Citation: Anika Therapeutics, Inc. (Re), 2023 CACP 17
Commissioner's Decision #1650
Décision du commissaire nº1650
Date: 2023-06-12

TOPIC: O00 Obviousness

SUJET: O00 Évidence

Application No. 2,633,957
Demande n^{o} 2 633 957

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 2,633,957 having been rejected under subsection 30(3) of the *Patent Rules* (SOR/96-423) as they read immediately before October 30, 2019 (the former *Patent Rules*), has consequently been reviewed in accordance with paragraph 199(3)(c) of the *Patent Rules* (SOR/2019-251). The recommendation of the Patent Appeal Board and the decision of the Commissioner are to refuse the application.

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INTRODUCTION

[1] This recommendation concerns the review of rejected Canadian patent application number 2,633,957, which is entitled “Treatment of arthritis and other musculoskeletal disorders with crosslinked hyaluronic acid” and owned by Anika Therapeutics Inc. A review of the rejected application has been conducted by a Panel of the Patent Appeal Board pursuant to paragraph 199(3)(c) of the *Patent Rules*.

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

BACKGROUND

The Application

[3] The application was filed under the *Patent Cooperation Treaty* and has an effective filing date in Canada of December 13, 2006. It was laid open to public inspection on June 21, 2007.

[4] Insofar as the claims on file are concerned, the rejected application relates to the use of a combination of a hyaluronic acid (HA) derivative and the anti-inflammatory drug triamcinolone hexacetonide for treating a musculoskeletal disorder in a subject’s articular site.

[5] The claims under review are claims 1 to 4 dated June 12, 2017 that were rejected in the FA (the claims on file).

Prosecution history

[6] On February 22, 2019, a Final Action was written under subsection 30(4) of the former *Patent Rules*. The Final Action states that the subject-matter of claims 1 to 4 is obvious contrary to section 28.3 of the *Patent Act*.

[7] In the Response to the Final Action dated August 19, 2019, the Applicant submitted arguments as to why the subject-matter of claims 1 to 4 is non-obvious

in view of the cited prior art references and therefore complies with section 28.3 of the *Patent Act*.

[8] On January 21, 2020, the application was forwarded to the Patent Appeal Board for review under paragraph 199(3)(c) of the *Patent Rules* along with a Summary of Reasons explaining that the rejection is maintained as the Applicant's arguments presented in the Response to the Final Action (RFA) are not persuasive.

[9] In a letter dated January 27, 2020, the Patent Appeal Board forwarded a copy of the Summary of Reasons to the Applicant and requested that they confirm their continued interest in having the application reviewed.

[10] In a letter dated April 27, 2020, the Applicant confirmed their interest in having the review proceed.

[11] The present Panel was formed to review the rejected application under paragraph 199(3)(c) of the *Patent Rules*. On March 28, 2023, the Panel sent a Preliminary Review letter detailing our preliminary analysis and opinion that the subject-matter of claims 1 to 4 is obvious, contrary to section 28.3 of the *Patent Act*.

[12] The Preliminary Review letter also provided the Applicant with an opportunity to make oral and/or written submissions.

[13] On April 18, 2023, a phone communication from the Agent on file indicated that the Applicant declined the opportunity for an oral hearing and further indicated that written submissions will be provided no later than April 28, 2023, if any. As no written submissions were received by April 28, 2023, the Panel completed its review based on the written record.

Issues

[14] In view of the above, whether the subject-matter of claims 1 to 4 is obvious, contrary to section 28.3 of the *Patent Act*, is the sole issue to be considered in this final review.

PURPOSIVE CONSTRUCTION AND ESSENTIAL ELEMENTS

Legal background and principles

[15] According to *Free World Trust v Électro Santé* Inc, 2000 SCC 66 and *Whirlpool Corp v Camco Inc*, 2000 SCC 67, a purposive construction of the claims is performed from the point of view of the person of ordinary skill in the art (POSITA) in light of the relevant common general knowledge (CGK) and considers the specification and drawings. In addition to interpreting the meaning of the terms of a claim, purposive construction distinguishes the essential elements of the claim from the non-essential elements. Whether or not an element is essential depends on the intent expressed in or inferred from the claim, and on whether it would have been obvious to the POSITA that a variant has a material effect upon the way the invention works.

[16] We consider that all elements set out in a claim are presumed essential unless it is established otherwise or such presumption is contrary to the claim language.

The claims on file

[17] There are 4 claims on file that read as follows:

> 1. Use of a combination of an effective amount of a hyaluronic acid (HA) derivative and an effective amount of an anti-inflammatory drug for treating a musculoskeletal disorder in a subject's articular site, wherein carboxyl functionalities of the HA derivative are each independently derivatized to include an N-acylurea or O-acyl isourea, or both N-acylurea and O-acyl isourea; the HA derivative including at least one crosslink represented by the following structural formula:
>
> HA'–U–R_2–HA'
>
> wherein:
>
> each HA' is the same or different such that the crosslink is an intermolecular or intramolecular crosslink;
>
> each U is independently an optionally substituted O-acyl isourea or N-acyl urea; and

each R_2 is independently phenylene; and

wherein the anti-inflammatory drug is triamcinolone hexacetonide.

2. Use of a combination of an effective amount of a hyaluronic acid (HA) derivative and an effective amount of an anti-inflammatory drug for the preparation of a medicament for treating a musculoskeletal disorder in a subject's articular site, wherein carboxyl functionalities of the HA derivative are each independently derivatized to include an N-acylurea or O-acyl isourea, or both N-acylurea and O-acyl isourea; the HA derivative including at least one crosslink represented by the following structural formula:

HA'–U–R_2–HA'

wherein:

each HA' is the same or different such that the crosslink is an intermolecular or intramolecular crosslink;

each U is independently an optionally substituted O-acyl isourea or N-acyl

urea; and

each R_2 is independently phenylene; and

wherein the anti-inflammatory drug is triamcinolone hexacetonide.

3. A combination of an effective amount of a hyaluronic acid (HA) derivative and an effective amount of an anti-inflammatory drug for use in treating a musculoskeletal disorder in a subject's articular site, wherein carboxyl functionalities of the hyaluronic acid derivative are each independently derivatized to include an N-acylurea or O-acyl isourea, or both N-acylurea and O-acyl isourea; the HA derivative including at least one crosslink represented by the following structural formula:

HA'–U–R_2–HA'

wherein:

each HA' is the same or different such that the crosslink is an intermolecular or intramolecular crosslink;

each U is independently an optionally substituted O-acyl isourea or N-acyl

urea; and

each R_2 is independently phenylene; and

wherein the anti-inflammatory drug is triamcinolone hexacetonide.

4. The use of claim 1 or 2, or the combination of claim 3, wherein the HA derivative is for administration to the subject by an intra-articular injection.

The POSITA and the relevant CGK

[18] The Preliminary Review letter, on pages 5 to 6, states the following with regard to the identity of the POSITA and their expected CGK:

> The FA defines the POSITA as follows:
>
> > The person skilled in the art is considered to at least include a team of pharmacologists and pharmaceutical/medical chemists having experience with, or knowledge of, the use of hyaluronic acid (HA) derivatives; and of anti-inflammatory drugs such as corticosteroids for treating a musculoskeletal disorder in a subject's articular side and for providing pain relief.
>
> The RFA does not contest or otherwise comment on the identity of the POSITA.
>
> With respect to the relevant CGK, the FA states the following:
>
> > The treatment of musculoskeletal disorder with crosslinked HA derivatives or with anti-inflammatory drugs such as corticosteroids is well-known in the art and is therefore part of the common general knowledge (CGK) of the person skilled in the art. The residence time of derivatized HA that leads to prolonged pain relief and the use of

corticosteroids that leads to rapid relief when administered to articular sites, are also part of the CGK.

It is our understanding that the RFA on pages 2 and 3 submits the following with regard to CGK:

- All corticosteroid are not alike and not interchangeable. Different corticosteroid have different properties and are not simply interchangeable; and

- HA viscosity varies widely in the presence of other compounds.

Having reviewed the specification as whole, as well as the prior art cited in the FA, we consider that the characterization of the POSITA found in the FA is reasonable and we adopt it for the purposes of this preliminary review.

With respect to CGK, it is our preliminary view that intra-articular crosslinked HA derivatives therapy in osteoarthritic joints as well as intra-articular (IA) corticosteroid therapy in osteoarthritis joints are part of the CGK (as evidenced by Uthman et al. "Intra-articular therapy in osteoarthritis, *Postgrad Med J.*, 2003 Aug;79(934):449-53 and introduced here in the record as D13). We agree with the FA that it was CGK that HA treatments typically lead to prolonged pain relief and that corticosteroids treatments typically lead to rapid relief when administered to articular sites.

It is also our preliminary view that triamcinolone hexacetonide and triamcinolone acetonide are among the most commonly used injectable corticosteroids (as evidenced by Schumacher et al., "Injectable corticosteroids in treatment of arthritis of the knee", *Am J Med.*, 2005 Nov; 118(11):1208-14 and introduced here in the record as D14).

Further, we are of the preliminary view that it is CGK that different corticosteroids may have different properties relevant to the treatment of osteoarthritis but it was also CGK that different corticosteroids may have similar or identical properties relevant to the treatment of osteoarthritis. Therefore, different corticosteroids are not necessarily interchangeable or not interchangeable. It is a contextual and factual driven inquiry. We find the same with regard to an impact of the presence of another compound on the HA viscosity that is significant enough to be relevant to the treatment of osteoarthritis; it is a contextual and factual driven inquiry.

[19] In the absence of submissions from the Applicant, we adopt these characterizations for the purposes of this final review.

Essential elements

[20] On page 6 of the Preliminary Review letter, we expressed our preliminary view on the essential elements of the claims:

> We consider that the POSITA reading claims 1 to 4 would understand that there is no use of language in any of the claims indicating that any of the elements are optional, or a preferred embodiment. Although the claims encompass alternatives, we consider that the POSITA would understand that the element represented by one of said alternatives is essential. Further, there is no indication on the record before us that any claim elements are non-essential. It is therefore our preliminary view that the POSITA would consider all of the elements of claims 1 to 4 as essential.

[21] In the absence of submissions from the Applicant, we maintain the above identification of the claim elements that are essential in this recommendation.

OBVIOUSNESS

Legal background and principles

[22] Section 28.3 of the *Patent Act* sets out the statutory requirement that the claimed subject-matter must not have been obvious to the POSITA:

> 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; and

(b) information disclosed before the claim date by a person not mentioned in paragraph (a) in such a manner that the information became available to the public in Canada or elsewhere.

[23] In *Apotex Inc v Sanofi–Synthelabo Canada Inc,* 2008 SCC 61 [Sanofi], the Supreme Court of Canada states that it is useful in an obviousness inquiry to follow the following four-step approach:

> (1) (a) Identify the notional "person skilled in the art";
>
> (b) Identify the relevant common general knowledge of that person;
>
> (2) Identify the inventive concept of the claim in question or if that cannot readily be done, construe it;
>
> (3) Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed;
>
> (4) Viewed without any knowledge of the alleged invention as claimed, do
>
> those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?

[24] In the context of the fourth step, the Court in Sanofi states that it may be appropriate in some cases to consider an "obvious to try" analysis.

[25] The Court in Sanofi identifies the following non-exhaustive factors to be considered in an obvious to try analysis [defined terms added]:

> Is it more or less self-evident that what is being tried ought to work? Are there a finite number of identifiable predictable solutions known to persons skilled in the art? [the Self-Evident Factor]
>
> What is the extent, nature and amount of effort required to achieve the invention? Are routine trials carried out or is the experimentation prolonged and arduous, such that the trials would not be considered routine? [the Extent and Effort Factor]

> Is there a motive provided in the prior art to find the solution the patent addresses? [the Motive Factor]

Analysis

The POSITA and the relevant CGK

[26] The POSITA and the relevant CGK have been identified above as part of the purposive construction of the claims. Although in this context the information forming the relevant CGK is identified using the publication date, this information is also considered CGK at the claim date and is therefore relevant for assessing obviousness.

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

[27] In the Preliminary Review letter on page 8, we identified the inventive concepts of the claims on file:

> In this assessment, we take into account all of the essential elements of the claims. We consider that the essential elements of independent claims 1 to 3 are the following:
>
> 1. Use of a combination of:
>
> a) an effective amount of an HA derivative as defined in claims 1 to 3; and
>
> b) an effective amount of triamcinolone hexacetonide.
>
> 2. for treating a musculoskeletal disorder in a subject's articular site.
>
> We also consider that administration to the subject by an intra-articular injection is an essential element of dependent claim 4.
>
> In our preliminary view, the combination of essential elements of claims 1 to 4 represent their inventive concepts as well.

[28] In the absence of submissions from the Applicant, we maintain the above identification of the inventive concepts of the claims on file for the purposes of this final review.

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

[29] In the Preliminary Review letter on pages 9 and 10 we introduced and described the prior documents cited in the Final Action that we found the most relevant to the instant obviousness inquiry and noted the differences with the inventive concept of the claims:

D1:	EP0416250	Prestwich et al.	13 March 1991
D2:	US2005/0136122	Sadozai et al.	23 June 2005

D10: Ozturk et al., "The safety and efficacy of intraarticular hyaluronan with/without corticosteroid in knee osteoarthritis: 1-year, single-blind, randomized study", *Rheumatology International,* 26/4, 314-319, 10 February 2005 (online).

D1 discloses crosslinked HA derivatives, said crosslinked HA derivatives being useful as vitreous replacements, joint treatments or adjuncts in wound healing. D1 further teaches that the disclosed crosslinked HA derivatives can be advantageously used to introduce and control the release of therapeutic drugs because they remain at the site of administration where it is needed, for example to an intra-articular site, rather than allowing the systemic dispersion of the therapeutic drug. The HA derivatives of the claims on file are specifically taught to be amongst the disclosed crosslinked HA derivatives that can be advantageously used to introduce and control the release of therapeutic drugs and are exemplified in Example 6 on page 10 of D1.

D2 discloses crosslinked HA compositions, including crosslinked HA derivatives encompassed by the claims on file (see paras [0085] to [0087]). D2 discloses known uses of HA, including as adjuncts to synovial fluid in joints. D2 also teaches that the disclosed crosslinked HA derivatives have advantages over the commercially available hyaluronan and other known crosslinked HA derivatives, namely a

desirable balance of *in vivo* mechanical and biostability properties balanced with surgical/administrative usability. D2 further teaches at para [0017] that the disclosed crosslinked HA derivatives are also effective as a drug delivery vehicle that exhibits the effect of increasing biostability along with effective drug release properties and effective administrative properties.

D10 teaches that, when used alone, the clinical improvement is “rapid but short-lived for corticosteroids, delayed but prolonged for HA” (see page 317). D10 discloses the use of combined IA injections of HA and triamcinolone acetonide for treating osteoarthritis in a subject. D10 also discloses that the patient group that received a combination of HA and triamcinolone acetonide experienced a significant pain relief earlier than the group that received HA alone and that the observed effects of combined IA corticosteroids and HA injections should be considered as a rapid and prolonged effect in improvement of knee osteoarthritis. D10 concludes on page 318 that [emphasis added]:

> [T]his study demonstrates that HA together with corticosteroid provides rapid pain relief, has beneficial effects during 1 year after treatment, is well tolerated, and has no deleterious effects on joint structure in the management of knee OA. For the choice of IA treatment in patients with knee OA, our findings support that HA combined with corticosteroid should be prefer instead of HA alone.

It is our preliminary view that the difference between the matter cited as forming part of the “state of the art” and the inventive concept of the claims is that none of these documents, or the CGK, discloses a combination comprising the HA derivative as defined in the claims on file and triamcinolone hexacetonide for treating a musculoskeletal disorder in a subject’s articular site.

[30] In the absence of submissions from the Applicant, we maintain the above view with regard to the difference between the matter cited as forming part of the “state of the art” and the inventive concept of the claims.

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?

[31] In the Preliminary Review letter on pages 10 to 17, we provided reasons as to why in our preliminary view it would not have required any degree of invention from the POSITA to use an HA derivative as disclosed in either D1 or D2 and to combine it with any of the most commonly used injectable corticosteroids, including triamcinolone acetonide as disclosed by D10 or triamcinolone hexacetonide as an obvious alternative [emphasis in the original]:

> The Federal Court of Appeal has reminded at para 65 of *Bristol-Myers Squibb Canada Co v Teva Canada Limited*, 2017 FCA 76, that the instant step of the obviousness analysis is concerned with whether bridging the difference between the prior art and a second point constitutes steps that require any degree of invention:
>
> > It may be helpful to keep in mind that the obviousness analysis asks whether the distance between two points in the development of the art can be bridged by the Skilled Person using only the common general knowledge available to such a person. If so, it is obvious. The first of those points is the state of the prior art at the relevant date. References in the jurisprudence to "the inventive concept", "the solution taught by the patent", "what is claimed" or simply "the invention" are attempts to define the second point.
>
> In the present case, what must be considered is whether it would have required any degree of invention from the POSITA, based on the disclosures of D1, D2, D10 and the relevant CGK, to use combined IA injections of HA and a corticosteroid for treating osteoarthritis in a subject as disclosed in D10 but wherein HA is replaced with an HA derivative as disclosed in either D1 or D2 and wherein triamcinolone hexacetonide is used instead of triamcinolone acetonide.
>
> It is our preliminary view that it would not have required any degree of invention from the POSITA to use an HA derivative as disclosed in either D1 or D2 and to combine it with any of the most commonly used injectable corticosteroids, including

triamcinolone acetonide as disclosed by D10 or triamcinolone hexacetonide as an obvious alternative.

Further, and for the reasons that follow, it is our preliminary view that the POSITA would not consider that the combination recited in the independent claims that comprises a specific HA derivative and triamcinolone hexacetonide is associated with any relevant surprising or unexpected effects in view of their CGK and/or the teachings of the instant description and thus, these findings do not support that the combination recited in the independent claims is inventive on that basis.

In that regard, it is our understanding that the RFA submits that the combination recited in the independent claims comprises an HA derivative and triamcinolone hexacetonide that cooperate in an unexpected manner to give a non-obvious effect, namely both rapid and prolonged pain relief.

The description on page 3 states the following:

> With the present invention, the residence time of HA in the joints can be improved, providing longer therapeutic effect, which in turn can reduce the frequency of administration, e.g., intra-articular injections, in OA patients, but yet effecting the efficiency and safety typical of uncrosslinked HA. In particular, co-therapy of the crosslinked HA in combination with a corticosteroid can provide rapid pain relief due to the presence of the corticosteroid, and prolonged pain relief due to the presence of the crosslinked HA.

In our preliminary view, the POSITA would understand from the above passage that each element of the claimed combination would cooperate to the treatment of a musculoskeletal disorder in a subject's articular site through their respective independent, typical and expected mechanism of action as well as their associated pain relief timing and duration; delayed and prolonged for the HA derivative versus fast-acting for the corticosteroid triamcinolone hexacetonide. The above passage of the description is aligned with the CGK described above in the "The POSITA and the relevant CGK" section and also aligned with the teachings of D10 on pages 314 and 317. In other words, both rapid and prolonged pain relief effects were expected from a combination of an HA derivative and the corticosteroid triamcinolone hexacetonide on the basis of CGK and/or the teachings of D10.

We also note that the specification does not exemplify the use of a combination of an HA derivative and triamcinolone hexacetonide for treating a musculoskeletal disorder in a subject's articular site. The only reference to triamcinolone hexacetonide is found on page 19, line 13 of the originally filed description wherein triamcinolone hexacetonide is presented as one of several corticosteroids that could be used as a second bioactive agent. The specification fails to suggest any unexpected effect associated with the combination of an HA derivative and triamcinolone hexacetonide versus a combination of an HA derivative with any of the other corticosteroids listed on page 19, lines 13 to 15 or the HA derivative/ corticosteroid combinations described in example 8 and prophetic examples 9 to 14.

It is also our understanding that the Applicant relies on a declaration from Chia-En Lin, Ph.D. signed on June 13, 2012 (Lin Declaration) as evidence of unexpected non-obvious effects associated with the claimed combination. We are of the preliminary view that the Lin Declaration is not relevant to the instant inquiry as to whether the claimed subject-matter was obvious before the claim date of December 14, 2005 for the following reasons.

First, we consider that the case law does not indicate that the inventiveness of a claimed subject-matter may be ascertained by turning to evidence outside of a patent application disclosure in cases where the alleged benefit or advantage is neither mentioned in the claim, indicated in the remainder of the specification nor reasonably derivable by the POSITA from the information contained in the specification. To the contrary, we consider that the basis for understanding the claimed invention for the purpose of determining its compliance with the patentability requirements of the *Patent Act* must be found within the four corners of the patent application: see Whirlpool at para 49(f).

Second, the Federal Court in *Janssen-Ortho Inc v Novopharm Ltd,* 2006 FC 1234 offered the following relevant reasoning, at para 113, as to why subsequently recognized advantages would not assist the inquiry as to inventive ingenuity and noted that such advantages may themselves be the subject of a subsequent patent:

> 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. This factor is of limited usefulness in considering inventive ingenuity as of the date

> of the invention. The recognition of later advantages, if unexpected, may themselves be the subject of a patent. To the extent that the United States Courts in cases such as Re Zenitz 33 F. 2d 924 have placed weight upon subsequently discovered advantages that is not the law here. Little, if any, weight should be put on this factor.

The Court applied the above reasoning to the facts of the case at para 114 [emphasis added]:

> Levofloxacin has achieved good acceptance in combating microbes associated with strep pneumonia and in treating infections of the eye. Neither of these uses are specifically suggested in the patent. No weight is given to these subsequent uses.

On appeal, the above rationale has been specifically acknowledged by the Federal Court of Appeal at para 26 of *Novopharm Ltd v Janssen-Ortho Inc,* 2007 FCA 217:

> 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 can imagine a situation where the commercial success of an invention is attributable to a subsequently recognized advantage, but that would not assist the inquiry as to inventive ingenuity. 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.

For the foregoing reasons, we therefore consider that no weight should be given to the data in the Lin Declaration.

The RFA also submits that based on the following passage of D1 (page 3, lines 22 to 25), the POSITA would have expected that a composition that includes an HA derivative and triamcinolone hexacetonide in combination as recited in the claims on file would provide slow release of triamcinolone hexacetonide, and would thus be unable to provide rapid pain relief:

> In use, the hydrophobic modified regions bind lipophilic drugs through weak non-bonded interactions, thereby slowing the diffusion of the drug from the site of administration of a water-soluble, modified hyaluronic acid-drug combination.

It is our preliminary view that the POSITA would consider that the above passage relates to the D1 teachings that the disclosed crosslinked HA derivatives can be advantageously used to introduce therapeutic drugs at a given site because the combination would remain at the site of administration where it is needed, for example to an intra-articular site, rather than allowing the systemic dispersion of the therapeutic drug. Thus, it is our preliminary view that the above passage would not suggest to the POSITA that combining the disclosed HA derivatives with a therapeutic drug would prevent said drug from exerting its expected therapeutic effect at the administration site. In any case, and as noted above, it is our view that D10 specifically teaches that combined IA corticosteroids and HA injections provide a rapid (corticosteroid effect) and prolonged (HA effect) pain relief effect.

With regard to the submission that the POSITA would not be motivated to replace a given corticosteroid used in combination with HA with another corticosteroid due to viscosity change considerations, we offer the following observations. There is no evidence on the record supporting the view that the POSITA would consider that exchanging triamcinolone acetonide for triamcinolone hexacetonide would significantly affect the viscosity of the resulting combination to be therapeutically relevant to the treatment of osteoarthritis. To the contrary, we note that the instant specification, taken as a whole, but more specifically the passages found on page 19 lines 12 to 15 and examples 8 to 14, rather suggest that the POSITA should not be *a priori* concerned with wide viscosity variations that would be therapeutically relevant when combining different corticosteroids with the recited crosslinked HA derivatives. Moreover, the disclosure and conclusions of D10 specifically suggest to the POSITA that other corticosteroids could be successfully used in combination with HA or HA derivatives.

Now, given that the subject-matter of the present claims relates to therapies for treating a musculoskeletal disorder, a field which could be considered an area of endeavor “where advances are often won by experimentation” (Sanofi at para 68), we therefore have also considered an “obvious to try” analysis.

For a finding that an invention was “obvious to try”, it must have been “more or less self-evident to try to obtain the invention. Mere possibility that something might turn up is not enough” (Sanofi at para 66).

Before considering the facts of the present case, it is worth noting that a finding that it would have been more or less self-evident that what is being tried “ought to work” does not mean that certainty of success is required, otherwise there would be no point in describing it as something “to try”. Indeed, an “obvious to try” analysis is used precisely in areas where advances are won by experiment, so that success cannot be guaranteed before trying (*Les Laboratoires Servier v Apotex Inc*, 2019 FC 616 at para 269). Rather, what must be considered is whether it is more or less self-evident that the “try” ought to work in view of the common general knowledge and the prior art; a mere possibility will not suffice but an amount of uncertainty is allowed in the obvious to try analysis: See *Janssen Inc v Apotex Inc*, 2021 FC 7 at para 135:

> 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.

In view of the foregoing and within the context of the claimed subject-matter, we consider that the relevant question is whether it would have been more or less self-evident to the POSITA, based on the disclosures of D10 and either D1 or D2, and the relevant CGK, that a combination comprising the crosslinked HA derivatives disclosed in either D1 or D2 and any of the most commonly used corticosteroids, including triamcinolone hexacetonide, ought to be effective in treating a musculoskeletal disorder in a subject’s articular site.

Given that D10 concludes that HA together with corticosteroid provides rapid pain relief, has beneficial effects during 1 year after treatment, and further teaches that HA combined with a corticosteroid should be preferred instead of HA alone, we are of the preliminary opinion that it would have been more or less self-evident to the

POSITA that alternate combinations of known crosslinked HA derivatives and CGK corticosteroids would also be expected to work to some degree in advance of routine testing, including combinations of the HA derivatives disclosed in either D1 or D2 and triamcinolone hexacetonide.

Although we considered that the above assessment is largely determinative of the "obvious to try" inquiry in this case, we make the following observations with regard to other non-exhaustive factors to be considered.

Regarding the Motivation Factor, which includes considerations provided in the prior art to find the solution the patent addresses and the motivation to combine the teachings of the cited prior art, we offer the following preliminary views.

We consider that was no specific motivation in the prior art to combine an HA derivative as defined in the claims on file and triamcinolone hexacetonide per se. However, as explained in *AstraZeneca Canada Inc v Mylan Pharmaceuticals ULC*, 2017 FC 142 [AstraZeneca], at paras 148 to 162, specific motivation is not required in order to find that an invention was "obvious", but it is a factor to consider. The question "how specific" to the claim was the motivation is relevant as the more specific to the claim, the more weight motivation may have as a factor in determining whether the claim was obvious to try (see AstraZeneca at para 160).

Although we consider that there was no specific motivation in the prior art regarding the exact claimed combination for treating a musculoskeletal disorder in a subject's articular site, we consider that D10 provides a strong motive to use intra-articular injections that combine HA or HA derivatives and a corticosteroid for the treatment of osteoarthritis as earlier therapeutic effects were observed in subjects that received a combination of HA and a corticosteroid when compared to HA alone. We note that the conclusion of D10 on page 318 broadly refers to corticosteroids and we consider that the POSITA would understand that the overall teachings of D10 suggest that similar results could be expected with other corticosteroids typically used in IA injections. The relevant advantages of crosslinked HA derivatives over HA were commonly known or otherwise disclosed in D1 and D2 and we consider that they provide the general motivation to determine alternate appropriate combinations of HA derivatives and corticosteroids for the treatment of osteoarthritis. Therefore, it is our preliminary view that POSITA would have been motivated by the results disclosed in D10 to use HA or HA derivatives, including the advantageous HA

derivatives disclosed in either D1 or D2, in combination with any of the most commonly used corticosteroids, including triamcinolone hexacetonide, for treating osteoarthritis in an articular site in a subject.

Finally and with respect to the Extent and Effort Factor, we consider that the extent, nature, and amount of effort required to combine the HA derivatives disclosed in either D1 or D2 with any of the most commonly used corticosteroids, including triamcinolone hexacetonide would have been within the POSITA's capabilities as of the claim date.

The Federal Court of Appeal has referred to the actual course of conduct factor as an elaboration of this factor (*Bristol-Myers Squibb Canada Co v Teva Canada Ltd*, 2017 FCA 76 at para 44). In that respect, the only evidence on record as of the claim date is the instant specification itself wherein triamcinolone hexacetonide is mentioned once on page 19 in the context of a list several corticosteroids that could be used as a second bioactive agent. Otherwise, the most relevant exemplary disclosure is, in our view, described in examples 8 to 14. With the exception of Example 8 which illustrates the preparation of a crosslinked HA derivative and the corticosteroid methylprednisolone acetate, the remaining combinations of a crosslinked HA derivative and a corticosteroid described in examples 9 to 14 are prophetic and do not include triamcinolone hexacetonide. Therefore, the description does not indicate or suggest that making and using a combination comprising a crosslinked HA derivative as defined in claims 1 to 3 and triamcinolone hexacetonide would be long or arduous.

Therefore, and taking into account the foregoing considerations of the relevant factors pertaining to an "obvious to try" analysis, we are of the preliminary view that it was obvious to try to obtain a combination comprising an HA derivative as defined in the claims on file and triamcinolone hexacetonide for treating a musculoskeletal disorder in an articular site in a subject.

Conclusion on obviousness

It is our preliminary view that the subject-matter of claims 1 to 4 on file would have been obvious to a POSITA as of the relevant date, in view of either D1 or D2, D10, and the CGK, contrary to paragraph 28.3(b) of the *Patent Act*.

Conclusion

[32] In the absence of submissions from the Applicant, we maintain the above preliminary view and conclude that the subject-matter of claims 1 to 4 on file would have been obvious to a POSITA as of the relevant date, in view of either D1 or D2, D10, and the CGK, contrary to paragraph 28.3(b) of the *Patent Act*.

RECOMMENDATION OF THE BOARD

[33] In view of the above, the Panel recommends that the application be refused on the grounds that the subject-matter of claims 1 to 4 is obvious, contrary to section 28.3 of the *Patent Act*.

Marcel Brisebois	Ryan Jaecques	Christine Teixeira
Member	Member	Member

DECISION OF THE COMMISSIONER

[34] I concur with the findings of the Board and its recommendation to refuse the application on the grounds that the subject-matter of claims 1 to 4 is obvious, contrary to section 28.3 of the *Patent Act*.

[35] Therefore, in accordance with section 40 of the *Patent Act*, I refuse to grant a patent for this application. Under section 41 of the *Patent Act*, the Applicant has six months to appeal my decision to the Federal Court of Canada.

Konstantinos Georgaras

Commissioner of Patents

Dated at Gatineau, Quebec
this 12th day of June, 2023