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Commissioner's Decision #1693
Décision du commissaire nº 1693
Date: 2025-08-22

TOPIC: O00 Obviousness

SUJET : O00 Évidence

Application No. 2807859
Demande n^{o} 2807859

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 2,807,859, having been rejected under subsection 86(7) of the *Patent Rules* (SOR/2019-251), has subsequently been reviewed in accordance with paragraph 86(7)(c) of the *Patent Rules*. 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 2,807,859, which is entitled “FORMS OF METHYL{4,6-DIAMINO-2-[1-(2-FLUOROBENZYL)-1H-PYRAZOLO[3,4-B]PYRIDINO-3-YL]PYRIMIDINO-5-YL}METHYL CARBAMATE” and is owned by Adverio Pharma GMBH. The Patent Appeal Board (the Board) has reviewed the rejected application pursuant to paragraph 86(7)(c) of the *Patent Rules* (SOR/2019-251). As explained below, we recommend that the Commissioner refuse the application.

BACKGROUND

The application

[2] Canadian patent application 2,807,859, has a filing date of February 21, 2013, and has been open to public inspection since August 21, 2014.

[3] The application concerns a new crystal form of the compound of formula (I), a soluble guanylate cyclase (sGC) stimulating agent that was known for the treatment or prevention of cardiovascular disorders.

Prosecution history

[4] This application was rejected in a Final Action (FA) issued on March 3, 2020 pursuant to subsection 86(7) of the *Patent Rules* for claiming obvious subject-matter contrary to section 28.3 of the *Patent Act* (RSC 1985, c P-4). The Applicant provided a response to the Final Action (R-FA) dated August 18, 2021 containing further arguments in favour of the patentability of those claims. Unpersuaded by the arguments, the Examiner maintained the rejection and forwarded the application to the Patent Appeal Board for review on behalf of the Commissioner of Patents.

[5] This Panel was formed and we conducted a preliminary review of the application. The results of our review were outlined in detail in a preliminary review letter (PR)

that was provided to the Applicant on July 25, 2024. Our letter invited the Applicant to provide written submissions in response to our preliminary views and to attend an oral hearing.

[6] The Applicant did not respond to our letter, but did confirm in a telephone call on August 9, 2024 that they would not be providing any further oral or written submissions.

[7] We have completed our review and have set out our conclusions below.

THE ISSUE IS OBVIOUSNESS

[8] This review considers whether the subject-matter of claims 1 to 4 on file is obvious contrary to section 28.3 of the *Patent Act*.

[9] We note that since the Applicant did not respond to our PR letter, the preliminary views presented in that letter are uncontested and considered to not be disputed. The recommendation below therefore provides an overview of the analysis and rationale presented in our PR letter.

PURPOSIVE CONSTRUCTION

Legal principles

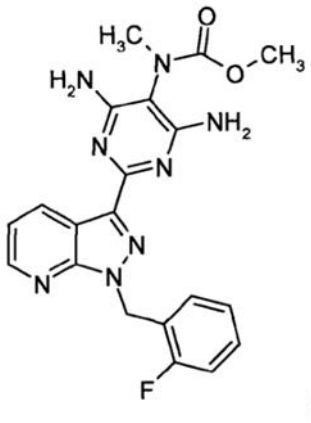
[10] In accordance with *Free World Trust v Électro Santé Inc*, 2000 SCC 66 and *Whirlpool Corp v Camco Inc*, 2000 SCC 67 purposive construction is performed from the point of view of the person skilled in the art in light of the relevant common general knowledge (CGK), considering the whole of the disclosure including the specification and drawings. In addition to interpreting the meaning of terms, 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.

[11] We consider that all elements set out in a claim are presumed essential unless it is established otherwise or if the skilled person would understand from the claim language that the Applicant did not intend to make the element essential.

Analysis

The claims on file

[12] The claims set consists of four independent claims. Claim 1 is directed to a specific crystal form “Modification II” of the known formula (I) compound:

> 1. A compound of the formula (I)
>
> 
>
>
> (I)
>
> which is methyl {4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridino-3-yl]pyrimidino-5-yl}methyl carbamate, in the Modification II, wherein
>
> the Modification II is characterized by a X-Ray powder diffractogram comprising peak maxima of the 2 Theta angle 11.2, 12.6, 12.7, 13.9, 15.2, 17.3, 22.5, 22.8, 25.0, 25.5.

[13] Claims 2 and 3 are directed to pharmaceutical compositions comprising Modification II as the active ingredient. Claim 2 is illustrative: (emphasis added)

> 2. A pharmaceutical composition comprising the compound of the formula (I) in **only** Modification II, as defined in claim 1, and one or more inert, nontoxic, pharmaceutically acceptable excipients.

[14] Claim 3 is similar but does not include the term “only”, specifying instead that the composition comprises Modification II “mainly and no significant fractions of another form”.

[15] Claim 4 reads as follows:

> 4. Process for preparing methyl {4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]pyrimidin-5-yl}methylcarbamate of the formula (I) in the form of Modification II, as defined in claim 1 or 2, comprising drying the compound according to formula (I) as mono-DMSO solvate, characterized by a X-Ray powder diffractogram comprising peak maxima of the 2 Theta angle of 9.0, 10.8, 11.1, 11.2, 13.0, 15.5, 15.9, 16.0, 20.7, 25.6, at about 80°C.

The person skilled in the art

[16] Our preliminary view was that the characterization of the skilled person that was set out in the FA was reasonable (PR, pages 4-5):

> The Final Action characterizes the skilled person as a person or team including at least an organic chemist in the field of pharmaceutical drug development with experience in polymorphs, crystal generation, XRD (X-ray diffraction), and the use of polymorphs in pharmaceutical formulations (page 3).
>
> This characterization was not disputed or commented on in the response to the Final Action. Our preliminary view is that this characterization is reasonable and so we adopt it for the purposes of our preliminary view.

> As with all of the preliminary views set out in this letter, the Applicant is invited to provide further comments or clarification on this characterization, if desired. Any such comments will be considered as part of our final review.

[17] We adopt this characterization for our analysis.

The common general knowledge

[18] The FA cited the following documents as support for information identified as being CGK:

D2: Byrn, S et al, “Pharmaceutical solids: a strategic approach to regulatory considerations” (1995) 12:7 Pharma Res pages 945-954 (Byrn et al)

D3: Caira, M R, “Crystalline polymorphism of organic compounds” (1998) 198 Topic in Current Chemistry, in Weber, E (Ed), Design of organic solids, pages 163-208 (Caira)

D4: Brittain, H G, (Ed), Polymorphism in Pharmaceutical Solids, 1st edition (1999) Guillory, J, Chapter 5, “Generation of polymorphs, hydrates, solvates and amorphous solids”, pages 183-226 (Guillory)

[19] Based on these documents, pages 3-4 of the FA identified the CGK as including: i) the methods of screening for polymorphs by preparing new forms using standard crystallization techniques (such as agitation, heating, cooling, etc.) from a number of solvents of various polarities; ii) any solid form of a molecule with an established activity, such as against cardiovascular disorders, would also have that same activity to some degree, since biological activity is an effect of the molecule, and the molecules are chemically identical; and iii) the use of thermal desolvation of crystalline solvates to isolate polymorphs.

[20] The R-FA did not comment on or dispute that any of these points are CGK, but did add the following in reference to further information and documents appearing to relate to the CGK (R-FA, pages 2-3, full citations of referred documents provided below):

> The prospect of success that a further crystalline form could be obtained in addition to a known crystal of an organic molecule is by no means obvious, see for instance Burger, where it is noted that about 36% of the crystalline organic compounds listed in the EuAB (European Pharmacopoeia) are polymorphs; Henck et al. where it was estimated that 42% of all active pharmaceutical compounds are monomorphs; Grunenberg which (in the same year as Henck) estimated that 80% of all active pharmaceutical compounds are polymorphs; and Kuhnert-Brandstätter which states that for about 40 steroid hormones it was not possible to prepare more than one crystalline form.

Burger, A, “Die polymorphen arzneistoffe des europäischen arzneilbuches”, (1979) Supplement 7 Acta Pharm Technol, pages 107-112

Henck, J-O et al, “Polymorphie von arzneistoffen, eine wirtschaftliche herausfordergung?” (1997) 50 Pharm Ind, pages 165-169

Grunenburg, A, “Polymorphie und thermische analyse pharmazeutischer wirkstoffe”, (1997) 26 Pharmazie in unserer zeit, pages 224-231

Kuhnert-Brandstätter, M, “Polymorphie und pseudopolymorphe kristallformen von steroidhormonen”, (1977) 39 Pharm Ind, pages 377-383

[21] As we stated in our PR letter, the principles governing the assessment of CGK were 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 (RPC) (PR, page 6). In sum, CGK is a concept derived from a common sense approach to the practical question of what would in fact be known to an appropriately skilled addressee at the relevant time. Generally, scientific articles form part of the CGK provided they are generally known and generally regarded as a basis for further action by the bulk of those who are engaged in a particular art.

[22] 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: (see MOPOP at §12.02.02c).

[23] The references cited in the FA and those provided by the Applicant are all from the relevant field. Byrn et al and Caira are review articles and Guillory is a chapter from a textbook. By contrast, the four German-language documents provided by the Applicant appear to be journal articles. Further, two of those documents were published in 1977, which is more than 35 years before this application was filed.

[24] In order to understand the state of the CGK circa the publication date and claim date, our preliminary review letter referred to the following handbook, review article and International guideline which all concern the use of polymorphs in medicines:

[25] Hilfiker, R, ed, Polymorphism in the Pharmaceutical Industry (Weinheim, Germany: WILEY-VCH Verlag GmbH & Co KGaA, 2006), see Chapters 1, 2, 8, 9, 11 and 15 at pages 1-3, 12, 14, 21, 211-212, 215-216, 222-223, 242, 288 and 390-392

[26] Morissette, S L et al, “High-throughput crystallization: polymorphs, salts, co-crystals and solvates of pharmaceutical solids” (2004) 56:3 Adv Drug Deliv Rev pages 275-300

[27] “ICH harmonised tripartite guideline, specifications: test procedures and acceptance criteria for new drug substances and new drug products: chemical substances Q6A”, (International conferences on harmonisation of technical requirements for registration of pharmaceuticals for human use) October 6, 1999 at pages 8-9 and 24-25 [ICH]

[28] According to Hilfiker, polymorphism is very common in connection with drug substances, which are mostly (about 90%) small organic molecules with molecular weights below 600 g/mol. Further, the probability that a drug substance can exist in several solid forms (polymorphs, solvates, hydrates, amorphous

forms, co-crystals) is probably close to 100% since 56-87% of all small organic molecules can form solvates and polymorphs alone: Hilfiker pages 1, 2, 287.

[29] Since Hilfiker is a Handbook on polymorphism in the pharmaceutical field and was published at least 9 years after the most recent references provided by the Applicant, our preliminary view was that the information in Hilfiker more reasonably reflects the state of the CGK as of the relevant dates (i.e., the publication date and the claim date for assessing CGK and obviousness, respectively) (PR, page 7).

[30] We expressed the preliminary view that the following information would also have been well-known CGK (PR, pages 10-11):

- In addition to having different physical properties (e.g., solubility, melting point, etc.), different polymorphs of a compound/molecule can have different performance characteristics. These characteristics include those that are critical to formulating a pharmaceutical dosage form, such as bioavailability, manufacturability and stability: Hilfiker pages 1-3, 14, 392; Morissette et al page 276; ICH pages 8-9

- By 1999 international guidelines recommended that polymorph screening be conducted for pharmaceutical candidate molecules ahead of seeking regulatory approval; these guidelines were adopted by the regulatory authorities in the United States, Europe and Japan by 2001, becoming requirements: www.ICH.org, ICH pages 8-9, 24-25; Hilfiker pages 390-392

- Two main reasons for conducting a polymorph screen are: i) to find and select the solid form with optimal performance characteristics in the dosage form, and ii) to identify any polymorphs that are produced during processing (i.e., synthesis, formulation etc.) so that the formation of undesirable forms may be monitored and controlled: Hilfiker pages 3, 14, 390-393; Morissette et al page 277; Caira page 165; Byrn et al page 947

- Processes including crystallization, drying, heating, compression and milling can induce polymorphic transformations and so careful monitoring and control is needed in all stages: Caira pages 165, 167; Morissette et al page 277

- Sometimes crystallizing from a solvent produces a type of polymorph (or "pseudopolymorph") called a "solvate" where the compound molecules crystallize and pack "together" with the solvent molecules, integrating them as part of the crystal structure: Hilfiker page 212; ICH page 8

- The potential for a polymorph or solvate other than the most thermodynamically stable form to convert to a more stable form under suitable conditions (e.g. in suspension, via solvent-mediation, etc.) can negatively impact bioavailability, and so all forms appearing in the system need to be identified and their interconversions understood: Caira pages 165-167, 170; Hilfiker pages 3, 242, 288

- Even though solvates other than hydrates are not typically used in drug products, this potential for interconversion makes it important to fully characterize them (and their desolvated forms) and their transitions (regardless of whether they are used on purpose as an intermediate or may form accidentally): Byrn et al page 949; Caira page 167

- "desolvated solvates" are forms that originally crystallize as a solvate but the solvent is removed later, generally by thermal desolvation induced by heat and vacuum which vaporizes the solvent (i.e., a solid → gas + solid transformation): Guillory page 199; Caira page 177; Hilfiker page 3

- Forming solvates is problematic at times but can also be a useful strategy for obtaining a crystalline material with increased purity (if the molecule is difficult to crystallize in a solvent-free form) and is a common technique for preparing and identifying more polymorphs through thermal desolvation via controlled heating: Hilfiker pages 3, 12, 211; Caira page 178; Morissette et al page 290

- The solvent within a solvate is frequently highly volatile and is therefore easily lost under mild conditions (including simply heating it in air), and so it is important

to use gentle drying procedures during processing (e.g., synthesis, purification, etc.) to avoid desolvating it accidentally or unknowingly, thus causing the solvate to be overlooked: Hilfiker pages 204 and 223, see also pages 3, 222; Morissette et al page 290; Byrn et al page 946

- Thermal desolvation of solvates (which generally fall into one of two classes) always leads to either i) a different crystal structure or disordered amorphous state (stoichiometric solvates), or ii) a form that primarily retains the original crystal structure of the solvate (non-stoichiometric solvates): Hilfiker pages 215-216; Guillory page 199; Caira page 177

[31] Since this information comes from a handbook, book chapter, review articles and an International guideline all concerning the use of polymorphs in medicines, and there is also a demonstrated commonality of knowledge from a number of these disclosures, our view is that it is reasonably considered as CGK.

Meaning of terms

[32] We expressed the preliminary view that the skilled person reading the claims would understand that the pharmaceutical composition of claim 2 comprises a higher purity form (i.e., a higher content of one polymorphic form over other forms of the same compound) compared to claim 3 since it is expressly limited to comprising Modification II “only”, whereas claim 3 may contain fractions of other forms (albeit in insignificant amounts) (PR, page 10).

[33] We adopt this interpretation for the purposes of our analysis.

Essential elements

[34] 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. Our PR letter expressed the view that the skilled person reading claims 1 to 4 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. For that reason, our preliminary view was that all of the elements of claims 1 to 4 are essential.

[35] We adopt this characterization for the purposes of our analysis.

CLAIMS 1 TO 4 ON FILE ARE OBVIOUS

[36] Our view is that claims 1 to 4 define obvious subject-matter.

Legal principles

[37] Section 28.3 of the *Patent Act* requires claimed subject-matter to not be obvious:

> 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;

[38] In *Apotex Inc v Sanofi–Synthelabo Canada Inc*, 2008 SCC 61 at para 67 [*Sanofi*], the Supreme Court of Canada stated 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?

[39] With respect to the second step of obviousness, *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.

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

> 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 in (*Bristol-Myers Squibb Canada Co v Teva Canada Limited,* 2017 FCA 76 [*Bristol-Myers*]*)*, these beneficial properties were the "solution taught by the patent" claim. They explain the source of motivation to pursue the solution (*Bristol-Myers* at para 75).

[41] At the fourth step the Court in *Sanofi* indicated that an "obvious to try" enquiry might be appropriate in areas of endeavour where advances are often won by

experimentation, such as the pharmaceutical industry, providing the following guidance at paras 69 and 70:

> [69] If an “obvious to try” test is warranted, the following factors should be taken into consideration at the fourth step of the obviousness inquiry. As with anticipation, this list is not exhaustive. The factors will apply in accordance with the evidence in each case.
>
> (1) Is it more or less self-evident that what is being tried ought to work? Are there a finite number of identified predictable solutions known to persons skilled in the art?
>
> (2) 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?
>
> (3) Is there a motive provided in the prior art to find the solution the patent addresses?
>
> [70] Another important factor may arise from considering the actual course of conduct which culminated in the making of the invention. It is true that obviousness is largely concerned with how a skilled worker would have acted in the light of the prior art. But this is no reason to exclude evidence of the history of the invention, particularly where the knowledge of those involved in finding the invention is no lower than what would be expected of the skilled person.

[42] The assessment of these factors is a fact driven exercise, dependent on the specific facts of the case. The fourth factor is closely tied to the second: *Janssen Inc v Apotex Inc*, 2021 FC 7 at para 136 [*Janssen* 2021], citing *Sanofi* para 71; *Janssen Inc v Apotex Inc*, 2019 FC 1355 at paras 195, 199-200 [*Janssen* 2019].

[43] 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*: Eli Lilly Canada Inc v Mylan*

Pharmaceuticals ULC, 2015 FCA 286 at para 4. Mere possibility that something might turn up is not enough: *Sanofi* at para 66.

Analysis

(1) Identify the notional person skilled in the art

[44] Our characterizations of the skilled person and relevant CGK are set out above.

(2) Identify the inventive concept of the claim in question or if that cannot readily be done, construe it

[45] We declined to adopt the inventive concepts from the FA because some essential elements set in the claims were not reflected in their respective inventive concepts and because there was no distinction between claims 2 and 3 on file.

[46] We considered the following statements from the Applicant in the R-FA as pertinent to the inventive concepts (R-FA, pages 3-4): (emphasis added)

> In the present case, Applicant has discovered a chemical compound, the novelty of which has been recognized. This novel chemical compound has different physical properties and characteristics than the referenced Modification (I), **and has beneficial properties, described in the application (see page 5)** and evidenced by data of record.
>
> The Final Action dismissed the additional data provided on the basis that a "subsequently recognized advantage" cannot assist in the obviousness inquiry, **but this ignores Applicant's disclosure on page 5 which clearly references solubility as a beneficial property**.

[47] As stated above under "Legal principles", it may be appropriate to construe the inventive concept of a claim as including one or more special advantageous properties that are associated with a claimed compound in certain situations,

such as where the description teaches the property as being part of the "solution taught by the patent": *Shire* para 84.

[48] The description says the following in reference to the various solid forms that are disclosed in the application on pages 4-5: (emphasis added)

> Surprisingly it has been found that the compound of formula (I) crystallizes in two modifications with melting points at 268 °C (**Modification I**) and 250 °C (**Modification II**). In this context modifications and polymorphs have the same meaning. In addition, three pseudo-polymorphs, **a mono-DMSO solvate, a sesqui-DMSO solvate, a 1/4-ethyl acetate solvate and the amorphous form** have been found. The amorphous form can exist at room temperature, but crystallizes very quickly. All together – modifications or polymorphs, pseudo-polymorphs and amorphous forms – are different forms of the compound of formula (I) according to the present invention.
>
> Aspects of some embodiments of the present invention which may be beneficial in the present pharmaceutical field may include stability (e.g. pressure stability, chemical stability, storage stability), compatibility over other ingredients, purity, solubility (thermodynamically, kinetically), crystallization properties, properties regarding isolation during the chemical synthesis and bioavailability **of the forms of the compound of formula (I)**.

[49] We expressed our preliminary view that the beneficial properties on page 5 are not associated with Modification II over any of the other solid forms that are disclosed (PR, page 15). We added that the only property in the above passages that is expressly associated with Modification II is its melting point which is a physical property, as opposed to one of the performance characteristics in the list. Further, the expressions "which may be beneficial" and "which may include" are very general. Our preliminary view was that, in the absence of a clear description of solubility as a beneficial property of Modification II over the other forms of formula (I), the skilled person would not reasonably regard it as part of the inventive concept in the manner described in *Shire* at para 84.

[50] On that basis, our preliminary view was that the inventive concepts of claim 1 to 4 are the claims as construed (PR, page 15).

[51] We adopt this characterization for our analysis.

(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

[52] The FA cites document D1 against the claims on file. D1 is an earlier Canadian patent application that was filed by the Applicant that also relates to the compound of formula (I):

D1: CA 2,781,799 Mais et al June 3, 2011

[53] D1 teaches a new simplified process for preparing the formula (I) compound in higher purity via a mono-DMSO crystalline solvate intermediate (page 13, lines 5-6, 28-29) that is subsequently converted to an unsolvated form. The formula (I) compound is described as a known sGC stimulating agent used for preventing and/or treating cardiovascular disorders (see page 2, lines 1-11 and page 12, line 5). Medicaments prepared using the formula (I) compound that is purified by that process are also disclosed.

[54] Two examples are disclosed for preparing the mono-DMSO solvate, both using a mixture of DMSO and ethyl acetate and both drying the solvate at low temperatures of 50°C and 30°C, respectively. Example 7 provides the steps for preparing the formula (I) compound in an unsolvated form by re-dissolving the mono-DMSO solvate produced in Example 6 in ethyl acetate, stirring at reflux (about 78°C), cooling, filtering, washing and drying under reduced pressure.

[55] The Applicant acknowledged in an earlier letter that Example 7 in D1 is the same as Example 1 in the application under review and that both examples produce Modification I: letter of June 17, 2019, page 3. We similarly noted in our letter that the process for preparing the mono-DMSO solvate in Example 9 of D1 is identical to Example 2 disclosed in the application (PR, page 16).

[56] Our letter agreed with the Applicant that D1 does not disclose the Modification II polymorph from claims 1 to 4. However, it does disclose the same mono-DMSO solvate form that is converted to Modification II by thermal desolvation in the process of claim 4 on file. In other words, both processes (i.e., Example 7 of D1 and that of claim 4) convert the same mono-DMSO solvate to a desolvated form, but by two different routes that produce two different polymorphs. More specifically, Example 7 of D1 uses a different “solvent-mediated” route that produces the molecule in Modification I, as opposed to thermally desolvating to Modification II, as claimed.

[57] On that basis, our letter set out the differences as follows (PR, page 19). The main difference from the inventive concept of claim 1 is that D1 does not disclose Modification II characterized by the X-ray profile data as set out in claim 1.

[58] For claims 2 and 3, D1 discloses preparing medicaments but does not explicitly recite compositions comprising one or more inert, nontoxic, pharmaceutically suitable excipients, and so this is a further difference from D1.

[59] Claim 3 is similar to claim 2 but contains the further limitation that the composition comprises “no significant fractions of another form of the compound of formula (I)” which, as stated, indicates that other forms may be present in small amounts. Our preliminary view was the skilled person would regard this as indicating a purity of form (i.e., being substantially free of other polymorphs of the formula (I) compound). D1 similarly teaches “high amounts” of the mono-DMSO solvate relative to other forms and so our preliminary view was that purity (in general) would not be regarded as a further difference, although these expressions describe the purity of the two different forms.

[60] With regard to claim 4, D1 discloses drying the mono-DMSO solvate under vacuum at 50°C (Example 6) and in a drying cabinet at 30°C (Example 9) in the final steps of synthesis. These processes are analogous to a thermal desolvation protocol, however claim 4 defines using a higher temperature of about 80°C, and so this is a further difference from D1.

[61] Finally, D1 does not explicitly disclose the mono-DMSO solvate as being characterized by the X-Ray data of claim 4. However, D1 does disclose the same mono-DMSO solvate prepared by the same protocol and so the crystal forms would necessarily have the same X-Ray data profile, and so this is not a further difference.

[62] We adopt these differences for the purposes of our analysis.

(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?

[63] The FA states that, from the perspective of the skilled person, screening for new crystalline forms and solvate forms of the compound of formula (I) lacks inventive ingenuity (page 3), ultimately concluding that claims 1 to 4 are not inventive (FA, page 5): (emphasis in the original)

> There is nothing unexpected that flows from this alternative arrangement of molecules, and no unexpected benefit has been disclosed in the specification regarding Modification (II). This form is a variation of the compound of formula (I) that, as expected, would possess utility in the treatment of cardiovascular diseases. As such, the POSITA would recognize that any alternative form obtained from screening would be applicable toward the same use as any other form of the compound of formula (I), since the use for the treatment of cardiovascular disorders is an effect of the molecule, and the molecules are identical. The routine screening of solid forms uses a methodology and crystallization techniques that are considered CGK according to the teachings of **D2**, **D3** or **D4**…
>
> Furthermore, it is well established within the CGK, as seen in **D4**, that **thermal desolvation** of crystalline solvates is a common method of obtaining crystalline forms of a compound.

[64] In response, the Applicant disputed the general contention that, from the perspective of the skilled person, screening for new crystalline forms and solvate forms lacks inventive ingenuity (R-FA, page 4):

> The sole reason for the objection under Section 28.3 of the *Patent Act* is premised on a conclusion that "screening for new crystalline forms…lacks inventive ingenuity". However, this statement is not supported by the jurisprudence, as set out above.

[65] The specific jurisprudence referred to in this passage are the two cases confirming the inventiveness of Pfizer's Canadian Patent No. 2,436,668 to the Form I polymorph of the drug "ODV": *Pfizer Canada Inc v Apotex Inc*, 2017 FC 774, aff'd in 2019 FCA 16; *Pfizer Canada Inc v Teva Canada Limited*, 2017 FC 777, aff'd in 2019 FCA 15 [*Teva FCA*].

[66] Our letter agreed with the Applicant that there is no general proposition in the jurisprudence that screening a molecule for polymorphs lacks inventive ingenuity (PR, page 18). We further agreed that the ODV Form I patent is an example where a new polymorph discovered through screening was inventive (PR, page 19). We note that the Federal Court's assessment of that patent used an obvious to try analysis in both cases.

[67] The FA cites *Teva FCA* at para 27 as supporting the proposition that an obvious to try analysis is not to be used automatically in every case and concludes that it is not necessary in the present case. However, the accompanying reasoning appears to be based on the specification failing to identify an unexpected benefit that is attributable to Modification II.

[68] To our knowledge, there is no jurisprudence that supports failing to disclose a benefit as a reason for not applying the obvious to try test. Our view is that this determination should consider whether the field is one where advances are often won by experimentation and whether the invention in question was developed by experimentation: *Bridgeview Manufacturing Inc v 9314409 Alberta Ltd (Central Alberta Hay Centre)*, 2009 FC 50 at para 49, aff'd in part in 2010 FCA 188; *Wenzel Downhole Tools Ltd v National-Oilwell Canada Ltd*, 2012 FCA 333 at

paras 95-100; *Uview Ultraviolet Systems Inc v Brasscorp Ltd*, 2009 FC 58 at para 189, citing *Sanofi* at para 68.

[69] Our preliminary view was that it is appropriate to apply the obvious to try test in this case, and as stated the Applicant did not dispute this in response to our letter (PR, page 19).

[70] Before we proceed, there was a disagreement about experimental data that was submitted by the Applicant in Appendix A with an earlier letter dated May 3, 2018. This data demonstrates that Modification II has superior solubility relative to Modification I. The FA declined to give this data any weight because it was not disclosed originally in the application and because the Appendix is not associated with a date establishing when the data was obtained.

[71] The Applicant disputed this in response, arguing that the data should be accepted because there is a basis for improved solubility of Modification II in the original application (R-FA, pages 2-3): (emphasis in the original)

> …Modification (II) shows a **considerably improved solubility** both in the amount released per time in µg/ml and in the cumulative amount released per time [µg] as compared to the Modification (I) and as shown in the Appendix submitted with that response. As noted on page 5 of the instant application, an aspect of the invention is **solubility** of the claimed modification…
>
> This novel chemical compound has different physical properties and characteristics than the referenced Modification (I), and has beneficial properties, described in the application (see page 5) and evidenced by data of record.

[72] We said the following in relation these points in our letter (PR, page 20):

> To the extent that the Applicant is saying that the description discloses an improved solubility of Modification II compared to other forms as an aspect of the invention or in a manner providing a basis for accepting the data, we

> do not agree. We have already addressed the list of performance characteristics from page 5 at step 2 and expressed our preliminary view is that the skilled person would not regard the disclosure as associating Modification II with any specific property from the list. Instead, the skilled person would regard this as a list of potentially beneficial properties that may be associated with any one or more of the six forms recited in the paragraph immediately preceding the list.

[73] Our preliminary review letter also considered *Novopharm Limited v Janssen-Ortho Inc*, 2007 FCA 217 at para 26 [*Novopharm*] where the Federal Court of Appeal instructs that a "subsequently recognized advantage" is a secondary factor of limited usefulness in considering inventive ingenuity and should generally be given little weight:

> I find it difficult to envisage a situation where a subsequently recognized advantage to a claimed invention would be of any assistance in determining whether inventive ingenuity was required to make it (…) I recognize that it is impossible to imagine every possible situation, but given the current state of the jurisprudence I would be inclined to give this factor no weight except in the most extraordinary case.

[74] Citing *Novopharm*, the Final Action concluded that because there is no evidence establishing that the solubility data in Appendix A is not a "subsequently recognized advantage" that was perceived only after the date of invention, the data cannot assist in the inquiry into inventive ingenuity. Our letter agreed, adding the following (PR, page 21):

> Since the only date associated with Appendix A is the date that it was submitted, which is well after the claim date, our preliminary view is this data should be given little to no weight in the assessment of whether inventive ingenuity was associated with Modification II as of the claim date: *Novopharm* at para 26.

[75] For these reasons, we are inclined to give this data little to no weight in our assessment.

[76] Turning to the assessment, our preliminary view was that the motivation to desolvate the mono-DMSO solvate was expressly disclosed in D1. More specifically, the same DMSO-solvate that is used to prepare Modification II is disclosed in D1, and D1 teaches that “for pharmaceutical use, the DMSO has to be removed” from the mono-DMSO solvate: page 13, lines 30-31. Our preliminary view was that the skilled person reading this through the lens of their CGK would have known that thermal desolvation is a common route for removing solvent from a solvate. It was also well known that this technique is so straightforward that it is easily done without even realizing it (PR, page 21): Hilfiker page 204; Morissette et al page 290; Byrn et al page 946.

[77] Further, D1 discloses using the mono-DMSO solvate as a precursor for preparing another form (i.e., Modification I) in Example 7. The skilled person wanting to repeat that process to produce Modification I would know from the CGK that since it uses a solvate as starting material, that solvate would need to be characterized and its conversions to other forms would need to be understood. As stated above under CGK, this is done to prevent, monitor for and control the formation of undesirable forms: Hilfiker pages 3, 14; Caira page 165; Byrn page 946. As discussed in the PR, the skilled person would know this would require determining the temperature where solvent vaporizes (i.e., the temperature where thermal desolvation takes place), characterizing the desolvated form and comparing that form to the starting material and product of Example 7 (PR, page 21).

[78] In our view, both of these considerations independently indicate that the skilled person reading D1 would have produced Modification II without exercising any degree of inventive ingenuity.

[79] We next consider the obvious to try factors.

SELF-EVIDENT IT OUGHT TO WORK

[80] The Applicant submitted in the R-FA that the prospect of success that a further crystalline form could be obtained in addition to a known crystal of an organic molecule is by no means obvious (R-FA, page 2).

[81] Our letter stated that, while that may be true in some cases, it was well known from the CGK that thermal desolvation of a crystalline solvate leads to a new form by one of two pathways (PR, page 22). When the solvent is removed the crystalline structure is either retained (at least primarily), or alternatively the loss of the solvent leads to a new crystalline structure or amorphous solid-state form: Hilfiker pages 215-216. Further, the ability to produce new polymorphs by the controlled heating of solvates to desolvate them was a well-known and commonly used tactic for identifying new solid-state forms: Caira page 178; Morissette et al page 290.

[82] On that basis, our preliminary view was that it would have been self-evident to the skilled person that thermally desolvating the mono-DMSO solvate of D1 ought to work to produce a desolvated form (PR, page 22).

EFFORT REQUIRED

[83] Our preliminary view was that there would have been minimal effort for the skilled person to dry or heat the mono-DMSO solvate at a higher temperature than those used in the D1 examples and characterize the resulting desolvated form by X-ray powder diffraction (PR, page 22). It was well known that solvates generally lose the solvent of crystallization readily under mild conditions, so much so that it is easy to do accidentally during synthesis and purification: Hilfiker pages 204, 223; Byrn et al page 946. For that reason, our preliminary view was that the skilled person would not have expected this to be difficult.

[84] As stated above under “Legal principles”, the effort factor and the actual course of conduct are closely related and are considered together in some cases: *Sanofi* at para 71; *Janssen 2021* at para 136; *Janssen 2019* at paras 195, 199-200.

[85] Example 3 in the application discloses the preparation of Modification II, which is reproduced in its entirety as follows:

> **Example 3**
>
> **Preparation of (the compound) of formula (I) in its Modification II**
>
> 0.5 g of the compound according to the formula (I) as mono DMSO solvate was tempered for 2 days at 80°C.

[86] There is no indication in this example or elsewhere in the description of any difficulties or that significant effort or prolonged experimentation was required. Our preliminary view was that, from the skilled person's perspective, this would not be regarded this as a situation where significant experimentation or undue burden was required to arrive at a polymorph (PR, page 23).

MOTIVATION

[87] The Applicant submitted in the R-FA that there is no suggestion in D1 that Modification II might be prepared via the mono-DMSO solvate of the compound of formula (I) (R-FA, page 2). Our letter agreed with the Applicant that this is true (PR, page 23). However, our preliminary view was that the skilled person would have been motivated nonetheless for three reasons. The first two are already mentioned above.

[88] First, D1 explicitly teaches that for pharmaceutical use there was a general need to remove DMSO from the solvate (page 13, lines 30-31). When read through the lens of the CGK, our preliminary view was that this teaching would have motivated the skilled person to remove DMSO by thermal desolvation since it is an efficient, economic and straightforward route for removing residual solvent compared to the solvent-mediated process that is taught in D1, Example 7 (PR, pages 21, 23): see Guillory page 199; Caira page 178.

[89] Second, as already mentioned above, the skilled person seeking to follow the solvent-mediated process of D1, Example 7 would also have been motivated to

thermally desolvate the mono-DMSO solvate in order to determine the temperature of desolvation. This is because, as a starting material in that process, its interconversions to other forms would need to be fully understood (PR, page 23): Morissette et al page 276; Caira pages 165-167; Byrn et al page 949; Hilfiker pages 3, 14.

[90] Third, the skilled person reading D1 would have been motivated to prepare and characterize the thermally desolvated form in order to study and compare its properties as part of the search for the form with optimal performance characteristics for the dosage form (PR page 23): Hilfiker pages 3, 14; Byrn et al pages 947-948; Morissette et al page 276.

[91] For all of these reasons, our preliminary view was that the skilled person reading D1 would have been motivated to remove DMSO from the mono-DMSO solvate by thermal desolvation, which would have produced Modification II (PR, page 24).

[92] Having considered and weighed all of the obvious to try factors, our view is that it would have been more or less self-evident to the skilled person reading D1 through the lens of the CGK to try to obtain Modification II.

Conclusions

[93] The skilled person would have produced the formula (I) compound in Modification II defined in claim 1 on file using well-known methods and would have arrived at the process defined in claim 4 on file without exercising any degree of inventive ingenuity. Our view is that any gaps between the claimed subject-matter and D1 would have been bridged by the CGK.

[94] Likewise, our view is that it would not have required any degree of inventive ingenuity for the skilled person to formulate a pharmaceutical composition of claim 2 or claim 3 comprising Modification II with one or more inert, nontoxic, pharmaceutically suitable excipient, whether or not insignificant fractions of other forms of the formula (I) compound were present.

[95] For all of the reasons set out above, our conclusion is that the subject-matter of claims 1 to 4 on file would have been obvious to the skilled person, contrary to section 28.3 of the *Patent Act*.

RECOMMENDATION OF THE BOARD

[96] In view of the above, we recommend that the application be refused on the ground that claims 1 to 4 do not comply with section 28.3 of the *Patent Act*.

Cara Weir	Marcel Brisebois	Philip Brown
Member	Member	Member

DECISION OF THE COMMISSIONER

[97] I agree with the Board's findings and its recommendation that the application be refused on the ground that claims 1 to 4 do not comply with section 28.3 of the *Patent Act*.

[98] 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 Applicant has six months within which to appeal my decision to the Federal Court of Canada.

Konstantinos Georgaras

Commissioner of Patents
Dated at Gatineau, Quebec
this 22nd day of August, 2025.