I submit these comments in my personal capacity and not on behalf of a client or firm.

High-Level Comments:

- To support its position, CIPO mainly relies on old scientific articles (as far back as the 1970s) and several Old Act cases. This suggests a results-oriented approach to examining polymorphs.
- The assessment for patentability has internal inconsistencies and is off-side the current law (legislation and jurisprudence) in several respects, particularly with respect to anticipation and obviousness. The patentability assessment is also contrary to the patent bargain and the principles of eligibility for listing patents for polymorphs on the Patent Register.
- As with CIPO's approach to promise of the patent (now shown to be wrong), these guidelines are setting standards for patentability, like a need to show improvement over the prior art, that are not required by the patent statute or case law.

Comments With Respect to Certain Sections:

Intro

- Why is this tied to "small" chemicals and what is a "small chemical molecule"? This does not seem to be a commonly-accepted phrase. I think CIPO means to refer to small molecules or small-molecule chemicals. (CIPO has it backwards.) It is the molecular size that determines this category of chemical (as distinguished from, say, biologics, which are large molecules).
- The science described in this section is convoluted and should not even be needed if the examiners are persons skilled in the art of polymorphs.

Section 17.08.01

- While the true test for anticipation under the New Act (disclosure + enablement) is certainly acknowledged here, CIPO goes on to explain that a polymorph is anticipated if it is "inherently" present in the prior art. Specifically, novelty will be destroyed if the polymorph is somehow "disclosed and enabled in the prior art…inherently".
    - First of all, how can an entire polymorph be inherently enabled?
    - Second of all, a proper inherency assessment finds an element of a claimed invention in what would otherwise be a prior enabling disclosure of the remaining elements of the claimed invention. It would be improper for an Examiner to find anticipation based on inherency if not a single element of a claimed invention is mentioned in the prior art.
- CIPO also explains that a polymorph is anticipated if it is already "known". This is incorrect under the present statute. Unlike the Old Act, s. 28.2 of the New Act requires an enabling disclosure of the claimed polymorph to find anticipation. Mere "knowledge" of something later claimed is insufficient, on its own, to anticipate the claim.
- Anticipation by inherency alone and anticipation by knowledge alone not only run counter to s. 28.2; they also violate the patent bargain. Under the proposed guidelines, the discloser and enabler of the polymorph is prevented from patenting his invention based on a prior knowledge or statement that neither discloses nor enables that polymorph. In the result, the public has no information regarding the invention itself or how to make/use it. The purpose of the patent system is unfulfilled.
- The obviousness assessment suggests that a routine process cannot produce a patentable invention; however, the non-obviousness of a product does not depend on an inventive process for patentability: a routine process could isolate something unpredictable (as often happens with polymorphs).
- In the absence of an inventive process, a claimed polymorph will likely be considered obvious under these guidelines unless the inventor has disclosed unexpected properties/benefits or a "significant difference or improvement" over the prior art. While these might be helpful to address a prior art objection, they are not pre-requisites to avoiding obviousness and obtaining patents in

Canada. Indeed, per s. 2, an invention is not required to be an "improvement"; it is sufficient to be "new".

Section 17.08.02

- In this proposed section, the MOPOP calls for demonstration of the specific physicochemical properties of a particular crystalline form to support utility, on the basis that these properties are generally considered unpredictable (so no sound prediction permissible).
- The combined result of this section and section 17.08.01, with its standard of anticipation by mere knowledge or inherency, will be that many polymorphs will not be patented if there is no demonstration of specific physicochemical properties, but many polymorph claims will be anticipated by prior disclosures that include no such demonstration.
- In other words, with these revisions, the prior art now has a lower burden of disclosure than the patentee, which is contrary to the patent bargain. Why is the patent bargain not met if the Applicant doesn't show these physicochemical properties but equally denied to the Applicant if the prior art doesn't show them either?

Section 17.08.03

- CIPO seems to be requiring that the claims to a polymorph include "physical characterization data and/or physicochemical properties which are specific to its solid state structure" in order to avoid a finding of indefiniteness. CIPO rejects the suggestion that an expression like "form X" would be sufficient to claim a polymorph.
- This statement reveals a possible confusion between the data required in the disclosure to support a claim to a polymorph and the terms by which that polymorph is defined in the claim. The support for the polymorph should be found in the disclosure, not within the claim itself.

Section 17.08.04

- A patent for multiple polymorphs will be divided on the basis that each polymorph is its own invention.
- This seems inconsistent with the prior art analysis, by which polymorphs can be considered obvious in view of each other unless unexpected properties/benefits/improvements are disclosed.

Mark-up with Comments:

17.08
Pharmaceutical solid forms

Many small chemicals ~~molecules~~ are able to exist in more than one solid form. A solid form may be generally described as either crystalline or amorphous. The structure of a crystalline solid is dictated by the regular arrangement of the atoms of a molecule within a crystal lattice. The crystalline solid may contain the molecules in free base (or free acid) form or the molecules may exist as a salt. The molecules ~~or salt~~ may crystallize as a hydrate/solvate or co-crystal (see 17.08.06 for further guidance on salts, hydrates/solvates and co-crystals). Conversely, an amorphous solid contains molecules exhibiting a high degree of disorder in the molecular arrangement and, therefore, lacks crystallinity.

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Polymorphism refers to the ability of some molecules to have more than one crystalline form. In each polymorph, the molecule has a different three-dimensional arrangement of its atoms within the crystal lattice. Different polymorphs of the same chemical ~~molecule~~ have different solid state structures that can generally be distinguished using spectral or thermal analysis. Different polymorphs may also have different physicochemical properties, such as solubility, stability, dissolution rate, hygroscopicity, compactibility, etc.

The investigation of solid forms is a significant focus in the development of new pharmaceuticals. Recognizing that different solid forms of the same small chemical ~~molecule~~ may have different physicochemical properties, it follows that the quality or performance of the product may be affected by the form it contains, such as pharmaceutical formulations that include the polymorph as an active ingredient. A particular solid form may possess a property which is beneficial or detrimental, for example, in formulating a new drug product. It is routine to screen for small chemical molecule polymorphs in the early stages of drug development to identify any forms that possess a property which would be detrimental to the performance, bioavailability or stability of the final drug product.Footnote 1

Screening a small chemical molecule for polymorphic forms is often performed using general methodologies that utilize basic crystallization techniques which are standard in the field. Such methodologies typically include dissolving and crystallizing a chemical molecule of interest from multiple solvents, including any solvents used in the synthesis, formulation or processing of the drug product. The solvents may be polar or non-polar, and may be hydrophilic or hydrophobic. Heating and stirring may be used to help dissolve the molecule in the solvents. In order to induce crystal formation, a further solvent or seed crystal may be added, or the pressure, temperature or pH may be modulated. Small molecule compounds are almost invariably purified by crystallization, and these basic crystallization techniques have long been part of the common general knowledge of synthetic chemists in all fields of technology. [It seems that these methodologies may be known already, but the different polymorphs that they may uncover cannot be predicted.]

[NTD: If patent applications are examined by persons skilled in the art, the foregoing description should not be required for an examination manual.]

17.08.01
Considerations respecting anticipation and obviousness

Anticipation is assessed on a claim-by-claim basis by asking whether a prior disclosure, when understood by the person skilled in the art in light of their common general knowledge, both describes and enables the practice of the claimed invention (see 15.01 for further guidance on anticipation). [Combination with anything extraneous to the single reference -- say, CGK -- is an obviousness assessment, not an anticipation assessment. There should be no anticipation under s. 28.2 of the

New Act unless the entire subject matter defined by the claim is disclosed in the single reference and the invention as claimed is enabled by information in the reference.]

Where a particular crystalline form (e.g., a polymorph) of a small chemical molecule has not been disclosed and enabled in the prior art, either explicitly or inherently, a claim to the crystalline form is novel and satisfies subsection 28.2(1) of the Patent Act. [This applies inherency improperly under the New Act by relying on Old Act cases like Hoffman. Under the New Act, an entire claimed invention cannot be inherently disclosed in prior art if there is no mention of same. The public would not even be aware of the invention, so how can it be disclosed to the public?]

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Where, on the other hand, a polymorph of the molecule is disclosed and enabled in the prior art, a claim that encompasses the same polymorph is anticipated. Further, a polymorph that is already known may not be claimed by making it dependent on a new process. Footnote 2 However, a claim to the process used to prepare the polymorph may still be novel if it can be distinguished from the prior art. [There are problems with footnote 2. First, Hoffman is an Old Act case and should not be cited here. It is not good law for New Act patent applications. Second, "known or used" was one of the tests for anticipation under the Old Act, but is insufficient to constitute anticipation under the New Act unless the knowledge or use was such that the entire subject matter of the claimed invention was disclosed to the public and enabled. In the absence of such a disclosure, the public has received no description of the polymorph and no explanation of how to isolate it. There can be no anticipation by mere knowledge or mere use under the New Act.]

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Obviousness is assessed on a claim-by-claim basis by asking whether the claimed invention is obvious (or uninventive) when considered from the viewpoint of the person skilled in the art in light of their common general knowledge and the state of the art as it was on the claim date (see 15.02.02 for further guidance on assessing obviousness). The obviousness inquiry goes beyond asking whether the properties of the new solid form are self-evident or not. Footnote 3 [In prosecution, an Examiner needs to find at least one prior reference/disclosure + something else (another disclosure, CGK, etc.) showing the elements of the claim in order to arrive at obviousness. Moreover, if the properties of the polymorph aren't even claimed, why does the obviousness inquiry consider them?]

When assessing the obviousness of a new crystalline form (e.g., polymorph) of a known small chemical molecule, one factor to consider is the process by which the new form is produced. Inventiveness may be acknowledged for a form that can only be produced using an inventive process. Such a process would generally go beyond the mere application of common general knowledge solutions and routine experimentation. [Obviousness of a product does not depend on the obviousness of the process by which it is made.]

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Even if the process used to prepare a new solid form of a known small chemical molecule relies on basic crystallization techniques that are standard in the field, the solid form may still be non-obvious. Inventiveness may be acknowledged if the originally-filed application discloses that the form provides an unexpected benefit, such as a beneficial physiochemical property attributable to the form itself. [There is no requirement in law to show an unexpected benefit to overcome an obviousness argument in Canada. Per s. 2, an invention can be something "new"; it does not have to be an "improvement". If the form itself could not have been predicted from the earlier polymorph, then the form itself is unexpected and its benefits do not need to be considered.] To determine whether or not a crystalline form possesses a beneficial physicochemical property the form must be prepared and tested. Since beneficial physicochemical properties are not predictable, they are generally considered as unexpected. [So are polymorphic forms themselves.] It follows that an unexpected beneficial property may represent the scintilla of invention sufficient to support the non-obviousness of the solid form. Footnote 4

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Only benefits disclosed in the originally-filed application will be taken into account during an obviousness assessment. The disclosure of the benefit may be either explicit (e.g., direct statements) or implicit (e.g., supportive data provided in the application). In a patent application, the most persuasive disclosure is one that provides data comparing the form of the invention to the prior art form (or all of the closest prior art forms when more than one exist) and confirms that there is a significant difference or improvement in one or more physicochemical properties compared to the prior art form(s) of the same chemical molecule. [No basis in law for the highlighted requirement.] Where the specification comprises statements indicating a solid form "may" have a particular benefit or "has at least one" benefit selected from a list of benefits (without clearly stating which it has), this amounts to an inexplicit indication of a potential benefit. Unless the benefit would be implicit from data provided in the application, such statements would not be considered during an obviousness assessment. [Applicants pay CIPO, through examination fees, to examine the application in full and take all content into consideration. A flat refusal to consider certain statements in the context of a specification seems to contravene the enabling legislation.] Likewise, a benefit that is recognized subsequent to the filing of the original application would be given no weight in the assessment. [These positions contradict the law of *Free World Trust* and purposive construction, by which everything in a patent specification must be read in context. How can there be blanket statements about the meaning of terms in people's patents without reading them in context?] Footnote 5

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It is important to note that the person skilled in the art would generally expect or predict that a crystalline form will have certain benefits over an amorphous form of the same small chemical molecule, including easier isolating, purifying, drying, and in batch processes, easier handling and formulating. Footnote 6 However, such expected benefits are generally not sufficient, when taken alone, to support a finding of non-obviousness. [A benefit over prior art is not required to obtain a patent in Canada in the absence of a selection.]

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In cases where a new solid form of a known small chemical molecule is the product of a routine, uninventive process and the specification only discloses, at best, benefits that the skilled person would have expected, a claim to the form may be obvious and not in accordance with section 28.3 of the Patent Act. [The public has not obtained sufficient information from the prior disclosure to understand and make the new polymorph. The inventors' discovery will be afforded no patent protection, thereby becoming a windfall to the applicant's competitors.]

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17.08.02
Considerations respecting utility

The utility of a polymorph invention does not need to be expressly set out in the application; however, the subject-matter of the invention must have utility. Please see Chapter 12 for general guidance on utility.

It is generally understood that the person skilled in the art would reasonably expect that polymorphs of a known small chemical molecule with a previously established utility (e.g., pharmacological or therapeutic utility) would also possess the same activity since it is a general effect of the molecule itself. Many patent applications rely on such a line of reasoning to support a sound prediction of utility for new solid forms of the same small chemical molecule. Thus, in such cases, the utility of the polymorph will generally be self-evident to the skilled person and the utility requirement of section 2 of the Patent Act would be satisfied.

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Where the specification is silent as to the utility of the claimed polymorph and the utility of other known forms of the same small chemical molecule is neither disclosed in the specification nor common general knowledge to the skilled person in the art, a utility defect under section 2 of the Act should be identified.

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Where the subject-matter of the invention as claimed has a utility that is different from other known form(s) of the same small chemical molecule, the utility related to the subject-matter must be established by demonstration or sound prediction (see 12.04.02 and 12.04.03). However, if the utility relies on a physicochemical property that was not established and could not have been predicted, then the utility of the subject-matter of the invention cannot be established by sound prediction. Recall that the specific physicochemical properties of a particular crystalline form are generally considered as unpredictable since the crystal form must be prepared and tested before its properties can be ascertained (see 17.08.01). Given that such properties cannot be predicted and would not be implicit to the skilled person, in order to establish utility the applicant must be in a position to show that the property associated with the utility was demonstrated no later than the filing date of the application. [This paragraph seems inconsistent with the anticipation/obviousness discussion. Are these properties predictable or not? If they're not, and the Applicant can't get a patent for the polymorph without an explicit teaching of them, then how did the prior art disclosures (which also wouldn't have shown these properties) anticipate/obviate the Applicant's claim? Why is the patent bargain not met if the Applicant doesn't show these properties but equally denied to the Applicant if the prior art doesn't show them either?]

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Statements of the polymorph's demonstrated utility may be adequate in some cases to establish utility in accordance with section 2 of the Patent Act. Where experimental data serves as the basis for the demonstration of utility, the data must have existed at the filing date but need not have been disclosed in the description.

17.08.03
Defining a polymorph in the claims

In accordance with subsection 27(4) of the Patent Act, the subject-matter of a claim must be defined distinctly and in explicit terms and the scope of a claim must be clear and definite from the perspective of the person skilled in the art.

Where an application discloses and claims a new polymorph of a known small chemical molecule, the polymorph must be defined in terms of physical characterization data and/or physicochemical properties which are specific to its solid state structure and which serve to distinctly and explicitly distinguish it from all other forms of that molecule or in terms of the process by which it is made.

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Defining a polymorph in a claim by the physical parameters relevant to its particular crystal structure is often sufficient to satisfy subsection 27(4) of the Act. Spectral analysis parameters such as the X-ray powder diffraction (XRPD) pattern, Raman spectrum and/or the solid-state nuclear magnetic resonance (NMR) of the particular crystalline form may be acceptable depending on the facts of the particular case. It may also be acceptable to define the polymorph by parameters associated with methods of thermal analysis, such as infrared (IR) absorption, differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), melting point, or combinations thereof.

Merely defining a claimed polymorph by an internal designation (e.g., Form I, polymorph B, etc.) cannot serve to define the polymorph in distinct and explicit terms. Furthermore, defining the polymorph solely in terms of its molecular formula (e.g., C28H38N6O11S) or chemical name does not satisfy subsection 27(4) of the Act: the same formula and name are shared with all other crystalline polymorphs and amorphous forms of the same small chemical molecule and is therefore not distinct.

17.08.04
Considerations respecting unity of invention

As directed by section 36 of the Patent Rules, an application will not be considered to "claim more than one invention if the subject-matters defined by the claims are so linked as to form a single

general inventive concept". Footnote 7 See MOPOP 14.05 for further guidance on unity of invention. It follows that where more than one solid form of a small chemical molecule is claimed, the forms will be considered different inventions (i.e., there is a lack of unity of invention) if, having regard to the specification as a whole, it is apparent that there is no single general inventive concept linking the different forms within the claims. [This is also inconsistent with CIPO's prior art analysis. Different inventions are necessarily patentably distinct. CIPO cannot both split polymorphs into different divisions on the ground that they are separate inventions but find anticipation or obviousness of a polymorph on the basis of a prior disclosure of a different form. The two positions are at odds with one another.]

Generally, a set of claims that encompasses multiple distinct forms of the same small chemical molecule will share a general inventive concept if a set of new and unobvious elements is common to each claim in the set and as long as the elements are those required for the proper operation of the invention. Depending on the facts of a particular case, the element may include, for example, the use of the same intermediate in the process to prepare each form and/or the fact that all of the forms are crystalline. Where the intermediate and/or crystallinity was previously associated with a form of the same small chemical molecule in the prior art, the claims should be identified as lacking compliance with subsection 36(1) of the Patent Act as a result of an a posteriori unity defect.

17.08.05
Examples

The following hypothetical examples are provided to help clarify some elements of the foregoing guidance.

Example 1:

The specification discloses that the inventors have discovered a crystal polymorph (Form II) of compound X, which was arrived at using basic crystallization techniques that are standard in the field. The techniques included dissolving compound X in ethanol, heating the solution to reflux, and then cooling the solution until crystals appeared. A working example in the description characterizes Form II by X-ray powder diffraction (XRPD) pattern, IR absorption spectrum and melting point. According to the description, prior art document D1 discloses the use of compound X as an antibacterial compound in the treatment of urinary tract infections. The examiner also learned from D1 that compound X was obtained in crystalline form, that it was recrystallized in the final synthesis step using dichloromethane, and that the crystalline form was characterized by XRPD. Upon comparing the two XRPD patterns, the examiner is satisfied that Form II is distinct from the crystalline form disclosed in D1.

Claims:
1.Crystalline Form II of compound X which is characterized by an X-ray powder diffraction pattern having characteristic peaks expressed in angle 2-theta at approximately 8.0°, 12.2°, 14.4°, 16.6° and 18.8°.
2.A process to prepare Form II of compound X comprising: a.providing a solution of compound X in an ethanol solvent;
b.stirring and heating the solution to reflux until X is fully dissolved;
c.cooling the solution so as to form crystals of said compound; and
d.collecting the crystals.

Each scenario below illustrates the analysis used when determining the patentability of the claims. The analysis is different for each scenario and is based on what was disclosed in the description according to each scenario.

Scenario A

Analysis: The subject-matter of claims 1 and 2 is defined in distinct and explicit terms. The examiner has also determined that the utility of the polymorph of claim 1 would have been self-evident to the skilled person in the art because it can be soundly predicted from D1 that compound X, in general, has utility as an antibacterial compound. Further, the examiner is satisfied that, based on the description, the process claimed in claim 2 has utility in producing Form II.

Claims 1 and 2 are novel. Recognizing that compound X was not previously known in the prior art to exist in the solid state as Form II and that Form II is distinguished from the form disclosed in D1, Form II is not anticipated. Moreover, since D1 discloses crystallizing compound X from a different solvent, the process of claim 2 is not anticipated.

Although novel, the subject-matter of claims 1 and 2 is not patentable in view of the obviousness analysis that follows. As discussed above, a crystalline form of compound X and therapeutic use thereof were already known from D1, which represents the closest prior art. There is no disclosure of any unexpected benefit resulting from the arrangement of compound X molecules in Form II, and so the only difference from the D1 form is the 3D arrangement of the molecules of compound X in relation to one another (i.e., the arrangement characterized by the XRPD peaks). However, simply having an alternative arrangement of the molecules of compound X in the solid state is not necessarily an indication of inventive ingenuity. The utility of compound X was already established in D1, and so it follows that the skilled person reading D1 would recognize that compound X was a pharmaceutical candidate worth pursuing. It was also well known in the pharmaceutical field to screen such candidates for polymorphs. Further, the examiner determines that the Form II polymorph was obtained using basic crystallization techniques that were well within the grasp of the skilled person. In view of the above, the examiner concludes that the difference between Form II and the prior art would have been bridged by the skilled person using only the common general knowledge available to them. Therefore, claim 1 is obvious. Regarding claim 2, even though the crystallization solvent is different from that used in D1, the examiner determines that the process did not require any degree of inventive ingenuity for the same reasons set out above. Ethanol was a well-known recrystallization solvent used for polymorph screening, and the basic techniques used were well within the grasp of the skilled person. [If the new polymorph was never disclosed or known, its entire existence was unpredictable. The public learned something new from the inventors that it never knew before. In the absence of the patent application in this example, there would be no such thing as Form II. In the absence of the patent application in this example, the Examiner couldn't have even conducted the obviousness assessment. It was performed with 20/20 hindsight based on the Examiner's reading of the present specification.]

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Scenario B

In this scenario, the description teaches that there is a need for a new crystalline form of compound X with improved solubility over existing forms of compound X. A working example in the description shows that the solubility of Form II exceeds the solubility of the crystalline form of D1 form by approximately 22%.

Analysis: As in Scenario A, the subject-matter of claims 1 and 2 is novel, has utility and is defined in distinct and explicit terms. Scenario B differs from Scenario A in that the description in Scenario B discloses a need for a more soluble crystalline form of X and shows that the solubility of Form II is, in fact, improved over the form of D1. Based on the available information, the examiner concludes that the increased solubility is an unexpected beneficial property attributable to Form II itself and, therefore, claim 1 is inventive. Since the product of the process of claim 2 is new, useful and inventive, claim 2 is also new, useful and inventive.

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Example 2:

An application discloses the preparation of a crystal polymorph (Form III) of known antiretroviral compound V. In order to arrive at Form III, the specification describes a process that uses a series of basic crystallization techniques that are standard in the field (i.e., common general knowledge to the person skilled in the art) involving a number of different steps, solvents and conditions. The description characterizes Form III by XRPD, IR absorption spectrum and melting point but is silent as to any benefits that are specifically provided by Form III. A search of the prior art identifies document D1, which discloses crystalline Form I and Form II of antiretroviral compound V. The process used to prepare Form III is not disclosed in D1. Based on the physical characterization data disclosed in D1, the examiner concludes that Forms I and II can be distinguished from Form III of the invention.

Claims:
1.A crystalline polymorph of compound V, wherein the polymorph exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2θ (+/-0.2°θ) at about 7.1, 9.0, 19.7, 20.7, 22.2, and 33.3 and infrared peaks at wavenumbers 1128, 1423, 2035, 2602, and 3231.
2.A process to prepare Form III of compound V comprising: a.refluxing amorphous compound V in ethanol;
b.evaporating the ethanol to dryness leaving a residue;
c.dissolving the residue in dimethyl formamide and heating at 110ºC for 24 hours;
d.evaporating the dimethyl formamide to dryness leaving a residue;
e.dissolving the residue in acetonitrile and stirring in an inert atmosphere for 17 hours;
f.adding methyl t-butylether dropwise;
g.cooling the solution to 0°C; and
h.isolating Form III.

Analysis: The subject-matter of claims 1 and 2 is defined in distinct and explicit terms. The examiner has also determined that the utility of the polymorph of claim 1 would have been self-evident to the skilled person in the art because it can be soundly predicted from D1 that compound V, in general, has utility as an antiretroviral compound. The examiner is satisfied that, based on the description, the process claimed in claim 2 has utility in producing Form III.

Recognizing that compound V was not previously known to exist as Form III, the form appears to be a variation of compound V that is distinguished from the prior art with respect to anticipation. Also, the process of claim 2 is not disclosed in D1. Therefore, claims 1 and 2 are novel.

On the question of obviousness, the examiner determines that the process to prepare Form III of claim 2 is inventive from the skilled person's perspective. The process is not straightforward, it involves a degree of inventive ingenuity despite the fact that the process uses a series of basic crystallization techniques, solvents and conditions. Likewise, inventiveness may be acknowledged for the polymorph of claim 1 because, based on all of the information available to the examiner, it appears that Form III can only be prepared by the new and inventive process defined in claim 2.

17.08.06
Considerations relating to particular solid forms

A determination of the patentability of pharmaceutical salts, hydrates, solvates, desolvates and co-crystals involves the same considerations as those described above in 17.08.01 to 17.08.04; however, further clarification is provided below for some issues specific to salts, hydrates, solvates, desolvates and co-crystals.

17.08.06a

Salts

Physicochemical properties of a small chemical molecule, such as solubility, stability, dissolution rate and hygroscopicity, can be modulated by the formation of acidic or basic salt forms of the molecule. Footnote 8 Salts of small chemical molecules readily form crystalline structures which may be subject to polymorphism.

Like polymorphs, screening a small chemical molecule for acceptable salt forms is often performed using general methodologies that utilize basic techniques standard in the field. Such methodologies include pairing an acidic or basic molecule with a finite number of known pharmaceutically acceptable counterions and characterizing the performance of the resulting salt forms. In cases where the free base (or free acid) form of a small chemical molecule exhibits poor solubility, the skilled person in the art would generally expect that the solubility and bioavailability of the molecule could be improved by converting it to a salt using a salt screen.Footnote 9

In assessing whether claims to a novel salt are inventive, the process used to prepare the salt and the salt's unexpected beneficial properties, if any, may be informative in the assessment. Where the originally-filed application discloses that the salt can only be produced using an inventive process that goes beyond routine methodologies or that the salt has a beneficial property that is unexpected, the claimed salt is inventive and complies with section 28.3 of the Patent Act.

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It is generally understood that the person skilled in the art would reasonably expect that salts of a known small chemical molecule with a previously established utility (e.g., pharmacological or therapeutic utility) would also possess the same utility despite the incorporation of a counterion in its structure.

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Defining a salt of a known small chemical molecule in a claim in terms of the counterion that is incorporated into the structure of the molecule is often sufficient to satisfy the requirements of subsection 27(4) of the Patent Act. For instance, the salt in the claim "A besylate salt of the compound of formula (I)…" is defined distinctly and in explicit terms that would be clearly understood by the person skilled in the art. However, in cases where a claim is directed to a specific polymorph of a salt, the physical parameters relevant to the polymorph's particular crystal structure must also be defined in order to satisfy subsection 27(4) of the Patent Act. See 17.08.03 for more information about physical parameters.

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17.08.06b
Hydrates, solvates and desolvates

A small chemical molecule may form an entity called a solvate with one or more solvent molecules (e.g., ethanol, benzene, acetone, tetrahydrofuran, etc.). Where the solvent is water, the solvate is usually referred to as a hydrate. Where the solvate is crystalline, the solvent molecules are incorporated into the crystal lattice. A desolvate occurs when the solvent molecules are subsequently removed from a crystalline solvate and the crystal lattice retains the structure of the original solvated form with vacant spaces where the solvent molecules used to be. Solvates and desolvates may also be subject to polymorphism.

The discovery of solvates and desolvates usually happens in the early stages of drug development, as the screening for new solid forms is performed. Processes for preparing these forms often follow general methodologies that utilize basic routine crystallization techniques that would be well within the grasp of the person skilled in the art in the relevant field.

In assessing whether claims to a novel solvate or desolvate are inventive, the process used for the preparation and any unexpected benefits of the particular entity may be informative in the

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assessment. Where the originally-filed application discloses that the solvate or desolvate can only be produced using an inventive process that goes beyond routine methodologies or that there is an unexpected benefit attributable to the particular solvate or desolvate crystalline form, a claim to the solvate or desolvate is inventive and complies with section 28.3 of the Patent Act.

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It is generally understood that the person skilled in the art would reasonably expect that solvates and desolvates of a known small chemical molecule with a previously established utility (e.g., pharmacological or therapeutic utility) would also possess the same utility despite the incorporation of a solvent into the crystal lattice (solvate) or the removal of the solvent from the solvated form (desolvate).

Defining a solvate of a known small chemical molecule in a claim in terms of the solvent and the number of solvent molecules per small chemical molecule is often sufficient to satisfy the requirements of subsection 27(4) of the Patent Act. For example, the skilled person in the art would understand the scope of a claim to "A dihydrate of the compound of formula (I)" since the solvate is defined distinctly and in explicit terms. However, in cases where a claim is directed to a specific polymorph of a solvate, the physical parameters relevant to the polymorph's particular crystal structure must also be defined to satisfy subsection 27(4) of the Patent Act. See 17.08.03 for more information about physical parameters.

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Likewise, defining a desolvate in a claim by the physical parameters relevant to its particular crystal structure is often sufficient to satisfy the requirements of subsection 27(4) of the Patent Act.

17.08.06c
Co-crystals

A co-crystal is a crystalline complex of two or more neutral small chemical molecules bound together in a crystal lattice, where both molecules individually, in their pure forms, are solid at room temperature. Footnote 10 In a pharmaceutical co-crystal, the molecules include an active pharmaceutical ingredient (API) and a co-crystal former.

Like salts, the physicochemical properties of a small chemical molecule (e.g., solubility, stability, dissolution rate and hygroscopicity) can be modulated by the formation of a co-crystal. Unlike salts, co-crystal formation does not rely on the presence of ionizable groups or a finite number of counterions. To produce a co-crystal, the list of co-crystal formers that can be potentially combined with a given API is extensive. Footnote 11

In assessing whether claims to a novel co-crystal are inventive, the process used for the preparation and any unexpected benefits of the particular co-crystal may be informative in the assessment. Given the state of the art and recognizing the extensive number of potential co-crystal formers that can be used, screening for co-crystals may involve an inventive process and co-crystals produced by such an inventive process would also be inventive.

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It is generally understood that the person skilled in the art would reasonably expect that co-crystals of a known small chemical molecule with a previously established utility (e.g., pharmacological or therapeutic utility) would also possess the same utility despite the incorporation of a co-crystal former into the crystal lattice.

Like polymorphs, defining a co-crystal in a claim by the physical parameters relevant to its particular crystal structure is often sufficient to satisfy the requirements of subsection 27(4) of the Patent Act. See 17.08.03 for more information about physical parameters.

Footnotes

Footnote 1

ICH Harmonised Tripartite Guideline, "Specifications: Test procedures and acceptance criteria for new drug substances and new drug products: chemical substances Q6A", Adopted by CPMP, November 1999, issued as CPMP/ICH/367/96, Published in the FDA Federal Register, Vol. 65, No. 251, 29 December 2000, pages 83041-83063. Is this the most up-to-date scientific view on this topic?

Footnote 2

Hoffman La Roche v Commissioner of Patents 1955 23 C.P.R. 1 This is a really old, Old Act case.

Footnote 3

CIBA Specialty Chemicals Water Treatments Limited v SNF Inc., 2017 FCA 225 at paragraphs 61-62; Bristol-Myers Squibb Canada Co. v Teva Canada Limited, 2017 FCA 76 at paragraph 62; AstraZeneca Canada Inc. v. Mylan Pharmaceuticals ULC, 2017 FC 142 at paragraph 134

Footnote 4

Apotex Inc. v Allergan Inc., 2012 FCA 308 at paragraph 74; Bristol-Myers Squibb Canada Co. v Teva Canada Limited, 2017 FCA 76 at paragraph 50

Footnote 5

Novopharm Limited v Janssen-Ortho Inc., 2007 FCA 217 at paragraph 26 This is an Old Act case.

Footnote 6

Bavin, M., "Polymorphism in Process Development", Chem. & Ind., August 1989; 21:527-529. Is this the most up-to-date scientific view on this topic?

Footnote 7

The "single general inventive concept" in the unity of invention inquiry is not to be confused with the "inventive concept" in an obviousness assessment. The inventive concept in the latter comprises the feature or features of the claim that appear to be inventive over the common general knowledge and/or which the applicant appears to consider inventive (see 15.02.02c). The average practitioner may say there is no difference.

Footnote 8

Berge, S. M. et al., "Pharmaceutical Salts", J. Pharm. Sci., January 1977; 66(1):1-19. Is this the most up-to-date scientific view on this topic?

Footnote 9

Bristol-Myers Squibb Canada Co. v Teva Canada Limited, 2017 FCA 76 at paragraphs 6 and 76

Footnote 10

It is noted that, unlike co-crystals, solvates contain solvent molecules that, in their pure form, are liquid at room temperature.

Footnote 11

Trask, A. V., "An Overview of Pharmaceutical Cocrystals as Intellectual Property", Mol. Pharm., 2007; 4(3): 301-309. Is this the most up-to-date scientific view on this topic? Is this written from a perspective of the Canadian Patent Act? Why is CIPO making policies on the basis of this publication rather than the terms of its enabling statute?

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