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By Email: jeremy.mclean@canada.ca

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Dear Mr. McLean:

Re: Consultation on the proposed changes to Chapter 17 of the Manual of Patent Office Practice (MOPOP) - Pharmaceutical solid forms

This letter is in response to the call for comments in relation to the above draft revisions to MOPOP Chapter 17. FICPI Canada wishes to thank the Canadian Intellectual Property Office (CIPO) for the opportunity to comment on the proposed revisions.

FICPI (the Federation Internationale des Conseils en Propriété Intellectuelle), comprises more than 5000 intellectual property attorneys in private practice in 86 countries. FICPI Canada is a self-governing national association of FICPI and represents the interests of Canadian patent and trade-mark professionals. Our membership includes senior professionals at most major Canadian intellectual property firms. Our clients span all types and sizes of businesses, including multi-national corporations, small and medium size enterprises, and individuals.

We appreciate that the proposed new section 17.08 of MOPOP is intended to provide more information and guidance than the current version in this regard, which will certainly be useful for Applicants.

We have reviewed with interest the consultation document, and believe that some of the principles discussed in the proposal could benefit from and be revised in view of recent

jurisprudence in the area of crystalline forms. We provide our comments below, first generally, then with respect to specific sections of the draft.

General comments

We note that the proposed revisions refer to various decisions of the Canadian Courts (in footnotes 2-5) in support of certain principles discussed therein. Since a significant portion of the proposed revisions relates to the patentability of crystalline forms, we believe that it would be helpful to refer to recent Court decisions which specifically addressed the patentability of crystalline forms of chemical compounds.

Particularly relevant are a pair of 2017 decisions from the Federal Court in respect of Pfizer's Canadian Patent No. 2,436,668, the validity of which was challenged by *Apotex*[1] and *Teva*[2] in the context of Patented Medicines, Notice of Compliance (PMNOC) proceedings. These cases are of particular interest in that they were subsequent to, and considered the analysis of, key decisions of the Supreme Court in respect of obviousness (*Sanofi*[3]) and utility (*AstraZeneca*[4]).

On the question of obviousness, the test established by the Supreme Court in *Sanofi* was applied, including its "obvious to try" component. Using the *Sanofi* test, the Federal Court assessed the validity of claims directed to a crystalline form, establishing the following principles:

The formation of crystalline forms is <u>unpredictable</u>

As noted by the Courts in these two cases:

> *The foregoing deals with the salts. The situation regarding crystals is, if anything* ***more complex,*** *and further from the capabilities of the unimaginative uninventive Skilled Person in my respectful view, based on the experience of Dr. Park which I have accepted and that of Dr. Myerson referred to at para 234 above. Apotex's witnesses confirm a number of points,* ***a central one being the fact that identification of crystals was not predictable****.* [*Apotex*; para 243; emphasis added]
>
> *Skilled persons* ***would not know in advance how a crystalline solid (if any) of a given compound could be made, how many different crystal forms of that***

[1] *Pfizer Canada Inc. v. Apotex Inc.*, 2017 FC 774.
[2] *Pfizer Canada Inc. v. Teva Canada Limited*, 2017 FC 777.
[3] *Apotex Inc. v Sanofi Synthelabo Inc.,* 2008 SCC 61.
[4] *AstraZeneca Canada Inc. v. Apotex Inc.*, 2017 SCC 36.

> ***compound might exist (including hydrated and solvated forms), what those forms would be, or what properties those forms would have****. They would know that some salts might crystallize, some might form amorphous forms, but they would also know that other salts would neither form into crystals.* [*Apotex*; para. 231; emphasis added]
>
> *…**It was not possible to predict at the outset of a polymorph screen how many solid forms would identified, what they would be, or what solid forms would result from any particular method or set of conditions****.* [*Apotex*; para. 232; emphasis added]
>
> *Pfizer says that all the experts agree that **the existence and properties of crystal forms cannot be predicted in advance** of their having been successfully made and tested. A Skilled Person would not know nor could he or she predict that Form I ODV succinate existed nor could they identify or predict what properties it would have, or how if at all, it could be prepared. **In my respectful view this is an accurate summary**.* [*Teva*; para. 258; emphasis added]

The fact that general methods to prepare crystalline forms are known in the art does not detract from such unpredictability

Regarding the issue of the knowledge of methods of preparation in the art, the same Court concluded that such knowledge is <u>insufficient</u> for a finding that a particular crystalline form would be obvious:

> *In my respectful view, the Skilled Person would not know nor could he or she predict that ODV succinate salt would form as a solid, whether that solid would form as a crystal, or what the properties of a hypothetical crystalline solid would be. **This is the case regardless of the fact that salt screens were generally known as were, also in general terms, crystallization and polymorph screens**.* [*Apotex*; para. 236; emphasis added]
>
> *… **A general knowledge of salt screens and what was known of crystallization and polymorph screening, merely provided possibilities** for the Skilled Person to conduct research, studies and further experiments which in this case were significant and in the nature of a research program particularly in the area of crystallization and polymorph screening. **This is not enough**; every Court that has reviewed this matter has agreed that mere possibilities do not satisfy the obvious to try set out in Sanofi.* [*Apotex*; para. 296; emphasis added]

> *… As Sanofi put it,* ***knowing these procedures existed is of no account because the evidence does not prove it was more or less self-evident to try them****: "a possibility of finding the invention is not enough. The invention must be self-evident from the prior art and common general knowledge in order to satisfy the 'obvious to try' test. That is not the evidence in this case." [para 85] That is not the evidence in this case either:* ***the invention was not self-evident from the prior art and the common general knowledge on the facts of this case****.* [*Apotex*; para. 299; emphasis added]
>
> *Teva argues that because salt screens and polymorph tests, among other things, were generally known in the prior art, it would be more or less self-evident to the Skilled Person that Form I ODV succinate, i.e., what is being tried, ought to work.* ***I disagree. A general knowledge of salt screens and what was known of polymorph tests merely provided possibilities*** *for conducting research, studies and further experiments which in this case was in the nature of a research program.* ***This is not enough; every Court that has reviewed this matter has agreed that mere possibilities do not satisfy the obvious to try set out in Sanofi****.* [*Teva*; para. 267; emphasis added]

On the question of utility, the Federal Court first reiterated the principles set forth by the Supreme Court in *AstraZeneca*, summarizing the proper approach as follows, and noting in particular that (1) utility may be established by demonstration or sound prediction and (2) the requirements are minimal:

> *The first question is to identify the subject-matter of the invention as claimed in the patent. The second question the Court must ask is whether that subject-matter is useful - is it capable of a practical purpose (i.e. an actual result). The utility must be either* ***demonstrated or soundly predicted****.* ***Only a scintilla of utility is required****.* [*Teva*; para. 324, emphasis added]

On applying this test, the Court then noted that basic properties such as stability are sufficient to establish utility:

> *Pfizer says that the usefulness, the utility, of Claims and 9 is its usefulness as a stable, solid state form of ODV succinate.* ***I agree*** *… Stability (i.e., the tendency not to change to other forms) is an important property for a new crystal form...* [*Apotex*; para. 340; emphasis added]

> *Apotex disagrees saying that stability is one of the physical properties of the drug (e.g., mass, colour, melting point, stability, etc.), and that utility it is what the drug can do as a practical matter (i.e, treat disease) and not its properties.* ***I disagree*** [*Apotex*; para. 341; emphasis added]

We now turn to the consultation document, with reference to the Section numbers.

Section 17.08.01 - Considerations respecting anticipation and obviousness

The draft guidelines for assessing obviousness of a new crystalline form appear to go beyond the criteria established by the authorities, such as the cases on point discussed above. The draft guidelines suggest that inventiveness may be acknowledged under two broad situations: (1) where the crystalline form can only be produced by an inventive process, and/or (2) if the new form provides an unexpected benefit (even if produced using standard techniques) and this unexpected benefit is disclosed in the application as-filed. Satisfying one or both of these criteria, which certainly support inventiveness, does not appear to be necessary for a finding of non-obviousness, based on the principles established by the Federal Court discussed above. Rather, based on the well-established unpredictability in the field, a new crystalline form will by definition generally be considered to be non-obvious. We thus suggest that the following section be amended to read:

> When assessing the obviousness of a new crystalline form (e.g., polymorph) of a known small chemical molecule, the unpredictability in the existence, production and identification of a particular new crystalline form will generally support the inventiveness of the new form, regardless of whether the form is produced by an inventive process or by basic crystallization techniques that are standard in the field. [insert references to *Apotex* and *Teva* noted above] It follows that in this unpredictable state of the art, the production and identification of a new crystalline form will in itself likely be sufficient to support the non-obviousness of the solid form.
>
> Another factor to consider is the process by which the new form is produced, in that production of the new form using an inventive process further supports inventiveness. Such a process would generally go beyond the mere application of common general knowledge solutions and routine experimentation.
>
> In addition, disclosure in the originally-filed application that the form provides an unexpected benefit, such as a beneficial physiochemical property attributable to the form itself, is a further factor supporting inventiveness. Since beneficial physicochemical properties are generally not predictable, they are generally considered as unexpected. It follows that an unexpected beneficial property may further support the non-obviousness of the solid form.

> 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 difference or improvement in one or more physicochemical properties compared to the prior art form(s) of the same chemical molecule. 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 or an explicit statement of benefit provided elsewhere in the application, such statements would not be considered during an obviousness assessment.
>
> 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 nonetheless be considered non-obvious due to the unpredictability in the existence, production and identification of a particular new crystalline form.

Section 17.08.02 - Considerations respecting utility

As established by the Supreme Court and as noted in the proposal, utility may be established by demonstration or sound prediction. However, the proposed section appears to sometimes set a higher bar for utility of a new crystalline form than that recently assessed by the Federal Court in the cases discussed above. In these cases on point, the Federal Court has established that only a “scintilla” of utility is required, and that for example the simple stability of a new crystalline form is sufficient to support its utility.

The draft also seems to suggest that in certain cases it is not possible to establish utility via sound prediction. It does not seem appropriate to preclude the possibility of relying on sound prediction in one technological area, particularly given the fact that drug development is constantly evolving. We thus believe that the section should be worded to permit the requisite flexibility required for addressing a constantly evolving technological field, always noting that the approach established by the Supreme Court (demonstration or sound prediction) be applied to a given case.

We thus suggest that proposed section 17.08.02 be amended to read:

> 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.

Further, basic properties such as stability may be sufficient to support the utility of a new crystalline form [insert references to *Apotex* and *Teva* noted above].

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.

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).

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.

Section 17.08.05 - Examples

Example 1:

We disagree with the obviousness analysis in Scenario A. As noted above, the requirement of an unexpected benefit is inconsistent with the principles established by the Federal Court. The precise identification of Form II is unpredictable, and therefore non-obvious. The fact that generally known methods and solvents were used to produce Form II is irrelevant.

Example 2:

While we agree with the conclusion of non-obviousness, we disagree that it was necessary that Form III be produced by an inventive process.

Further, it would appear that the main reason to include Examples 1 and 2 would be to illustrate the non-obviousness criteria discussed earlier in the draft, which we believe, as discussed above, go beyond and are inconsistent with those established by the Federal Court in clear cases on point. Thus perhaps the Examples section may be condensed, or revised to simply provide examples of sample claim formats.

Conclusion

To summarize, our main concerns are the guidelines concerning the assessment of obviousness and utility. Since they issued relatively recently, we appreciate that the *Apotex* and *Teva* decisions of the Federal Court noted above may not have been available for consideration during preparation of the initial draft. We believe that these decisions, which concerned a claim directed to a novel crystalline form of a compound, are informative and would be useful to consider in the context of these examination guidelines.

FICPI Canada wishes to thank CIPO for the opportunity to provide these comments and invites CIPO to contact the undersigned should it have questions about them.

Yours truly,

FICPI Canada
Serge Shahinian, Secretary, on behalf of Coleen Morrison, President