Citation: Shionogi & Co, Ltd & ViiV Healthcare Company (Re), 2025 CACP 11
Commissioner's Decision #1692
Décision du commissaire nº 1692
Date: 2025-08-22

TOPICS:	B00	Ambiguity or indefiniteness (incomplete)
	D00	Double-patenting
	O00	Obviousness

SUJETS :	B00	Caractère ambigu ou indéfini (incomplet)
	D00	Double-brevet
	O00	Évidence

Application No. 2955957
Demande n^{o} 2955957

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 2,955,957, 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 2,955,957, which is entitled “SYNTHESIS OF CARBAMOYLPYRIDONE HIV INTEGRASE INHIBITORS AND INTERMEDIATES” and is owned by Shionogi & Co., Ltd and VIIV Healthcare Company. The Patent Appeal 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 2,955,957, has a filing date of December 8, 2009, and has been open to public inspection since June 17, 2010.

[3] The application concerns crystal forms of the sodium salt of Dolutegravir, an anti-HIV agent that inhibits HIV integrase.

Prosecution history

[4] This application was rejected in a Final Action issued on June 9, 2020 pursuant to subsection 86(7) of the *Patent Rules* on the basis that claims 1 to 13 are obvious and non-compliant with section 28.3 of the *Patent Act* (RSC 1985, c P-4) and claim 8 is indefinite and non-compliant with subsection 27(4) of the *Patent Act*. The Applicant provided arguments in favour of the patentability of 1 to 13 along with an amendment to claim 8 to address the indefiniteness defect in their response to the Final Action dated December 7, 2020. The Examiner acknowledged that the amendment would address indefiniteness in his Summary of Reasons, but maintained the rejection based on obviousness and so the application was forwarded to the Patent Appeal Board (the 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 letter) dated May 30, 2024.

[6] Pursuant to subsection 86(9) of the *Patent Rules*, our PR letter notified the Applicant of two further defects, namely that the subject-matter of claims 1 to 6 and 13 was anticipated and that the subject-matter of claims 1 to 13 is not patentably distinct from the subject-matter of claims 123, 124, 315 and 316 of the Applicant's Canadian Patent 2,606,282 (the '282 Patent). Our letter provided a preliminary analysis of those issues and invited the Applicant to make further oral and written submissions and to attend a hearing on July 23, 2024, which was postponed to September 5, 2024 at the Applicant's request.

[7] The Applicant provided a response to our letter (R-PR letter) dated August 21, 2024 addressing our preliminary views that included a new set of proposed claims that would cancel claims 7 to 12 on file and arguments in favour of the patentability of the remaining claims. At the hearing, we reminded the Applicant that the amendment could not be entered at that time because, pursuant to section 86(11) of the *Patent Rules*, amendments can only made at the end of the review process on the direction of the Commissioner of Patents. Following a brief discussion at the hearing, it was agreed that the arguments would be considered as applying to claims 7-12 on file as well, where applicable.

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

THE ISSUES ARE INDEFINITENESS, OBVIOUSNESS AND DOUBLE-PATENTING

[9] This review considers whether the subject-matter of claim 8 on file is indefinite, whether the subject-matter of claims 1 to 13 on file is obvious contrary to section 28.3 of the *Patent Act* and whether the subject-matter of claims 1 to 13 is not patentably distinct from the subject-matter of claims 123, 124, 315 and 316 of the Applicant's Canadian Patent 2,606,282 (the '282 Patent).

[10] As stated above, we originally notified the Applicant of the additional issue of anticipation in our PR letter. However, we informed the Applicant before the hearing that, on further consideration, we were satisfied that the anticipation defect should not have been added. We have therefore limited our analysis below to the two issues addressed in the Final Action and the issue of double-patenting.

PURPOSIVE CONSTRUCTION

Legal principles

[11] 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.

[12] 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.

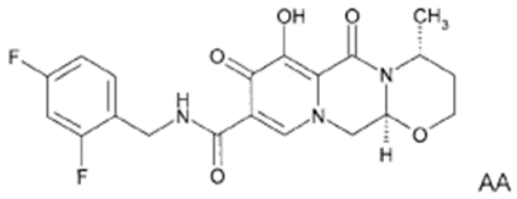
Analysis

Claims 1 to 13 on file

[13] The claims set comprises seven independent claims: claims 1, 4, 6, 7, 10, 12 and 13. Claims 1 to 6 and 8 are directed to a crystal form of a sodium salt of Dolutegravir. The Dolutegravir molecule is depicted as the non-salt or “parent”

molecule (i.e., without the sodium atom) and is labelled “AA”. Independent claims 1 and 6 are illustrative:

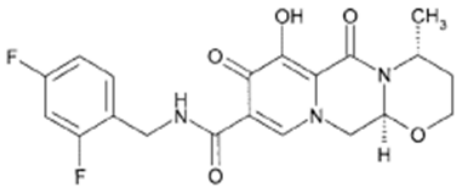
1. A crystal form of a sodium salt of a compound of formula AA



AA

having characteristic diffraction peaks at 6.4° ± 0.2°, 9.2° ± 0.2°, 13.8° ± 0.2°, 19.2° ± 0.2° and 21.8° ± 0.2° degrees two-theta in an X-ray powder diffraction pattern.

6. A crystal form of a sodium salt of a compound of formula AA



AA

having one or more spectra selected from the group consisting of (a) to (c):

(a) X-ray powder diffraction pattern substantially as shown in Figure 1;

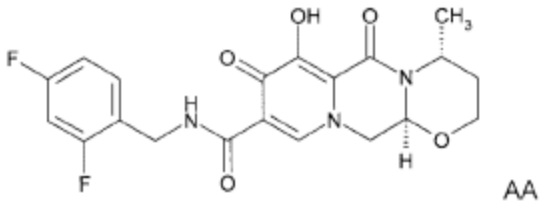
(b) Infrared absorption spectra substantially as shown in Figure 2; and

(c) Solid state ^{13}C-NMR spectra substantially as shown in Figure 3.

[14] Independent claim 4 is similar to claim 1 but defines a crystal form using infrared (IR) data instead of X-ray diffraction (XRD) data. Dependent claims 3 and 5 (which depend on claims 1 and 3, respectively) define further IR data and

dependent claims 2 and 8 (which depend on claims 1 and 6, respectively) define further XRD data.

[15] Claims 7 and 9 to 12 are directed to a crystal form of a hydrate of a Dolutegravir sodium salt. Independent claim 12 is illustrative:

> 12. A crystal form of a hydrate of a sodium salt of a compound of formula AA
>
> 
>
>
> AA
>
> having one or more spectra selected from the group consisting of (d) and (e):
>
> (d) X-ray powder diffraction pattern substantially as shown in Figure 4; and
>
> (e) Infrared absorption spectra substantially as shown in Figure 5.

[16] Independent claims 7 and 10 are similar to claim 12 but the crystal hydrate is defined using XRD (claim 7) and IR (claim 10) data instead of referring to Figures 4 and 5 from the drawings section of the application and dependent claims 9 and 11 (which depend on claims 7 and 10, respectively) define additional IR data.

[17] We note here, for the sake of clarity, that the Applicant confirmed at the hearing that claim 8 on file contains an error as it was meant to depend on claim 7, not claim 6, and the XRD data in claim 8 defines the crystal hydrate form of claim 7.

[18] Independent claim 13 on file is directed to a pharmaceutical composition comprising a crystal form as defined in any one of the claims 1 to 12 and a pharmaceutical excipient.

The person skilled in the art

[19] Our preliminary view was that the characterization set out in the Final Action was reasonable (PR letter, page 6):

> The Final Action characterizes the skilled person as a person or team of persons having varying expertise that would at least include an organic chemist in the field of pharmaceutical drug development with experience with, or knowledge of, polymorphs and their use in medicine (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. Subject to any further comment from the Applicants, we intend to adopt this characterization for the purposes of our review.

[20] In response, the Applicant did not disagree with this characterization in that the skilled person is a chemist that understands organic chemistry and the development of polymorphs (R-PR, page 7). However, the Applicant emphasized that such a skilled person would understand the unpredictability of the characteristics of crystals. On pages 7-8, the R-PR further argued that since the skilled person has no scintilla of inventiveness or imagination a clear teaching must be provided, citing *Beloit Canada Ltd v Valmet Oy* (1986), 8 CPR (3d) 289 (FCA): (emphasis in the original)

> The POSITA is devoid of any intuition, thus the reflexes and the decision making of the POSITA cannot be compared to any real chemist person. Clear teachings must be provided to the POSITA for that person to arrive at a certain invention ***without difficulty***.

[21] We agree with the Applicant that the skilled person has no scintilla of inventiveness or imagination and is devoid of any intuition. We further agree that the skilled person would have understood that the characteristics of a crystal cannot be predicted in advance of its making, as is discussed further in the next section.

The common general knowledge

[22] The Final Action cited two documents on pages 1-2 as supporting the CGK and described them as follows: (emphasis in the original)

D2: Byrn et al., “Pharmaceutical Solids: A Strategic Approach to Regulatory Considerations” (1995) 12:7 Pharma Res at pages 945-954

> (Byrn et al.) is a review article that teaches that is has been at least advisable since 1995 to screen drug substances for polymorphs and solvates in the early stages of drug development. Screening is generally carried out using standard crystallisation techniques to crystallise the drug substance from solution from a number of different solvents of various polarities. It is recommended to attempt crystallising from solvents used in the final steps of the synthesis, formulation and processing, and the following solvents are also indicated: water, methanol, ethanol, propanol, isopropanol, acetone, acetonitrile, ethyl acetate, hexane and mixtures thereof, if appropriate. Standard crystallisation techniques such as agitation, varying the crystallization temperature, cooling hot solution and partial evaporation of clear saturated solutions are all indicated (page 946).

D3: Bavin, “Polymorphism in Process Development” (1989) Chemistry & Industry, pages 527-529

> (Bavin) teaches screening for polymorphs by attempting to crystallise substances from a range of different solvents (polar and non-polar, hydrophilic and hydrophobic) using standard crystallisation techniques, such as varying the crystallization temperatures and chilling solutions rapidly (page 528).

[23] The Final Action states that the skilled person would have knowledge of the methods of screening for polymorphs by preparing new forms using standard crystallisation techniques as set out in Byrn et al. and Bavin, for example.

[24] In their response to the Final Action, the Applicant did not dispute that the above information was part of the CGK but clarified that, at best, Byrn et al. and Bavin suggest crystallizing generally, without providing specific guidance on which conditions, techniques, reagents etc. to employ. Our PR letter agreed that the teachings relate to screening small molecules in general and do not discuss Dolutegravir sodium specifically (PR, page 8).

[25] The first point of dispute was in relation to the following statement from page 3 of the Final Action:

> This skilled person would expect that any solid form of a molecule with an established pharmacological activity would also have that same activity to some degree, since pharmacological activity is an effect of the molecule, and the molecules are chemically identical.

[26] On page 2, the Applicant's response to the Final Action disputed this statement and pointed to a lack of any references supporting this assertion:

> Unfortunately, the assertion is unclear and not scientifically supported:
>
> i) it is not clear what "any solid form" refers to in the Office Action. The claims are directed to crystal forms of a sodium salt (or hydrate) of (Dolutegravir) well defined with specific XRD, IR and/or solid state ^{13}C-NMR profiles, as well as compositions comprising same.
>
> ii) Although this section of the Office Action apparently intends to identify the common general knowledge possessed by the person skilled in the art, no citation was made to any common general knowledge document to support this position, which rather appears to be a personal opinion of the Examiner. Certainly, Applicants do not acknowledge that the assertion under (1) above is common general knowledge. Also, the description of the alleged content of cited art documents D1 to D3 in the Office Action does not support the assertion.

[27] In order to ascertain further relevant information forming part of the CGK in relation to this and other points in dispute, we referred to information in the following handbook, review article and journal articles in our PR letter:

Hilfiker, R, ed, *Polymorphism in the Pharmaceutical Industry* (Weinheim, Germany: WILEY-VCH Verlag GmbH & Co KGaA, 2006), see Chapters 1, 2, 8, 11, 12 and 15 at pages 1, 2, 9-12, 14, 34, 212-213, 216, 219, 222, 287, 289, 292-294, 299, 309 and 390-392

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

Mirmehrabi et al. “An approach to solvent screening for crystallization of polymorphic pharmaceuticals and fine chemicals”, (2005) 94:7 J Pharm Sci at 1560-1576

Gu, C-H et al., “Grouping solvents by statistical analysis of solvent property parameters: implications to polymorph screening”, (2004) 283:1-2 Intl J Pharm at 117-125

[28] The R-PR did not dispute our citation of these references as further evidence supporting the CGK in the field of pharmaceutical drug development and the use of polymorphs in medicines.

[29] We further considered the following International and National guidelines concerning polymorphs in medicines:

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

The *Patented Medicines (Notice of Compliance) Regulations*, SOR/2006-242 [the *PM(NOC) Regulations*]

[30] Subsection 2(1) of the *PM(NOC) Regulations* provides the following definitions relating to the types of granted patents that may be added to a patent list associated with a new drug submission or supplement thereto: (emphasis added)

> ***claim for the medicinal ingredient*** includes a claim in the patent for **the medicinal ingredient**, whether chemical or biological in nature, when prepared or produced by the methods or processes of manufacture particularly described and claimed in the patent, or by their obvious chemical equivalents, **and also includes a claim for different polymorphs of the medicinal ingredient, but does not include different chemical forms of the medicinal ingredient**

[31] With regard to the meaning of "medicinal ingredient" the Regulatory Impact Analysis Statement of SOR/2006-242, Canada Gazette, Part II, vol. 140, no. 21 – 18 October 2006 says the following at pages 1516-1517: (emphasis added)

> For the purposes of amended section 4, the terms "formulation" and "medicinal ingredient" are intended to bear their established meaning under the extensive body of case law interpreting a "claim for the medicine itself"…The term "medicinal ingredient", in turn, **refers to the substance in the formulation which, once administered, is responsible for the drug's desired effect in the body**. […]
>
> […] It also serves to clarify, in so far as small molecule drugs are concerned, that patents claiming **different crystalline, amorphous, hydrated and solvated forms of the approved medicinal ingredient (i.e. "polymorphs")** are eligible for listing when submitted in relation to the NDS, but that different chemical forms, such as salts and esters, are not. This accords with Health Canada policy on what constitutes an "identical medicinal ingredient" for the purposes of establishing pharmaceutical equivalence under section C08.001.1 of the *Food and Drug Regulations*.

[32] We said the following in our letter about how the activity of molecules and their polymorphs is regarded in the *PM(NOC) Regulations* (PR, pages 10-11):

> According to these passages, once they are administered small molecule medicinal ingredients and their polymorphs (which includes hydrated forms) are regarded as identical and equally responsible for the drug's desired effect in the body. In our preliminary view, the skilled person in the field of drug development with experience or knowledge of the use of polymorphs in medicine would know this and would be familiar with the guidelines and regulations relating to medicinal ingredients and their polymorphs.
>
> Since this information is consistent with the disputed statement in the Final Action, our preliminary view is that it was common general knowledge that any solid form of a molecule with an established pharmacological activity would be expected to have that same activity to some degree since activity is an effect of the molecule and the molecules are identical.

[33] In response, the Applicant disputed our reference to the *PM(NOC) Regulations* in ascertaining the CGK, saying the following (R-PR, page 9):

> The PMNOC regulation concerns patents that have been granted and that are or aim to be listed on the patent list. The laws that govern the PMNOC are completely irrelevant to the question of patentability of a pending patent application. The same goes for the regulations that permit a drug to be accepted for human use by Health Canada.

[34] To be clear, we did not apply any laws under the *PM(NOC) Regulations* or other Health Canada regulations as part of the preliminary analysis. Rather, we sought to clarify how a polymorph of a given therapeutic molecule would be regarded in relation to the molecule itself by the skilled person in this field. In any event, this reference is no longer needed since the Applicant clarified this point in response (R-PR, page 9): (emphasis added)

> The Applicant does not disagree that most crystal forms will have the same activity simply because **they are the same molecule which will have the same mechanism of action**. However, the Applicant does disagree in the similarities of pharmacological activity. The pharmacological activity does not only depend on the **method of action (which is shared between**

> **crystal forms since it is the same compound)**, pharmacological activity also relies on bioavailability…In fact, the PAB even contradicted this statement at page 12 of the preliminary review with the following statement:
>
> > "If it does form polymorphs and differences between forms **affect** performance, **bioavailabilty** or stability then the appropriate crystal form should be specified when seeking regulatory approval: ICH pages 8, 24-25; Hilfiker pages 14" (emphasis added).

[35] We agree with this helpful clarification and modify our previous statement as follows: any solid form of a molecule with an established therapeutic activity would be expected to have that same activity to some degree since therapeutic activity is an effect of the molecule and the molecules are identical and will have the same mechanism of action. However, the skilled person would not expect the pharmacological activity will be the same because this does not depend on therapeutic activity alone, it also depends on bioavailability. Since bioavailability is a performance characteristic that cannot be predicted, the skilled person would not know if the bioavailability and pharmacological activity of a polymorph is the same, better or worse than another solid form of the same molecule until it is tested: ICH pages 8, 24-25; Hilfiker page 14.

[36] We expressed our preliminary view that the following information would also have been CGK (PR, pages 11-13):

- Polymorphism is very common in drug substances which are mostly (about 90%) small organic molecules (i.e., less than 600 g/mol) and 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
- Each solid-state form of a drug substance has unique physicochemical properties that can influence bioavailability, manufacturability, stability and other performance characteristics of the drug: Morissette page 276; ICH pages 8-9

- Most drug substances are weak electrolytes capable of forming salts and, like the drug substance itself, salts may exist in several polymorphic and hydrate forms as well: Hilfiker pages 2, 309; Morissette page 276
- As salts generally have higher water solubility than their corresponding non-salt or parent molecule and higher bioavailability (since solubility affects in vivo dissolution and hence bioavailability), about half of all active molecules on the market are salts: Hilfiker page 2; Morissette page 276
- Solvate is the term describing a form where a compound crystallizes and packs “together” with a solvent, forming a solid phase where the solvent molecule is part of the crystal structure: Hilfiker page 212
- Water is the smallest solvate molecule and has an extraordinary ability to form hydrogen bonds, making hydrates unrivaled as the most common solvate with their own subclass: Hilfiker pages 212-213, 216, 219
- In the pharmaceutical industry, polymorphs and hydrates are the most common solid forms used in finished drug products: Hilfiker page 287
- By 1999, international guidelines were established recommending that polymorph screening be conducted for pharmaceutical candidate molecules (i.e., medicinal ingredients) ahead of seeking regulatory approval; by 2001 these guidelines were adopted and implemented by the regulatory authorities in the United States, Europe and Japan: www.ICH.org, ICH pages 8-9, 24-25; Hilfiker pages 390-392
- The first fundamental question is whether the molecule even has polymorphic forms and so step 1 in the ICH Q6A decision tree #4 is “Conduct polymorphism screen on drug substance”: ICH page 24; Hilfiker page 390
- If it does form polymorphs and differences between forms affect performance, bioavailability or stability, then the appropriate crystal form should be specified when seeking regulatory approval: ICH pages 8, 24-25; Hilfiker pages 14
- Crystallization, packing arrangements and form diversity remain unpredictable, by ab initio calculations for example, and so screening methods are employed for solid form discovery: Morissette pages 276-277
- Most pharmaceutically active compounds and their salts are purified and isolated by crystallization from an appropriate solvent during the final step in the synthetic process, and the same classical approach to crystallization is used in polymorph

crystallization screening (but with more variables): Morissette page 276; Hilfiker page 34

- Systematic screening for polymorphs generally involves recrystallizing the drug substance using fast and slow methods, a variety of solvents or solvent mixtures and different experimental conditions (such as cooling, evaporation, altering pH and slurrying): Hilfiker pages 34, 289, 292; Morissette page 276; Bavin page 528; Byrn page 946
- Screening is generally performed early in clinical development to, at a minimum, identify the thermodynamically stable polymorph and important hydrates with a large probability by: i) using solvents with a wide range of polarities and hydrogen-bonding potentials; ii) favouring slow crystallization experiments over fast ones; and iii) using gentle drying procedures to prevent desolvating hydrates: Hilfiker pages 9, 11, 222, 293, Figure 1.3
- High-throughput polymorph screening systems have been developed to automate and miniaturize crystallization experiments that are run in parallel with less drug, allowing thousands of experiments with a maximal number of variables to be run in a short time: Morissette page 278; Hilfiker pages 222, 294
- Hydrates are generally prepared by either dynamic vapour sorption or by crystallizing from water and water-solvent mixtures and it is extremely advisable to use slow crystallization methods such as suspension equilibration: Hilfiker page 293, Table 11.2; Byrn page 949
- Ethanol and THF are among the well known solvents useful for polymorph screening and water/THF is among known mixtures for preparing hydrates: Byrn page 946; Hilfiker Table 11.2; Mirmehrabi pages 1565-1566, 1569; Gu pages 119-120, 122-123

[37] The Applicant did not dispute any of these points in response, but clarified that Bavin and Byrn et al. (i.e., D2 and D3) should be viewed as providing recommendations on potential routes because it is never guaranteed that a crystal form can be obtained (R-PR, page 8):

> Although D2 and D3 generally describe crystallization procedures these references do not pretend to be able to predict whether a crystal form would be obtainable. In fact, the purposes of these references are to help the skilled person reduce the percentage of failed attempts of making a crystal

> form. Thus, it is clearly part of the common general knowledge that it is never guaranteed that a crystal form can be obtained as evidenced by D2-D3. […]
>
> The common general knowledge includes the general principles of obtaining polymorphs, however, it cannot be considered common general knowledge to predict that any specific protocol would necessarily result in a particular crystal and it is even more far-fetched to consider that the common general knowledge includes prediction of crystal properties such as X-ray diffraction peaks or infrared peaks. It should be noted that, at page 12, the reference cited by the PAB clearly acknowledges the complexity of crystal formation and whether a crystal can even be formed: "The first fundamental question is whether the molecule even has polymorphic forms and so step 1 in the ICH Q6A decision tree #4 is "Conduct polymorphism screen on drug substance": ICH page 24; Hilfiker page 390".

[38] We have already acknowledged that crystallization, molecular packing arrangements (which give rise to the unique performance characteristics and X-ray diffraction and infrared peaks) and form diversity are unpredictable by ab initio calculations (for example), and that this is why screening methods are employed for solid form discovery: Morissette pages 276-277.

[39] However, we do not agree that the ICH reference acknowledges the "complexity of crystal formation". In our view, this overstates what is said in that reference. The ICH decision tree is not referring to the complexities of crystallization. Rather, it is referring to screening a small molecule for polymorphs to ascertain if it exists in one or more **further** solid state forms (hence the prefix "poly" in polymorph).

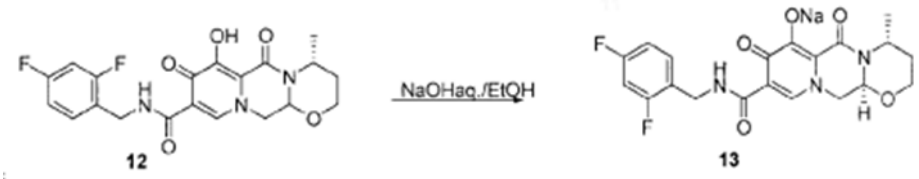
[40] Hilfiker supports the Applicant's position that polymorphism is not guaranteed, reporting that there are a few examples of substances that have been crystallized countless times and for which no polymorphs have been found so far, such as naphthalene, sucrose and aspirin: Hilfiker, page 288. However, even though it is not guaranteed, it was well known that polymorphism is very common in this field. As stated above, the probability of existing 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.

[41] That said, it is important to note that screens are not all the same. Early, less thorough (or basic) screens that focus primarily on processing solvents in order to identify the thermodynamically stable form and hydrates may not even look for solvates: Hilfiker pages 11, 292. Thus, when it comes to obtaining polymorphs, the skilled person would know that the degree of complexity will vary.

[42] With regard to crystal formation, like polymorphism it is not guaranteed but it is not uncommon either. In some cases a molecule may crystallize readily, whereas others described as “difficult-to-crystallize” are more problematic: Hilfiker page 259. Hilfiker explains that it can generally be assumed that two main factors cause crystallization difficulties: i) the presence of trapped impurities that inhibit crystal nucleation; and ii) conformational diversity where larger molecules such as polysaccharides or synthetic polymers are capable of many different conformations in solution (relative to small molecules), leading to an overall amorphous character: Hilfiker page 279. However, as stated above, about 90% of drug substances are small molecules under 600 g/mol and polymorphism is common in this group: Hilfiker, page 1. Thus, when it comes to obtaining crystal forms, the skilled person would know that the level of difficulty will vary.

Meaning of terms

[43] Our letter expressed the preliminary view that, although it is not expressly stated in the claims, the skilled person would understand that claims 1 to 6 on file are all directed to the same crystal form of Dolutegravir sodium (labelled below as compound 13) and claims 7 to 12 are all directed to a second crystal form that is a hydrate (PR, page 13):

> On page 17, the description discloses a process for preparing compound 13, which is the Dolutegravir sodium salt (depicted with the sodium "Na" at position 5 on the anthracene ring) as follows:
>
> 
>
>
> Compound 12 is the non-salt or "parent" molecule Dolutegravir that is depicted in the claims and labelled as AA.
>
> Example 1l (which is identical to Example 3l) provides the steps for preparing compound 13 which is produced directly in crystal form without the need for recrystallization. Figures 1-3 in the drawings section contain the XRD, IR and solid state ^{13}C-NMR profiles of that crystal form labelled as compound 13. In our view, the skilled person would recognize that the specific data that is recited in each of claims 1-5 corresponds to the peaks depicted in Figures 1-3. Claim 6 refers to Figures 1-3 directly. The skilled person would know that this data profile is unique and serves to characterize and define the 3D solid-state structure of the crystal form such that it can be distinguished from other forms of the same molecule. Consequently, our preliminary view is that the skilled person would understand that claims 1-6 are all directed to the same subject-matter (i.e., the specific crystal form of compound 13 that is produced in Examples 1l and 3l) defined in different ways.

[44] Our PR letter similarly reasoned that the skilled person would understand that claims 7 and 9 to 12 are all directed to the same crystal form labelled "13b" produced in Example 1m, which is identified as a hydrate form of compound 13. Figures 4 and 5 in the drawings section contain the XRD and IR profiles of that crystal hydrate form 13b. The specific data recited in each of claims 7 and 9 to 11 corresponds to the data from Figures 4 and 5, and claim 12 refers to Figures 4 and 5 directly (PR, page 14).

[45] In response, the Applicant agreed and confirmed that claims 1 to 6 are directed to the crystal form 13 which was characterized in Figures 1-3 (R-PR, page 9). The same acknowledgement was not made for claim 8 or for claims 7 and 9 to 12 on file (crystal hydrate form 13b) since the Applicant attempted to cancel these claims without prejudice.

[46] Our letter also indicated that the XRD data in dependent claim 8 also corresponds to Figure 4 and crystal form 13b even though it is dependent on claim 6, which defines the crystal form of Figures 1-3 and compound 13. On that basis, our preliminary view was that the skilled person reading the whole application would recognize that claim 8 defines features of the crystal hydrate 13b that is the subject-matter of claims 7 and 9 to 12 on file, not the crystal form of claims 1 to 6. Notably, this contradiction in is addressed further below under indefiniteness.

[47] The Applicant clarified at the hearing that they agree that claim 8 on file defines the features of crystal hydrate 13b and should depend on claim 7.

[48] For the reasons set out above, we conclude that the skilled person would understand claims 1 to 6 on file as encompassing one crystal form of Dolutegravir sodium and claims 7 to 12 as encompassing a second crystal form of Dolutegravir sodium that is a hydrate. For sake of ease, claim 8 will be considered as part of the grouping of claims 7 to 12 in the sections that follow.

Essential elements

[49] 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. We expressed the view in our letter that the skilled person reading the claims on file 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 as being non-essential. On that basis, we expressed our preliminary view that all of the elements of claims 1 to 13 are essential.

[50] The Applicant agreed on page 10 of the R-PR and so we adopt this characterization for the purposes of our analysis.

CLAIM 8 IS INDEFINITE

[51] Our view is that the subject-matter of claim 8 is indefinite.

Legal principles

[52] Subsection 27(4) of the *Patent Act* requires claims to distinctly and explicitly define subject matter:

> The specification must end with a claim or claims defining distinctly and in explicit terms the subject-matter of the invention for which an exclusive privilege or property is claimed.

Analysis

[53] Claim 8 is a dependent claim that refers to independent claim 6 and the crystal form that it defines:

> 8. The crystal form according to claim 6 having characteristic diffraction peaks at 8.0° ± 0.2°, 9.3° ± 0.2°, 11.3° ± 0.2°, 15.4° ± 0.2°, 16.0° ± 0.2°,

> 18.7° ± 0.2°, 19.1° ± 0.2°, 19.8° ± 0.2°, 22.8° ± 0.2° and 26.8° ± 0.2° degrees two-theta in an X-ray powder diffraction pattern.

[54] It is undisputed that the skilled person reading claim 8 in the context of the whole application, including the specification and drawings, would recognize that the recited XRD data are characteristic of the crystal form that is defined in claim 7 and Figure 4, not claim 6. Our PR letter agreed with the Final Action that claim 8 is indefinite on that basis and lacks clarity with regard to which crystal form it seeks to monopolize (PR, page 16).

[55] As mentioned above, the Applicant confirmed at the hearing that they agree claim 8 on file is indefinite and that, given the opportunity, they would prefer to amend claim 8 to make it dependent from claim 7 instead of claim 6 in the same manner they proposed originally in response to the Final Action. We agree that this is reasonable and conclude that claim 8 on file is indefinite in its present form and does not comply with subsection 27(4) of the *Patent Act*.

CLAIMS 1 TO 13 ON FILE ARE NOT OBVIOUS

[56] Our view is that claims 1 to 13 on file are not directed to subject-matter that would have been obvious to the skilled person in view of document D1 in view of the CGK.

Legal principles

[57] 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;

[58] 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?

[59] 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.

[60] 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).

[61] 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.

[62] 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].

[63] 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.

[64] These are the legal principles presented on pages 20-22 in our PR letter. In response, the R-PR letter agreed with the case law cited and had no specific comments on the “Legal principles” section of our letter.

Analysis

(1) Identify the notional person skilled in the art and the relevant common general knowledge

[65] 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

[66] The Final Action says the following in relation to the inventive concept of the claims on file (page 3):

> Based on the teachings of the specification as a whole, the inventive concept of the claims on file relates to two crystalline forms of (Dolutegravir), namely a crystal form of a sodium salt and a crystal form of a

> hydrate of the sodium salt, a pharmaceutical composition comprising said crystal forms and a process for their production.

[67] On page 2 of their response to the Final Action, the Applicant agreed that the claims relate to crystal forms of Dolutegravir sodium and a pharmaceutical composition, but disputed including a process for their production since there are no claims directed to the production of the claimed crystal forms. The Applicant also stated that "for greater clarity, Applicants remind that the claimed crystal forms are well defined with specific XRD, IR and/or solid state ^{13}C-NMR profiles".

[68] Our PR letter agreed that the characteristic profile data are essential elements of the respective claims and thus form part of the inventive concepts of those claims. We further agreed that there is no claim directed to the production of the claimed crystal forms and saw no reason to include this as part of the inventive concepts for any of the claims on file (PR, page 23).

[69] In response, the Applicant confirmed that the profile data defining the crystal forms is part of the invention, but disputed our formal inclusion of this data as part of the inventive concept (R-PR, pages 10-11): (emphasis in the original)

> The Applicant confirms that the data recited in the claims is part of the invention as those data define the characteristics of the crystal form of the present invention […]
>
> As set out in step 2 of the obviousness test analysis in (*Pfizer Canada Inc v Teva Canada Limited*, 2017 FC 777, [*Teva 2017]*), the inventive concept is the crystal form in and of itself. The crystal form is defined by the claimed characteristics.
>
> > [210] Both of Claims 8 and 9 cover Form I ODV (mono) succinate monohydrate, that is, the crystalline form of ODV succinate. Claims 8 and 9 specifically claim a new and distinct composition of matter. Claim 8 says this crystal form exhibits a fingerprint, namely characteristic XRPD as set out in Figure 1, while Claim 9 identifies another fingerprint namely that the polymorph crystal exhibits a

> characteristic endotherm (melting point) at about 131°C. In my view, these identification of characterization data, which are inherent to the form of the novel crystal at issue, are not the invention; these properties are not the inventive concept, nor are they solution taught by the 688 Patent.
>
> [211] In my respectful view, the solution taught by these two claims, **their inventive concept, is the novel crystalline form of ODV succinate referred to as Form I**. In short, the inventive concept or the solution taught by the 688 Patent is the novel crystal Form I ODV succinate. (Teva 2017, at paragraphs [210]-[211], emphasis added)

> […] The Applicant thus submits that **the inventive concept is the crystal form** in and of itself which is defined by the claimed characteristics.

[70] We agree that the Applicant's preferred approach is reasonable since, based on the specification as a whole, there is no indication that the characterization data per se is the invention, inventive concept or the solution taught by the patent. This is consistent with the what is said in *Shire* at para 84, above, when it comes to inherent properties that are not claimed. In the case of a bare chemical formula claim, not all the chemical's properties will inform its inventive concept: *Shire* para 76, citing *Bristol-Myers* at para. 74; *Teva Canada Limited v Pfizer Canada Inc*, 2019 FCA 15 at para 34 [*Teva 2019*].

[71] In our view, when it comes to a claim to a new three dimensional packing arrangement of a molecule in crystal form, it may be necessary to look to the specification to determine what, if anything, makes the claim as construed inventive since, like a bare chemical formula, this may not be clear from the bare packing arrangement alone.

[72] We note that our PR letter also considered whether or not the description disclosed any other properties that should have been included in the inventive concept based on this same guidance from *Shire*, since this was addressed in the Final Action. For reasons expressed on pages 23-25 of our PR letter, our preliminary view was that the disclosure was not sufficient to justify including the

properties in question in the inventive concepts of the claimed crystal forms. The Applicant did not dispute this, submitting in response that the inventive concepts are the crystal forms in and of themselves, which are defined by the claimed characteristics (R-PR, page 11). At the hearing, the Applicant confirmed when asked that the inventive concept is the three dimensional structure of each of the two crystal forms claimed and would not further include “pharmacological activity or benefits or anything else”.

[73] The Applicant also made the following statements in response to our preliminary analysis (R-PR, pages 10-11):

> The entire analysis presented by the PAB relies on whether an expected advantage was demonstrated by compound 13 […]
>
> The Applicant respectfully submits that an “unexpected advantage” is not the only marker for inventiveness […]
>
> The position of the PAB is against the leading case law in Canada regarding crystal forms of compounds. The PAB is taking the approach of a “selection patent” by requiring that the inventive concept have an unexpected advantage over the prior genus.

[74] We agree with the Applicant that it would be improper to require an unexpected advantage. The only requirement in the obviousness analysis is inventiveness. We also agree with the Applicant that an unexpected advantage is not the only marker for inventiveness. However, it would also be improper to overlook a beneficial property or other advantage that is expressly disclosed in the specification in relation to what makes the claim inventive: *Shire* at para 76. Reading a patent narrowly may exclude a special property that belongs in the inventive concept of a bare compound claim and is critical to determining inventiveness: see *Apotex Inc v Allergan Inc*, 2012 FCA 308 at paras 72-75, 93. It was in that sense that we considered whether other properties belonged in the inventive concept since, as noted above, this prospect was squarely raised in the Final Action.

[75] We further note that, if properties relating to drug product quality and performance are disclosed, this would be appropriate to consider since there is a clear emphasis on those properties in this field (Hilfiker, page 392, discussing the ICH guidelines and decision tree #4, as cited in the PR, page 32):

> The first decision is whether the identified polymorphic forms have different properties. The parenthetical insert in this decision point serves to focus attention on properties that are directly relevant to drug product quality or performance (e.g., solubility and stability). Because there will always be some difference in properties, it seems appropriate to focus on the properties that would significantly affect the use of the polymorphic forms in the intended dosage form.

[76] We accept the Applicant's submissions and conclude that the inventive concept of claims 1 to 6 on file is the crystal form of compound 13, which is defined by the claimed characteristics. Likewise, the inventive concept of claims 7 to 12 on file is the crystal hydrate form 13b, which is defined by the claimed characteristics. Finally, the inventive concept of claim 13 on file is a pharmaceutical composition comprising the crystal form of claims 1 to 6 or 7 to 12 on file.

(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

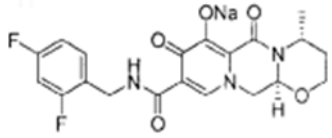
[77] The Final Action identifies document D1, which is a disclosure by the Applicant, as being relevant to obviousness:

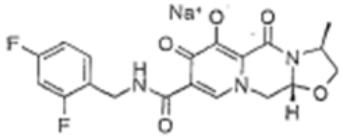
D1: WO 2006/116764 A1 (2 November 2006), Johns et al.

[78] D1 is an international patent application disclosing a group of polycyclic carbamoylpyridone HIV integrase inhibitors ("anti-HIV compounds" herein) that includes Dolutegravir (i.e., compound 12 in the present application), its sodium salt and solvates thereof. The Dolutegravir molecule is explicitly disclosed on page 26 and is prepared in Example Y-3. The Dolutegravir sodium salt, a solvate

thereof and pharmaceutical compositions comprising Dolutegravir sodium or a solvate thereof are each identified in the description and claimed in the claim set (see page 27 and claims 32-35). On page 55, D1 specifically defines solvates of the invention as including hydrates.

[79] Importantly, an example preparing Dolutegravir sodium from Dolutegravir is not disclosed. However, there are 5 examples provided in D1 for preparing salts of structurally similar anti-HIV compounds and all five are sodium salts that are





prepared according to the same procedure (see Examples Z-1, Z-4, Z-8, Z-9 and Z-38 on pages 130, 138, 142, 143 and 184, respectively). The closest compound by structure to Dolutegravir sodium is Cabotegravir sodium in Z-9. The Cabotegravir molecule is identical to Dolutegravir except for the terminal 6-membered oxazine ring on Dolutegravir (i.e., the last ring on the right), which is replaced with a corresponding 5-membered ring:

Dolutegravir sodium Cabotegravir sodium

[80] In the five examples, sodium hydroxide is added to a solution of the non-salt/parent compound (e.g., Cabotegravir in Z-9) in ethanol in an equimolar amount (i.e., 1:1 molar ratio) to convert the hydroxy group (O-H) to the sodium salt (ONa or O^-Na^+). Regarding pharmaceutical compositions, the description discloses that these combine the anti-HIV compound with standard formulating agents such as carriers and diluents (see pages 27, 38 and 78).

[81] We note, as we did in our PR letter, that there are no examples or instructions provided preparing a hydrate or any other solvate for Dolutegravir, Dolutegravir sodium or for any of the other structurally related anti-HIV compounds.

[82] The Final Action identifies the crystalline aspect of Dolutegravir sodium as the only difference between D1 and the inventive concept. The Applicant disputes this in the response to the Final Action, stating that D1 does not disclose

producing Dolutegravir sodium salts with the well defined XRD, IR and/or solid state ^{13}C-NMR profiles as claimed.

[83] We agree with the Applicant that the main differences are that D1 does not disclose the specific crystal form or crystal hydrate form of Dolutegravir sodium of the inventive concepts of claims 1 to 6 or 7 to 12, respectively, which are defined by the claimed characteristics, or pharmaceutical compositions comprising them as set out in claim 13.

(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?

[84] The first point of disagreement stemming from the Final Action was whether or not the obvious to try test is appropriate in the present case. Our PR letter expressed the preliminary view that it is appropriate since this is an area of endeavor where advances often rely on trial and error experimentation, and the Applicant agreed in response: R-PR, page 15.

[85] Before we proceed, we will first consider some supplemental data provided with the Applicant's R-PR letter. The Applicant said the following in regard to this data (R-PR, pages 20-21): (emphasis added)

> With regards to the pharmacological advantage of the claimed crystal form, and in order to show that not every crystal form of Dolutegravir are the same, the Applicant submits the following **data demonstrating the superior properties of compound 13 (i.e., the crystal form claimed) compared to compound 12** (another crystal form of Dolutegravir, see Example 1k in the present application). As set out in *JanssenOrtho Inc v Novopharm Ltd* (2006), 57 C.P.R. (4th) 6 (F.C.), with regards to *"Subsequently recognized advantages. The inventors may have perceived only certain advantages, yet later those inventors or others may determine that other, previously unrecognized advantages lay in the alleged invention"*. Accordingly, **the following experiment was performed**…

[86] The R-PR provides experimental results described as showing that the claimed Dolutegravir sodium crystal form of claims 1 to 6 on file has improved absorbability compared to the crystal form of the parent/non-salt form of Dolutegravir from Example 1k. The properties assessed are bioavailability, maximum plasma concentration (C_{max}) and time to maximum plasma concentration (T_{max}).

[87] In our view, the data is not helpful in determining inventiveness of the claimed subject-matter as of the claim date for two reasons.

[88] First, the skilled person would have known that these properties relating to absorbability and bioavailability are linked to solubility: Morissette page 276. As stated above under CGK, the skilled person would have already known that salts of a molecule generally have higher water solubility than the corresponding parent/non-salt version, which is why half of all active molecules on the market are salts: Hilfiker page 2; Morissette page 276. In our view, this evidence would just confirm what was already expected.

[89] Second, with regard to this data showing a “pharmacological advantage” over the Dolutegravir crystal, we point out that quoted excerpt from para 113 of *JanssenOrtho Inc v Novopharm Ltd* went on to say in the next sentence that advantages that are only recognized later are of limited usefulness in considering inventive ingenuity as of the date of invention and that little, if any, weight should be put on this factor. In reviewing that decision,the Federal Court of Appeal considered the state of the jurisprudence and stated that this factor should generally be given no weight: *Novopharm Limited v Janssen-Ortho Inc*, 2007 FCA 217 at para 26 [*Novopharm*]

> 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.

[90] It is not expressly stated as such, but the Applicant's letter implies that the experiment was performed after the claim date in response to our letter, which would qualify the improved absorbability over Dolutegravir as a "subsequently recognized advantage" under *Novopharm*.

[91] For these reasons, we are inclined to give the newly submitted data little to no weight in our assessment. For completeness, we note that *Teva 2017* similarly considered solubility and bioavailability, including C_{max} and t_{max} data for the ODV succinate crystal Form I, among others, but those were not subsequently recognized advantages. Unlike the present situation, those advantages were perceived before the application was filed and disclosed in the description in relation to problems with another known salt and with the on-market prodrug form of ODV. Comparative data was disclosed in the examples section as well.

[92] Turning to the obvious to try factors, our PR letter considered and weighed these factors, expressing our preliminary view that it would have been more or less self-evident to the skilled person to try to obtain the invention in the claims from D1 in view of the CGK (PR, pages 27-35).

[93] With regard to the motivation factor, our letter said the following on page 28:

> The Supreme Court of Canada in *Sanofi* recognized that there is a general motivation in the intensely competitive pharmaceutical field to find and develop new and improved medications: see *AstraZeneca v Mylan* 2017 FC 142 at para 151 [*AstraZeneca*], citing *Sanofi* at para 90. Further, as mentioned above under common general knowledge, when it comes to small molecule drug candidates specifically there was a general motivation in the field to characterize their solid state form and to screen for their polymorphs and hydrates as a regular part of drug development: Hilfiker pages 9, 287, 390; Morisette page 276. This is done in order to identify the thermodynamically stable form and to test for differences between forms that may affect bioavailability, manufacturability and other performance characteristics: Hilfiker pages 14, 390; Morisette page 276.

[94] Since D1 had already disclosed Dolutegravir sodium and solvates thereof as anti-HIV agents, we expressed the preliminary view that the skilled person reading D1 through the lens of their CGK would have been motivated to prepare Dolutegravir sodium, characterize its solid-state form and screen for its polymorphs and hydrates using standard solvents and techniques.

[95] We next considered whether it would have been more or less self-evident to the skilled person that preparing Dolutegravir sodium and screening for polymorphs and hydrates using well-known screening solvents and techniques ought to work.

[96] In reference to the CGK, we considered that this question would be answered in the affirmative, saying the following (PR, pages 32-33):

> As outlined above under common general knowledge, it was well known to the skilled person by the claim date that 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, 287. Also, by the claim date, automated high-throughput systems had been developed allowing for thousands of crystallization experiments with different solvents and conditions to be run in a short time using less drug: Morisette page 278; Hilfiker pages 222, 294. Further, since hydrates are often the thermodynamically stable form at ambient conditions and are commonly used in finished drug products, general protocols had been developed and were well-established for identifying them with large probability: Hilfiker pages 11, 222, 287, 293; Byrn page 949. Of course, the skilled person would understand that “large probability” falls short of a guarantee of success.
>
> The Federal Court said the following in *Janssen 2021* at para 135 with respect to this factor:
>
> > 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.

[97] Turning to the experimentation and effort required, we pointed to the lack of any indication that there was a problem obtaining Dolutegravir sodium in crystal form or that producing the specific crystal forms claimed required experimentation that was prolonged, arduous or unusual in any way (PR, page 34):

> The only evidence that is specific to the claimed crystal forms is found in the examples provided in the Applicants' description. As stated above, 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.
>
> Examples 1l and 3l are identical and each disclose that compound 13 crystallizes directly from solution in ethanol, without needing to be recrystallized, when the sodium salt is formed by adding sodium hydroxide to Dolutegravir in a 1:1 equimolar amount…this is the same procedure that is disclosed for forming sodium salts in all five of the examples provided in D1. After crystallizing from the ethanol, the crystals were filtered, washed with ethanol, dried, and were characterized as having the data profiles set out in Figures 1-3 and claims 1-6 on file.
>
> In our preliminary view, the skilled person reading the examples would recognize that this is not a scenario that required significant experimentation or where there was difficulty in coaxing an amorphous compound to form a crystal. […]
>
> With respect to the crystal hydrate form of claims 7-12, the evidence in Example 1m is that it was produced by recrystallizing Dolutegravir sodium from a mixture of THF and water. Specifically, compound 13 (i.e., the crystal form of claims 1-6 on file and Figures 1-3) was dissolved in a solution of

> THF-water at 30°C, sodium hydroxide was added and the mixture was stirred at room temperature for 2 hours. The crystals were filtered, washed with THF-water, THF and then dried at 85°C. Those crystals were the crystal form 13b that is the subject of claims 7-12 on file with the data profile set out in Figures 4 and 5.
>
> Based on this example, the hydrate was prepared using a well-known polymorph screening solvent mixed with water and techniques that were part of the common general knowledge: Hilfiker Table 11.2; Mirmehrabi pages 1566, 1569; Gu pages 119-120, 123. It was also well known to keep temperatures below 100°C when preparing hydrates to avoid evaporating water and desolvating the crystals: Hilfiker page 222.

[98] The key argument in the R-PR, in our view, was that Dolutegravir and its sodium salt did not stand out from the "multitude of compounds described in D1 and covered by the Markush formulas described" and so there was no particular motivation for the skilled person to screen Dolutegravir sodium from Example Y-3 for its polymorphs: R-PR, page 23. The Applicant further said the following (R-PR, page 16):

> It is true that D1 stated that the compounds described are useful in the treatment of HIV. However, D1 makes no emphasis on Y-3. A skilled person would have no motivation to specifically select Y-3 and when performing a screening the POSITA would have to first select a compound to screen (out of a list of more than 180 compounds)…By stating that "D1 had already disclosed Dolutegravir sodium and solvates thereof as anti-HIV agents", the PAB is exercising impermissible hindsight in selecting Y-3 as an obvious choice for the POSITA to start their screening procedure.

[99] We have reconsidered in view of the Applicant's arguments and agree that D1 makes no emphasis on Dolutegravir sodium specifically. In this view, it is more reasonable and more likely that the skilled person reading D1 would perform further testing to narrow to a smaller group of promising candidates before advancing to screening experiments. For that reason, we agree that the skilled

person would not reasonably be motivated to screen Dolutegravir sodium for its polymorphs and hydrates.

[100] On re-weighing the obvious to try factors, our conclusion is that it would not have been more or less self-evident for the skilled person reading D1 through the lens of the CGK to try to obtain the subject-matter of claims 1 to 13 on file. We therefore conclude that claims 1 to 13 on file comply with section 28.3 of the *Patent Act*.

THE CLAIMS ARE NOT PATENTABLY DISTINCT FROM THE CLAIMS OF THE '282 PATENT

[101] For the following reasons, our view is that claims 1 to 13 on file are not patentably distinct from claims 123, 124, 315 and 316 of the '282 patent.

Legal principles

[102] There are no express provisions in the *Patent Act* dealing with double-patenting. However, the Supreme Court of Canada has indicated that the statutory basis for double-patenting is subsection 36(1) of the *Patent Act* which indicates, in the singular, that "a patent shall be granted for one invention only": *Whirlpool* at para 63. The courts have also considered double-patenting to be a proper basis for the Commissioner of Patents to refuse an application: *Bayer Schering Pharma Aktiengesellschaft v Canada (AG)*, 2010 FCA 275, aff'g 2009 FC 1249.

[103] The double-patenting doctrine is aimed at the problem of evergreening; extending the monopoly that was granted on the first patent by filing a new patent that does not offer a new invention to the public: *Mylan Pharmaceuticals ULC v Eli Lilly Canada Inc*, 2016 FCA 119 at para 26 [*Mylan*].

[104] It has been noted that a further patent can provide additional rights to a patentee beyond an extension of the term of a monopoly, and that the overriding principle is the need for a further patent to exhibit novelty and ingenuity in order to be justified: *Manual of Patent Office Practice* (CIPO) at §18.06.02, citing

GlaxoSmithKline Inc v Apotex Inc, 2003 FCT 687 at paras 87-91. More recently, the Federal Court recognized that double-patenting may lead to a second unfair advantage for drug patents under the *PM(NOC) Regulations* since a patentee with more patents listed on the Register for a given drug will make more work for those seeking a notice of compliance for a generic version of the same drug: *AbbVie Corporation v Jamp Pharma Corporation*, 2023 FC 1520 at para 614.

[105] In *Whirlpool*, the Supreme Court noted that there are two branches to the test for double-patenting. The first is “same-invention” double-patenting, which occurs when the claims of a first and second patent, both of which are owned by the same party, are “identical” or “conterminous” to one another. The second branch of the test for double-patenting concerns “obviousness double-patenting”. This is a more flexible and less literal test than same-invention double-patenting that prohibits the issuance of a second patent unless its claims are “patentably distinct” and “ingenuity” is exhibited in moving from the first patent to the second: *Whirlpool* at paras 66 to 67; *Mylan* at para 36.

[106] Double-patenting is assessed from the perspective of the person skilled in the art, taking into account their CGK and requires a comparison of the claims as properly construed: *Whirlpool* at paras 63, 69. The analysis compares the claims in the subject application to the claims of the issued patent: *Mylan* paras 28 to 29.

Analysis

[107] The above identifications of the notional skilled person and relevant CGK are considered applicable for the purposes of construing the claims of the ‘282 Patent and for assessing double-patenting.

[108] The claims on file are already construed above. As stated, the skilled person would understand that although they use different data (or combinations of data), claims 1 to 6 on file all define the same crystal form of Dolutegravir sodium and claims 7 to 12 all define the same crystal hydrate form of Dolutegravir sodium. With that understanding, our preliminary view was that it was appropriate to

consider claim 1 as representative of claims 1 to 6 on file and claim 7 as representative of claims 7 to 12 on file for the purposes of comparing to the claims of the ‘282 Patent (PR, page 38). This approach was not disputed or commented on by the Applicant in response.

[109] Patent ‘282 is the granted Canadian patent that corresponds to document D1 of record considered above for obviousness. Double-patenting is considered in view of claims 123, 124, 315 and 316 of the ‘282 Patent:

Claim 123, 124, 315 and 316 of the ‘282 Patent	**Claims 1, 7 and 13 on file**
123. A pharmaceutically acceptable salt of a compound which is (Dolutegravir) wherein the pharmaceutically acceptable salt is a sodium salt.	1. A crystal form of a sodium salt of (Dolutegravir) having characteristic diffraction peaks at 6.4° ± 0.2°, 9.2° ± 0.2°, 13.8° ± 0.2°, 19.2° ± 0.2° and 21.8° ± 0.2° degrees two-theta in an X-ray powder diffraction pattern.
124. (when dependent on claim 123) A solvate of a compound or pharmaceutically acceptable salt of a compound as defined in any one of Claims 120 to 123.	7. A crystal form of a hydrate of a sodium salt of (Dolutegravir) having characteristic diffraction peaks at 8.0° ± 0.2°, 9.3° ± 0.2°, 11.3° ± 0.2°, 16.0° ± 0.2° and 22.8° ± 0.2° degrees two-theta in an X-ray powder diffraction pattern.
315. A pharmaceutical composition comprising the sodium salt of the compound according to Claim 123 with a pharmaceutically acceptable diluent or carrier.	13. (when dependent on claim 1) A pharmaceutical composition comprising a crystal form as defined in any one of the claims 1 to 12 and a pharmaceutical excipient.
316. A pharmaceutical composition comprising the solvate of the compound according to Claim 124 with a	13. (when dependent on claim 7) A pharmaceutical composition comprising a crystal form as defined in any one of the

pharmaceutically acceptable diluent or carrier.	claims 1 to 12 and a pharmaceutical excipient.

[110] Our preliminary view was that the skilled person reading claims 123, 124, 315 and 316 in the context of the specification as a whole 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 as being non-essential and all of the elements of those claims were considered essential on that basis (PR, page 39). This view was not disputed or commented on in response and so we proceed with this understanding.

[111] All of these claims are directed to the same molecule, Dolutegravir sodium. Our preliminary view was that the skilled person would understand that claims 1 and 7 on file are for specific crystal forms of the Dolutegravir sodium molecule whereas claims 123 and 124 of the ‘282 Patent more broadly encompass the Dolutegravir sodium molecule without restricting to any particular form and, in the case of claim 124, without restriction to water (hydrate) or any specific solvent packed within the crystal solvate structure (PR, page 39).

[112] Since the claims on file are narrower in scope compared to the corresponding claims of the ‘282 Patent, our preliminary view was that the claims are not identical or conterminous and are therefore appropriately assessed under the second branch for obviousness double-patenting (PR, page 39): *Sanofi* at para 110; *Whirlpool* at para 63-65. In response, the Applicant did not dispute or comment on this.

[113] Our letter expressed the preliminary view that no inventive ingenuity is exhibited in moving from claims 123 and 124 of the ‘282 Patent to the crystal forms in claims 1 and 7 on file, respectively, and similarly that the pharmaceutical composition of claim 13 on file is not patentably distinct from those of claims 315 and 316 in the ‘282 Patent.

[114] We first pointed to the following information from the CGK (PR, page 40):

> (T)he skilled person would have been aware of the need to screen small molecule drug candidates for their polymorphs and hydrates as part of drug development: Hilfiker pages 9-10, 303, 390-392; ICH page 8, 24-25; Morisette page 276; Bavin page 528; Byrn page 946. Further, they would have been aware of the well-established general protocols to, at a minimum, identify the thermodynamically stable form and stable hydrates with a large probability, and to test for differences that may affect performance characteristics: Hilfiker pages 11, 222, 292-293, 390-392 ICH page 8, 24-25. It was also well known that automated high-throughput systems had been developed allowing for thousands of crystallization experiments with different solvents and conditions to be run in a short time using less drug: Morisette page 278; Hilfiker pages 222, 294.

[115] We further stated that there is no indication in the description or examples that there was any difficulty producing Dolutegravir sodium in crystal form, referring to Examples 1l and 3l where it is shown to crystallize directly from solution in the form of claim 1 on file when the sodium salt is prepared from the Dolutegravir parent molecule. We expressed our preliminary view that the examples for producing the crystal forms of claims 1 and 7 on file are appropriately considered in this case (PR, page 40):

> In *Sanofi*, the Supreme Court of Canada considered the actual course of conduct as part of the analysis even though obviousness double patenting involves a comparison of the claims rather than the disclosure: *Sanofi* paras 106 and 113-114.

[116] The Applicant did not dispute or comment on this in response to our letter.

[117] In the same manner as D1 (set out above), the ‘282 Patent discloses preparing Dolutegravir but not Dolutegravir sodium, although five examples are provided that prepare salts of similar compounds and the specific salt is sodium in all five. The closest by structure is Cabotegravir sodium which, as shown above, is nearly identical to Dolutegravir sodium. The examples all use ethanol as the solvent and sodium hydroxide as the reagent, added in an amount of 1:1 molar

equivalents to the parent molecule. On that basis, our preliminary view was that the skilled person seeking to produce the Dolutegravir sodium salt of claim 123 would have produced it from these instructions, and likely in the same crystal form as claim 1 on file. Even if that were not the case, ethanol was a well-known screening solvent and our preliminary view was that the form of claim 1 on file would have been produced in a polymorph screen from ethanol without inventive ingenuity (PR, page 40).

[118] On page 30, the R-PR made three main arguments which we summarize as follows. First, the same obviousness analysis in view of D1 should be applied to the issue of obviousness-type double-patenting and the ‘282 Patent. Second, the level of experimentation and burden for the skilled person to arrive at a crystal of a salt of a compound is too great and so the crystal of the salt cannot be obvious in view of the salt of the compound. Third, a generic compound formula cannot predict or render obvious any specific crystal because each crystal is a separate physical entity with its own unique properties. We address these arguments in the following sections.

1. The obviousness analysis and corresponding conclusions in view of D1 does not apply to obviousness double-patenting in view of the ‘282 Patent claims

[119] There are two fundamental differences between obviousness and obviousness double-patenting that preclude us from using the same analysis for both issues. First, the tests are different. The obviousness test is structured to determine whether there is an invention at all, as opposed to preventing evergreening and the issuance of a second patent for a non-inventive variation of an invention covered in another patent. Second, obviousness considers the prior art at large (including combinations of references) whereas obviousness double-patenting is focused on the claims of an issued patent.

[120] Even though the ‘282 issued patent is the Canadian patent that corresponds to D1, there is a key difference between them. Like D1, the ‘282 Patent discloses the same “multitude of compounds that are individually described and covered by the Markush formulas” within an expanded set of around 185 claims (compared

to a total of 56 corresponding claims in D1) for compounds, compositions, processes and medical uses. Unlike D1, the issued ‘282 Patent contains around 255 additional claims that were added before the patent was granted that are directed to three specific compounds (about 85 claims each): Dolutegravir, Cabotegravir and the molecule from the Z-4 sodium salt example. Among those additional claims, there are 17 claims (including claim 123) that are directed exclusively to Dolutegravir sodium and its uses etc., with another 17 claims covering its solvates (including claim 124). Other than sodium, no other specific salts are expressly claimed apart from being generically encompassed within “or a pharmaceutically acceptable salt thereof” for either of the three molecules.

[121] In contrast to the arguments made in the context of D1 and obviousness, it cannot be said that there is no emphasis on Dolutegravir sodium in the ‘282 Patent or that it would not stand out to the skilled reader compared to the other specific compounds disclosed in the patent. In our view, the skilled person reading the specification as a whole, including the whole claims set, would regard Dolutegravir, Cabotegravir, the Z-4 molecule and their sodium salts as featuring prominently as candidate molecules of particular interest in a manner separate from the broader genus invention that is disclosed in the ‘282 Patent.

[122] *May & Baker Ltd v Boots Pure Drug Co* (1950), 67 RPC 23 (HL), at page 32 (also referred to in *Sanofi* at para 110) considered whether amending a patent to replace broad genus claims with narrower claims to two individual compounds within the genus would still cover the same invention, or different inventions. Even though it was not in the context of obviousness double-patenting, the scenario described was similar:

> Is there then a difference in the inventions claimed in the original and amended specifications? On the one hand a vast range of possible compounds, a fragment no doubt in the whole sphere of organic chemistry yet so numerous that the number becomes meaningless, within which no one can say what hidden things might be brought to light, what benefits discovered for the relief of humanity. On the other hand two specific drugs. Are these inventions the same or different inventions? My Lords, I hesitate

> to appeal to common sense, lest others should take a different view of the case. Yet in the consensus of opinion of all the learned judges who have dealt with this matter I find justification for the view which I most emphatically hold that it is plain common sense to say that the inventions are not the same but different: and I think that, if they are different, the substantial difference could not be denied.

[123] In our view, this emphasis on the three molecules and their sodium salts, including Dolutegravir sodium, would influence how the skilled person would construe the claimed invention of claims 123, 124, 315 and 316, which is the starting point of the double-patenting analysis. More specifically, our view is that these claims would not be construed as covering the same invention as the genus claims. Also, since it was well known that molecules of particular interest should be screened for their polymorphs to, at a minimum, identify the thermodynamically stable form and hydrates, there would have been motivation to screen Dolutegravir sodium and the sodium salts of the other two molecules as well, from the skilled person's perspective: Hilfiker pages 9, 11, 222, 293.

[124] For these reasons, it would be incorrect to apply the obviousness analysis considering D1 to the issue of obviousness-type double-patenting and claims 123, 124, 315 and 316 of the '282 Patent, in our view. That said, there is significant overlap between these issues since they both consider inventiveness and so we will consider the Applicant's arguments made in relation to obviousness where applicable.

2. The level of experimentation and burden for the skilled person cannot be assumed based on facts, evidence and arguments from Teva 2017

[125] With respect to the second argument, the R-PR says the following on page 30:

> The chemical formula of claim 123 cannot render obvious the crystal form presently claimed. As explained above and detailed in *Teva 2017*, the level of experimentation and burden for the POSITA to arrive at a crystal of a salt from a salt of a compound is too great.

[126] We agree that the facts and evidence in *Teva 2017* established that the work performed in that case would have been seen by the skilled person as difficult and prolonged. However, to the extent that the Applicant is saying *Teva 2017* establishes that will be true in all cases, we do not agree. At a minimum, it is understood that the state of the CGK evolves over time and nearly 8 years passed between the claim dates/publication dates of the this application and the patent that was the subject of the *Teva 2017* decision. For example, the technology and systems associated with high-throughput polymorph screening would have evolved during that time: Morissette page 278; Hilfiker page 294.

[127] Further, as discussed under CGK, the difficulty involved with obtaining a compound in a usable form varies, depending on the molecule and other factors such as stability or purity. We addressed factual differences from *Teva 2017* under obviousness in our PR letter, although it was in reference to the decision of the Federal Court of Appeal affirming its companion case, considering the same Canadian Patent No 2,436,668 (PR, page 31):

> (W)e note that the Federal Court of Appeal reviewing that case cautioned against extrapolating from conclusions on the basis of broad factual similarities to the detriment of otherwise significant differences in a given case. Specifically, the Court stated that each case is to be decided on the basis of its facts and that the lower Court in (*Pfizer Canada Inc v Apotex Inc, 2017 FC 774*) understood that the jurisprudence does not establish any "hard and fast rules" on obviousness when it comes to evaluating whether a salt screen or any other form of experimentation is obvious or not: *Apotex Inc v Pfizer Canada Inc, 2019 FCA 16* [*ODV1 FCA*] at paras 41-42.

[128] The R-PR argued on page 20 that we misunderstood what is said in *ODV1 FCA* and that our statement is not support by the case law cited because it does not apply to new crystal forms:

> It is correct that the Federal Court of Appeal cautioned with evaluating salt screens. However, as emphasized above, this statement does not apply to the discovery of crystal forms of compounds (see in particular paragraph

> [41]). The extrapolation of the *Teva 2017* decision was not applied to (*Pfizer Limited v Ratiopharm*, 2010 FCA 204 [*Amlodipine*]) and (*Bristol Myers Squibb Canada Co v Teva Canada Limited*, 2017 FCA 76 [*Atazanavir*]) because these are not crystals but just salts of compounds. The PAB's statement and citation regarding why *Teva 2017* cannot necessarily be extrapolated to the presence case is not supported by the case law cited. In fact it is contracted by paragraph [41] of *Teva 2019* as presented above.

[129] *Merck Sharp & Dohme Corp v Pharmascience Inc*, 2022 FC 417 [*Merck*] is another more recent case relating to a new crystal form where the Federal Court reviewed *Teva 2019* (i.e., the companion of *ODV1 FCA* that aff'd *Teva 2017*), *Amlodipine* and *Atazanavir*, and said the following in relation to all three decisions: (emphasis added)

> [182] In the third case, (*Teva 2019*), claims to a particular crystalline form of a particular salt of ODV (succinate salt) were held to be unobvious…The Court concluded that none of the prior case law, including *Amlodipine* and *Atazanavir*, supported a view that all salt screens and all polymorph screens were obvious to try or routine…
>
> [183] While these cases serve as useful illustrations of the application of the obvious to try analysis to cases involving new salt and polymorphic forms, I adopt the same approach as the Court in (*Teva 2019*) that each proceeding must turn on its own facts, evidence and arguments. There is no overriding principle that all salt screens are obvious to try as a matter of routine, **or that polymorph identification will always be unobvious. None of these cases can be used to force a conclusion that is not supported by the facts and evidence**

[130] The Federal Court's interpretation of guidance from the Federal Court of Appeal in *Teva 2019* supports our preliminary view. The facts and evidence in *Teva 2017* do not establish that the level of experimentation and burden for a skilled person to arrive at a crystal of a salt from a salt of a compound will amount to an

invention in all cases. *Teva 2017* cannot be used to force a conclusion that is not supported by the present facts and evidence: *Merck* at para 183.

[131] Further, even though both cases involve crystal forms of a salt compound where the salt had not previously been made, there are also significant differences between the present case and *Teva 2017* to consider, in our view.

[132] First, the description section of the patent at issue in *Teva 2017* disclosed that there were difficulties associated with other forms of ODV and that the new crystal Form I of ODV succinate solved problems relating to formulation properties and avoiding side effects: Canadian Patent No 2,436,668, see Background and Summary of invention sections, Description pages 1-2. The description also disclosed experiments in the examples section demonstrating good formulation properties and superior bioavailability compared to the on-market ODV prodrug (Effexor™).

[133] By contrast, there is no indication in the present description of any difficulties associated with other forms or salts of Dolutegravir (for example, in relation to purification), or that producing the Dolutegravir sodium salt or crystal form presented any challenges. Further, as mentioned above, the evidence in Examples 1I and 3I indicates that Dolutegravir sodium is not the type of compound that the skilled person would regard as difficult-to-crystallize.

[134] Second, the Federal Court in *Teva 2017* found that the work “performed by SSCI” would have been seen as difficult and prolonged, based in part on the evidence that it took over two years of experimentation to find a usable form that overcame the difficulties identified in the description: *Teva 2017* at paras 33 and 279.

[135] In our view, the facts that are specific to *Teva 2017* should not be assumed for all cases involving crystal forms.

[136] With respect to the facts that are specific to this case, we note that, in the context of obviousness and D1, the R-PR provided evidence of eighteen previously undisclosed salt screening experiments involving three different salts that were

conducted “before arriving at the presently desirable crystal form”, summarized as follows by the Applicant (R-PR, page 26):

> As can be seen from the table above, many attempts at obtaining a salt of potassium, arginine, or meglumine failed. The formation of a crystal form is not trivial at all and requires arduous experimentation.

[137] We are not inclined to give much weight to this evidence. First, there is no express statement or indication that these experiments were conducted using Dolutegravir and not a different molecule. Second, the experiments relate to the work that led to choosing sodium over other salts, but that choice is already made in the ‘282 Patent, in particular in claim 123 which is the starting point of the analysis. In this view, the evidence does not assist with the inquiry because it does not address the level of effort or burden in moving from Dolutegravir sodium of claim 123 to the crystal form of claim 1 on file.

3. Crystal forms cannot be predicted or obvious from a compound formula

[138] With respect to the third argument, the R-PR says the following on page 30:

> Moreover, as explained above, many different crystals could have been obtained and exist for the sodium salt of Dolutegravir. The generic compound formula cannot predict or render obvious any of these crystals. Each crystal has different properties including a different bioavailability, different maximum Cmax, different Tmax and different stability in the presence of heat and light.

[139] We agree that any solid form of any molecule will have its own unique properties (for better or worse) and three dimensional packing arrangement that cannot be predicted before it is made and characterized. However, that does not necessarily mean that a new invention is made every time a molecule that is already claimed in another patent is synthesized for the first time, especially not if that patent provides an enabling disclosure of how to make it.

[140] The ‘282 Patent provides instructions for making Dolutegravir and for making sodium salts of similar compounds, including Cabotegravir sodium, which the skilled person would reasonably be able to adapt to prepare Dolutegravir sodium using their CGK, in our view.

[141] Of course, it is always possible to encounter unexpected challenges or difficulties in synthesis that require inventive ingenuity to overcome. It is trite law that the inventive ingenuity necessary to support a valid patent may be found in the implementation of an obvious idea if ingenuity is required to put it into practice*: Canadian Gypsum Co v Gypsum, Lime & Alabastine, Canada Ltd* [1931] Ex CR 180 at para 12; see also the *Manual of Patent Office Practice* at §18.02.02e. However, if that was the case here, it was not disclosed. There is no indication of any difficulties in the description and none are evident from the examples. There is no evidence that anything was done other than synthesizing the molecule of claim 123 in the ‘282 Patent and characterizing its solid-state form.

[142] That said, the Applicant has also disputed that the instructions provided for Cabotegravir and the other sodium salts would have produced Dolutegravir sodium in the same crystal form as claim 1 on file: R-PR, pages 27-28. Even though the same solvent, reactants and molar proportions are used, the protocol in the ‘282 Patent is carried out at entirely at room temperature and adds ethyl ether: R-PR, page 27. By contrast, the protocol for producing the crystal form of claim 1 involves heating the ethanol solution to 80°C (the boiling point) and gradually cooling the solution back down to room temperature, and it does not add ethyl ether. This argument was made in the context of obviousness and D1 but applies here as well, in our view.

[143] We agree with the Applicant that changing the reaction temperature and adding ethyl ether addition may affect the crystal packing arrangement of the Dolutegravir sodium molecules. Our observation that it was likely produced in the same form was speculative. The CGK supports the Applicant’s position that those two changes may result in a different crystal form from that of claim 1 on file, and the Applicant has argued that “many different crystals forms could have been obtained” for Dolutegravir sodium.

[144] However, in our view, the skilled organic chemist in this field synthesizing Dolutegravir sodium would also have tried heating the Dolutegravir solution to its boiling point and cooling gradually to room temperature because this is a common and efficient technique for promoting the formation of pure crystals. As stated above under CGK, purification and polymorph screening use the same classical crystallization approach and techniques. The skilled organic chemist would have known that heating a saturated solution to increase solubility and adding an anti-solvent such as ethyl ether to decrease solubility are basic standard crystallization techniques that are employed as needed in purification: Morissette page 276, Table 1; Bavin page 528; Byrn page 946.

[145] Even if this was not done during the initial synthesis step, our view is that the skilled person would have cooled a Dolutegravir sodium/ethanol solution from boiling to room temperature in a basic polymorph screen to identify the thermodynamically stable form with a large probability (PR, page 40). This is because ethanol is a commonly used screening solvent, based on its polarity, and because identifying the thermodynamically stable form favours slow crystallization experiments: Byrn page 946; Mirmehrabi pages 1565-1566, 1569; Gu pages 119-120, 122-123; Hilfiker pages 9, 11, 292-293. Based on the evidence in Examples 1l and 3l, Dolutegravir sodium is not a molecule that is "difficult-to-crystallize" and would crystallize readily under these conditions.

[146] In our view, on the balance of probabilities, it is reasonable that the skilled person would have produced the crystal form of claim 1 on file in at least one of those two steps without inventive ingenuity. Based on the record as it stands, there is no indication that inventive ingenuity was exhibited in going from claim 123 of the '282 Patent to claim 1 on file, and so our conclusion is that these claims are not patentably distinct. Since claims 2-6 are directed to the same crystal form as claim 1 on file, our view is that these claims are not patentably distinct from claim 123 of the '282 Patent for the same reasons.

[147] With regard to the crystal hydrate of claim 7 on file, our PR letter pointed out that there was no indication in the description or evidence from the Applicant that producing the crystal form of claim 7 on file involved or required inventive

ingenuity: PR, page 40. As mentioned, there would have been motivation to screen Dolutegravir sodium specifically for its hydrates, and Example 1m shows that the hydrate of claim 7 on file is produced using a solvent and techniques that are standard for producing hydrates (PR, pages 40-41):

> (T)he evidence in Example 1m is that the hydrate form crystallized from a mixture of THF and water. Specifically, the crystal form of claim 1 on file was dissolved in a solution of THF-water at 30°C, sodium hydroxide was added and the mixture was stirred at room temperature for 2 hours. The crystals were filtered, washed with THF-water, THF and then dried at 85°C. Those crystals are the crystal form 13b that is the subject of claim 7 on file.
>
> Based on this example, the hydrate was prepared using a well-known solvent mixed with water and techniques that were part of the common general knowledge. It was also well-known to keep drying temperatures lower than the boiling point of water when preparing hydrates to avoid evaporating water and desolvating the crystals: Hilfiker page 222.

[148] The Applicant did not provide arguments addressing our preliminary views relating to the crystalline hydrate form of Dolutegravir sodium, opting instead to propose deletion of claims 7 to 12 on file.

[149] Since there is no indication that inventive ingenuity was required or exhibited in going from claim 124 of the ‘282 Patent to claim 7 on file, our conclusion is that these claims are not patentably distinct. Since claims 8 to 12 are directed to the same crystal hydrate form as claim 7 on file, our view is that these claims are not patentably distinct from claim 124 of the ‘282 Patent for the same reason.

[150] Further, our view is that the pharmaceutical composition of claim 13 on file comprising the crystal forms of claims 1 to 6 and 7 to 12 is likewise not patentably distinct from the corresponding claims 315 and 316 comprising the salt and solvate of claims 123 and 124, respectively, for the same reasons.

[151] For all of these reasons, our conclusion is that claims 1 to 13 on file are not patentably distinct from claims 123, 124, 315 and 316 of the ‘282 patent.

THE PROPOSED CLAIMS ARE NOT PATENTABLY DISTINCT FROM THE CLAIMS OF THE '282 PATENT

[152] As mentioned, the Applicant submitted a proposed claims set that would cancel claims 7 to 12 on file, keep claims 1 to 6 on file and renumber claim 13 on file as claim 7. We agree with the Applicant that this amendment would address the indefiniteness defect against claim 8. However, this amendment would not address the double-patenting defect. We have already concluded that claims 1 to 6 and 13 on file are not patentably distinct from claims 123 and 315 of the '282 Patent, and so the proposed amendment would not render the claims allowable. Consequently, the proposed amendment does not qualify as a "necessary" amendment under subsection 86(11) of the *Patent Rules*.

RECOMMENDATION OF THE BOARD

[153] In view of the above, we recommend that the application be refused on the grounds that claim 8 is indefinite and does not comply with subsection 27(4) of the *Patent Act*, and claims 1 to 13 are not patentably distinct from claims 123, 124, 315 and 316 of Canadian Patent 2,606,282, contrary to the doctrine of obviousness double-patenting.

Cara Weir	Marcel Brisebois	Philip Brown
Member	Member	Member

DECISION OF THE COMMISSIONER

[154] I agree with the Board's findings and its recommendation that the application be refused on the ground that claim 8 is indefinite and does not comply with subsection 27(4) of the *Patent Act*, and claims 1 to 13 are not patentably distinct from claims 123, 124, 315 and 316 of Canadian Patent 2,606,282, contrary to the doctrine of obviousness double-patenting.

[155] 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.