of the evidence that this was not a routine process and accepted the evidence of one of Pfizer's witnesses, Dr. Park, that "[c]onditions like the solvent(s) used, the temperature, the rate of cooling, the time course of the experiment and the presence of other reagents are all examples of things that can affect the solid state form of the compound, if any, that is produced." (Reasons at para. 125 no. 34; see also, Reasons at para. 123). It is significant that the evidence provided by Dr. Park attests to the following (Reasons at para. 125 no. 36):
>
> > The creation and analysis of new solid forms was not a rote process. It was not possible for us to predict at the outset how many solid forms we would be able to identify, what they would be, or what solid forms would result from any particular method or set of conditions. Therefore, this process often required numerous experiments and analyses, and strategy and judgment had to be employed in order to make decisions about how to proceed based on the results that we obtained.
>
> [Emphasis omitted]

> [51] It is also noteworthy that in the course of the process of creating and identifying new solid state forms, SSCI discovered a new solid form that was not crystalline and identified several other crystalline forms (Reasons at paras. 132 and 137). Given the uncertainty in the circumstances surrounding the new crystal form identified by Wyeth, SSCI's empirical and extensive research work was in fact a continuation of Wyeth's work and was required in order to conclude that Form I ODV succinate was the most stable hydrated form. The Federal Court Judge's consideration of this was accordingly justified.

[64] Before considering the facts of the present case, 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 common general knowledge 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

> [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.

[65] In the present case, the prior art disclosed the existence of crystalline forms of azoxystrobin. In addition, page 2 of the description provides the background knowledge regarding the search for alternate methods of preparing azoxystrobin:

> There is an urgent unmet need in the art for efficient methods for the preparation and purification of azoxystrobin, which are simple and can be used on a large scale for industrial manufacture, and which produce highly pure product that can be safely utilized.

[66] Further, as detailed in the Preliminary Review letter on pages 16 to 17, the relevant common general knowledge establishes that it was common practice for

an organic chemist in product development to conduct routine experimental screening for polymorph formation with the goal of discovering the most optimal form of a compound:

> In this regard, D3 teaches that the first step in a polymorph screen is to crystallize the substance from a number of different solvents (page 946):
>
> > Solvents should include those used in the final crystallization steps and those used during formulation and processing and may also include water, methanol, ethanol, propanol, isopropanol, acetone, acetonitrile, ethyl acetate, hexane and mixtures if appropriate. New crystal forms can often be obtained by cooling hot saturated solutions or partly evaporating clear saturated solutions.
>
> D4 also describes the use of hot stage microscopy, which allows for the identification of polymorphs using only small amounts of material. This capability can be added to a screen in order to minimize the likelihood that a solvent is overlooked because an initial crystallization is not successful. Once the existence of multiple forms is established, practical methods for the preparation of specific forms on a larger scale may be explored (page 177):
>
> > Frequently, recrystallization of the compound from solvents or solvent mixtures spanning a wide polarity range is effective in producing several of the different forms in sufficient quantity for complete characterisation by the analytical methods.
>
> D5, which was published twenty one years after D3 and eighteen years after D4, provides a more contemporary review of approaches to polymorph screening, including the design of high-throughput crystallization platforms. D5 recognizes that "[f]or a reliable polymorphism screening both crystallization conditions and solvent type have to be varied as broadly as possible" (page 288) and that "[t]he choice of crystallization method has a major influence on which form is produced, and it therefore clearly makes sense to perform crystallizations using various methods when looking for polymorphs" (page 289). In this regard, high-throughput screening provides a more efficient means of screening for polymorphs as it allows for the simultaneous testing of multiple parameters that affect crystallization, including method (*e.g.*, cooling, evaporation, precipitation, and slurry), conditions (*e.g.*, time, temperature, rate) and solvent.

[67] The Preliminary Review letter also notes that in the prior art the crystallization of azoxystrobin was achieved using solvents or mixtures of solvents used in the formulation of azoxystrobin, as taught in the common general knowledge:

> Given that D1 discloses the successful preparation of a polymorphic form of azoxystrobin from methanol—one of the commonly used solvents identified in D3, in our view, the person skilled in the art would consider testing additional common solvents, for example the remaining solvents identified in D3, to be a routine aspect of a polymorph screen. Likewise, D2 discloses the recrystallization of azoxystrobin but from a mixture of ether/dichloromethane/n-hexane. Notably, these solvents were used in the formulation and processing of azoxystrobin which, as taught by D3, would also be considered to be a routine aspect of a polymorph screen. In this view, the person skilled in the art would also consider that testing solvents or mixtures of solvents used in the formulation and processing of azoxystrobin as part of a polymorph screen.
>
> As indicated in the description, there are several reported ways of making azoxystrobin, e.g., EP-A-0382376, EP-A-0242081 or U.S. 7,084,272, as well as formulating of intermediates, e.g., WO 97/30020 and WO 97/01538 (pages 1–2). In particular, these references disclose the formulation and processing of azoxystrobin and its intermediates using a variety of different solvents including, 1-propanol, N,N-dimethyl acetamide, water, heptane, isopropyl alcohol and butanol.

[68] The Preliminary Review letter, on page 17, further notes that based on the common general knowledge from D4 and D5, the skilled person would know that a polymorph screen should also include recrystallization of the compound from solvents or solvent mixtures spanning a wide polarity range, as well as the testing of additional parameters that affect crystallization, such as method (*e.g.*, cooling, evaporation, precipitation, and slurry) and conditions (*e.g.*, time, temperature, rate). As taught by D5 and Lee et al., these methods are amenable to automated high-throughput technology which allows for simultaneous assessment of multiple parameters that affect crystallization with minimizing the amount of material that needs to be used, and the amount of time required for testing.

[69] Although the response to the Preliminary Review letter submits that there is no such thing as “routine” experimental screening for polymorph formation, as indicated above, the common general knowledge supports that a polymorph screen would include the testing of common solvents and solvents or mixtures of solvents used in formulation and processing using standard crystallization methods and conditions. In addition, the common general knowledge regarding polymorph screening is that it is necessary to use a diverse range of approaches that when coupled with robotic platforms for sample generation and analysis allow for large sets of crystallization experiments to be performed using small amounts

of compound in a short period of time. In our view, these aspects of a polymorph screen, which are limited to the generation of as many possible crystalline phases would be considered routine, unlike approaches that require strategy and judgment to be employed to make decisions about how to proceed, for example, based on experimental results or comparative analysis of properties.

[70] Another consideration that was addressed in the Preliminary Review letter was whether an unexpected benefit was a relevant factor. The Preliminary Review letter, on pages 18 to 19, explains why we agree with the assessment in the Summary of Reasons that in the present case an unexpected benefit or advantage cannot be considered a relevant factor. It notes that routine methods were used to prepare the claimed forms of azoxystrobin. Moreover, there was no “cautionary tale” from the prior art or the common general knowledge suggesting that a routine polymorph screen would not work.

[71] In addition, there is no teaching or suggestion in the description that Form B of azoxystrobin or a mixture of Form A and Form B are beneficial or advantageous as compared to the known polymorphic forms of azoxystrobin disclosed in D1 and D2. More specifically, the characterization of Form B and mixtures of Form A and Form B of azoxystrobin is limited to spectral characteristics. Beyond that, there is no testing to see whether any properties are affected by these crystal structures, for example, stability and solubility. This is consistent with the inventive concepts identified above which focus on the expected fungicidal activity of the claimed polymorphs.

[72] In light of the above, it is our view that it would have been more or less self-evident to the person skilled in the art, based on the disclosure of either D1 or D2 and the relevant common general knowledge, that performing those aspects of a polymorph screen that are considered routine, for example, testing of common solvents and solvents or mixtures of solvents used in the formulation and processing of azoxystrobin using standard crystallization methods and conditions, ought to work to generate crystalline forms of azoxystrobin.

[73] Contrary to the assertion in the response to the Preliminary Review letter that it would be unclear to the person skilled in the art whether azoxystrobin even

crystallizes, the evidence is that the prior art already confirms the existence of crystalline azoxystrobin. The fact that D1 and D2 each disclose the purification of a crystalline form of azoxystrobin supports our view that the person skilled in the art would reasonably expect to produce additional crystalline forms of azoxystrobin by following those aspects of a polymorph screen that are considered routine.

[74] Although we consider that the above assessments are largely determinative of the obvious to try inquiry in this case, we make the following observations with regard to the other non-exhaustive factors to be considered in an obvious to try analysis.

Extent and Effort Factor

[75] The Preliminary Review letter, on page 19, considers that the extent, nature, and amount of effort required to perform a routine polymorphic screen would have been within the capabilities of the person skilled in the art as of the claim date. The Preliminary Review letter reviews the evidence relating to the actual course of conduct of the Applicant, which is limited to the exemplary portion of the description, and considers that the person skilled in the art would act in a similar manner.

[76] The response to the Preliminary Review letter submits that this conclusion is based on hindsight analysis and that a polymorph screen meets the criteria of prolonged and arduous:

> The Board's conclusion that since the Forms of the present application were prepared using common techniques is clear hindsight analysis. Merely because the present application does not disclose a series of failed experiments that illustrate the path to the invention, this does not mean that the process was effortless. Rather, a number of calculated decisions were required based on experimental results that were obtained.
>
> The Applicant respectfully submits that the path to the invention as defined in claim 1 was not simple and routine, and again submits that in view of the evidence provided above, polymorph screens are by nature not routine experiments.
>
> Indeed, as the Board's own D5 reference notes, up to 400+ solvents can be tried, which when combined with an array of temperatures and cooling/heating times, over a million different experimental conditions can arise. Such screens can take years and extensive manpower and resources. This would certainly meet the criteria of

> prolonged and arduous. Accordingly, the present claims do not meet the second criteria.

[77] We disagree that these aspects of a polymorph screen, which are limited to screening methods for the purpose of uncovering as many crystalline forms of a compound as possible, would be considered prolonged and arduous. As explained above, experimentation of this nature was a routine aspect of polymorph screening.

[78] The response to Preliminary Review letter further submits that path to the invention involved a number of calculated decisions, based on experimental results that were obtained, however, there is no evidence that any decisions of an inventive nature were required. As mentioned in the Preliminary Review letter, the present application discloses that both Form B of azoxystrobin and the mixture of Form A and Form B were produced using common crystallization techniques, namely precipitation and cooling. In addition, there is no evidence that these were not routine processes. Likewise, there is no evidence that an arduous investigation of solvents or other formation conditions such as the temperature or evaporation rate was required.

[79] We also note that characterization of the polymorphs was limited to the determination of their different spectral characteristics. Specifically lacking from the description is the testing of any properties that would be relevant to the industrial manufacture of azoxystrobin, for example, comparative data demonstrating improved solubility or improved stability over the known forms.

[80] In the absence of any further polymorph characterization, it is our view that by performing those aspects of a polymorph screen which are routinely used when attempting to find new crystalline forms of a compound, the person skilled in the art would have produced Form B of azoxystrobin or a mixture of Form A and Form B without difficulty.

Motive Factor

[81] Regarding the Motivation Factor, which includes considerations provided in the prior art to find the solution the patent addresses, the Preliminary Review letter considers the arguments in the response to the Final Action concerning the twenty year gap between the time that azoxystrobin was first available commercially and the filing of the present application. The Preliminary Review letter, on page 20, explains that just because azoxystrobin had been widely used, it does not necessarily follow that differences over it of the type presently claimed are non-obvious: *Apotex Inc v H Lunbeck A/S 2013 FC 192* para 99:

> A motive is defined as that which moves or tends to move a person to a particular course of action (*Oxford Dictionary*). On the other hand, there may not have been reason to do something at a particular point in time. For instance, there may have been little interest in increasing automobile fuel efficiency in the 1950s. Lack of interest would not give rise to a patent if what was eventually done was obvious.

[82] In this view, the Preliminary Review letter considers there may simply have been little incentive to look for additional polymorphic forms in the 1990's:

> Likewise, in the present case, we are not convinced that the age of the prior art or the fact that azoxystrobin was a commercially successful fungicide means that the POSITA would not be motivated, to any degree, to seek improvements. It may simply mean that there was little incentive to investigate other polymorphic forms in the 1990's. However, as explained above, the CGK regarding polymorph screens has evolved significantly since that time. At the claim date, the relevant CGK establishes that it was common practice for an organic chemist in product development to conduct routine experimental screening for polymorph formation, with the goal of discovering the most optimal form, which constitutes a motive in the prior art to find a solution through a routine polymorph screen.

[83] The response to the Preliminary Review letter argues that not only is this line of thinking speculative and unsupported, it also goes against the common general knowledge as asserted from D3 and D4 which teach that the person skilled in the art would invariably screen for any polymorphs.

[84] We agree that we do not know why there is a twenty year gap between the time azoxystrobin was first commercially available and the filing of the present application. However, that does not mean that identifying Form B of azoxystrobin was inventive. In our view, what must be considered is whether the prior art and relevant common general knowledge at the claim date provide any motive to search for additional polymorphic forms of azoxystrobin. Therefore, we disagree

with the position in the response to the Preliminary Review letter which frames our assessments as mutually exclusive objectives as they pertain to motive. The relevant date for assessing motive is the claim date, not the date at which azoxystrobin was first made commercially available.

[85] The Preliminary Review letter, on page 21, explains that the “Background of the Invention” of the present application specifically acknowledges the ongoing research into the synthesis of azoxystrobin. Consistent with the teachings of the description (see page 2, lines 10 to 13), at the claim date, the person skilled in the art was aware that there was a need to improve on the preparation and purity of azoxystrobin. The general motive to use polymorph screens to achieve such needs was also common general knowledge at the claim date.

[86] In this regard the response to the Preliminary Review letter asserts that a general motivation to find polymorphs is not sufficient and that in view of ODV FC there must be evidence of a specific motivation to find Form B of azoxystrobin.

[87] As explained in *AstraZeneca Canada Inc v Mylan Pharmaceuticals ULC*, 2017 FC 142 [AstraZeneca], at paras 148 to 162, specific motivation is not required in order to find that an invention was obvious. A distinction between general and specific motivation is not consistent with Sanofi’s contextual approach to motivation. It is not our view that general and specific motivations are the same. However, we consider that the effect of motivation on the obviousness analysis depends on how it interacts with the other relevant facts, and not which category it falls into. The question “how specific” to the claim was the motivation is still relevant. The more specific to the claim, the more weight motivation may have as a factor in determining whether the claim was obvious to try (see AstraZeneca at para 160).

[88] Although we agree that there was no specific motivation in the prior art to find Form B of azoxystrobin, there was a specific motivation to search for forms of azoxystrobin amenable to industrial manufacture. We consider that the person skilled in the art would have started with those aspects of a polymorph screen that are considered routine and in doing so they would have found Form B of azoxystrobin, as well as mixtures of Form A and Form B. This is consistent with the evidence in the description concerning the course of conduct that led to Form B, as well as mixtures of Form A and Form B of azoxystrobin.

Conclusion on obvious to try

[89] In view of the foregoing, it is our view that the person skilled in the art would have been motivated to produce polymorphic forms of azoxystrobin and that it would have been more or less self-evident to use those aspects of a polymorph screen that are considered routine to try and obtain them. In doing so the person skilled in the art would have produced Form B of azoxystrobin or a mixture of Form A and Form B without difficulty and routinely. Accordingly, we conclude that the differences between either D1 or D2 and the inventive concepts of independent claims 1, 10, 13 to 16, 22, 25, 26 and 28 to 30 are not steps which would require any degree of invention from the person skilled in the art.

[90] With respect to the remaining dependent claims, the response to the Preliminary Review letter did not identify or associate any specific limitations in these claims with additional ingenuity. Having considered dependent claims 2 to 9, 11, 12, 17 to 21, 23, 24 and 27, we do not consider that any degree of invention would have been required from the person skilled in the art in respect of the spectral characterization of Form B, Form A or the mixture of polymorphs or specifying the type of solvent, specific process steps, type of alcohol and type of anti-solvent.

Conclusion on obviousness

[91] Our conclusion is therefore that the subject-matter of claims 1 to 30 on file would have been obvious to the person skilled in the art as of the relevant date, in view of either D1 or D2 and the common general knowledge, contrary to section 28.3 of the *Patent Act*.

Consideration of obligations under TRIPS

[92] The response to the Preliminary Review letter submits that Canada has an obligation to award a patent for a technical solution to a technical problem, which arises from Article 27.1 of *The Agreement on Trade-Related Aspects of Intellectual Property Rights* (TRIPS) and further notes that its corresponding and related applications in several TRIPS countries have issued to patent.

[93] Article 27.1 read as follows:

> [Emphasis added] Subject to the provisions of paragraphs 2 and 3, patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, **involve an inventive step** and are capable of industrial application.

[94] The TRIPS Agreement is sometimes described as a “minimum standards” agreement and the agreement gives members the freedom to determine the appropriate method of implementing the provisions of the agreement within their own legal system and practice. Further, the fact that the corresponding foreign applications issued to patents, or the fact that corresponding applications filed in other jurisdictions did not issue to patent, is not determinative on the question of obviousness under Canadian law.

[95] We have considered the evidence before us in light of the law on obviousness established by Canadian courts in reaching our conclusion.

RECOMMENDATION OF THE BOARD

[96] In view of the above, the Panel recommends that the application be refused on the basis that:

- Claims 1 to 30 are obvious and do not comply with section 28.3 of the *Patent Act*.

Christine Teixeira	Marcel Brisebois	Philip Brown
Member	Member	Member

DECISION OF THE COMMISSIONER

[97] I concur with the findings of the Board and its recommendation to refuse the application because the claims on file do not comply with section 28.3 of the *Patent Act*.

[98] Accordingly, I refuse to grant a patent for this application. Under section 41 of the *Patent Act*, the Applicant has six months to appeal my decision to the Federal Court of Canada.

Virginie Ethier
Assistant Commissioner of Patents

Dated at Gatineau, Quebec

this 29th day of March, 2022.