Commissioner=s Decision #1292

Décision de la Commissaire #1292

TOPICS: O00, J80, K11

SUJETS: O00, J80, K11

Application No : 2,300,723

Demande no : 2,300,723

COMMISSIONER=S DECISION SUMMARY

C.D. 1292 App'n No. 2,300,723

The application relates generally to the use of Botulinum toxin in relieving pain related to muscle activity or contracture, in particular the pain associated with a spasticity condition secondary to a stroke or cerebral vascular event. The focus of the claims is on a specific dosage range of Botulinum toxin.

All of the claims were rejected by the Examiner as being obvious. As a result of the amendments to the claims in response to the Final Action, the Examiner contended that the claims were also directed to an unpatentable method of medical treatment since they included a dosage regimen. The Board found that the claims were obvious and that they were directed to an unpatentable method of medical treatment because the claims sought to fence in a range within which physicians must exercise their professional skill and judgement in any given case. Accordingly the Board recommended that the application be refused.

The Commissioner agreed with the Board=s recommendation and the application was refused.

IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application number 2,300,723 having been rejected under Subsection 30(4) of the *Patent Rules*, the Final Action of the Examiner has been reviewed. The rejection has been considered by the Patent Appeal Board and by the Commissioner of Patents. The findings of the Board and the decision of the Commissioner are as follows:

Agent for the Applicant

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INTRODUCTION

This decision deals with a review by the Commissioner of Patents of the Examiner=s Final Action on patent application no. 2,300,723 entitled AMETHOD FOR TREATING PAIN ASSOCIATED WITH A MUSCLE DISORDER@. The Applicant is Allergan, Inc. The inventors are K. Roger Aoki, Michael W. Grayston, Steven R. Carlson, and Judith M. Leon.

The application relates generally to the use of Botulinum toxin in relieving pain related to muscle activity or contracture, in particular the pain associated with a spasticity condition secondary to a stroke or cerebral vascular event, which is the focus of the pending claims. Botulinum toxin is a generic term for the family of toxins produced by the bacterium *Clostridium botulinum*. The toxins are classified into what are called seven serotypes designated A through G on the basis of their immunological properties. The toxins function by blocking the release of the neurotransmitter acetylcholine from the peripheral nerves, which results in local paralysis and hence relaxation of the muscle afflicted by spasm.

As conceded by the Applicant, Botulinum toxins, particularly type A, have been used in the past to treat a number of neuromuscular disorders and conditions involving spasms. Some of these include strabismus (crossed eyes), blepharospasm (uncontrolled blinking), spasmodic torticollis (abnormal movements or twisting of the neck and head), oromandibular dystonia (sustained mouth closure), and spasmodic dysphonia (uncontrolled vocal fold spasms). It has also been disclosed by the Applicant that other strains of clostridial species such as *C. baratii*, *C. butyricum*, and *C. novyi* can produce botulinum toxins as well. Treatment involves direct injection of the toxin into the affected muscle group which leads to the local paralysis mentioned earlier.

Botulinum toxins are more commonly known in association with botulism outbreaks in humans, which, as disclosed, provided the opportunity to isolate the toxins. The toxins are normally identified through specific antibodies developed against earlier toxins. For example, if the antibody for serotype B neutralizes the biological activity of a toxin, then one knows that what is present is serotype B. Currently there are two common forms of

botulinum toxin type A, one known as DYSPORTJ manufactured by Porton Products Ltd., and the other known as BOTOX7 manufactured by the Applicant, Allergan, Inc.

The potency of the toxin is expressed as a multiple of the LD_{50} value for a mouse, one unit (U) of toxin being defined as being the equivalent to that amount, on a per mouse basis, that kills 50% of a group of Swiss-Webster mice weighing between 17 and 22 grams each. Applicant has disclosed a conversion between toxin mass in nanograms (ng) and units (U). For DYSPORTJ, 1ng = 40 U, and for BOTOX7 , 1ng = 4 U. In the present case the Applicant seeks an exclusive right to a specific dosage range for botulinum toxin, used in the treatment of pain associated with a spasticity condition secondary to a stroke or cerebral vascular event.

BACKGROUND

This application is a divisional application of Patent no. 2,180,011, and as such maintains the parent=s filing date of December 16, 1994. We also note that this case has been given Special Order status as requested by the Applicant. It has been the subject of considerable prosecution which dates back to October of 2000 when the first office action was written. It was rejected by the Examiner on March 9, 2006 in a Final Action in which the Examiner found that all of the claims (1-49) were obvious in view of eight different references, discussed in various combinations. The references applied are set out below. The label numbers assigned to the references have been preserved as they were in the Final Action for ease of reference.

D1 = Revue Neurologique	1992	148:212-214	Mémin et al.
D2 = Lancet	1986	2:245-7	Tsui et al.
D3 = Microbiological Reviews	1992	56:80-99	Shantz et al.
D4 = Arch. Phys. Med. Rehabil.	1990	71:24-6	Dykstra et al.
D7 = Nervenartz	1993	64:64-68	Konstanzer et al.
D11 = Lancet	1988	24:714-717	Hallan et al.
D12 = New Engl. J. Med.	1992	326:349-350	Ludlow et al.
D15 = Mov. Disord.	Oct. 1993	8:479-83	Greene et al.

In response to the Final Action, the Applicant chose to focus the claims on the specific range of dosages of botulinum toxin which were useful in treating pain associated with a muscle disorder, wherein the muscle disorder is a spasticity condition secondary to a stroke or cerebral vascular event. Prior to the Final Action the independent claims were not limited to any particular amount or range, and included claims directed to treating pain and separate claims directed to the treatment of spasticity, with, for the most part, a focus on particular serotypes. Seven claims were substituted for those on file and the Applicant, in its submissions, emphasized that the claims were directed to treating Apain@ and not a spastic muscle. Despite these amendments, the case was forwarded to the Patent Appeal Board on July 17, 2007. In the Summary of Reasons submitted to the

Board by the Examiner, which was forwarded to the Applicant on August 28, 2007, the objection as to obviousness of the claims was maintained based on the previous references applied. The Examiner also, as a result of the amendments made to the claims, contended that the claims no longer complied with section 2 of the *Patent Act* since they now focussed on a Adosage regimen@ and were therefore directed to an unpatentable method of medical treatment. We believe this would be more accurately described as a Adosage range@. In support of this contention the Examiner relied upon an unpublished decision of the Commissioner of Patents. The Board will speak to the matter of this citation later in the analysis with respect to patentable subject matter.

An oral hearing was requested by the Applicant, which took place February 20, 2008 at which time the Applicant was represented by Hélène D=Orio and Élisabeth Wellman-Desbiens of the firm GOWLING LAFLEUR HENDERSON LLP, and Stephen Donovan of Allergan, Inc.. The Patent Office was represented by the Examiner in charge of the application, Dr. Ralph Salvino and his Section Head, Mr. Daniel Bégin. At the hearing, the Applicant submitted both written and oral arguments in response to the objections based on obviousness and unpatentable subject matter. The Applicant, in addition, in response to a suggestion in the Summary of Reasons that the examples disclosed in the present application were hypothetical, made additional submissions in response thereto. However, the Applicant objected to the consideration of this objection by the Board based on the grounds that it was not raised in the Final Action and that AClaims directed to the use of the botulinum toxin for treating spasticity of an arm and a leg, wherein the spasticity is secondary to a stroke were present in the application as originally filed@. We take the Applicant=s position to be that such an objection could have been made at any point in the prosecution and was not prompted by any amendment to the application in response to the Final Action. Therefore, it would not be proper that the Applicant is only being notified of such a problem at this point. This matter is discussed later in this recommendation following considerations of obviousness and patentable subject matter.

ISSUES

The two issues which have been considered by the Board are as follows:

(1) Would claims 1-7 have been obvious in view of the art cited by the Examiner?

(2) Do claims 1-7 fail to comply with section 2 of the *Patent Act* for being directed to a method of medical treatment?

THE CLAIMS

There are only seven pending claims relating to the use of botulinum toxin, which are reproduced below for convenience:

1. The use of from 50 to 300 units of a botulinum toxin for treating pain associated with a muscle disorder, wherein the muscle disorder is a spasticity condition secondary to a stroke or a cerebral vascular event.
2. Use according to claim 1 which is intramuscular.
3. Use according to claim 1 wherein the botulinum toxin is selected from the group consisting of botulinum toxin types A, B, C, D, E, F, and G.
4. Use according to any one of claims 1 to 3 in a human patient.
5. Use of from 50 to 300 units of a botulinum toxin for treating pain associated with spasticity of an arm, hand, or leg, wherein the spasticity is secondary to a stroke.
6. Use according to claim 5 wherein the botulinum toxin is selected from the group consisting of botulinum toxin types A, B, C, D, E, F, and G.
7. Use according to claim 6 wherein the botulinum toxin is type A.

The only point of contention which appears to be present regarding the claim language is whether the limitation as to treating Apain@ differentiates the claimed subject matter from an application in which muscle spasticity is treated. As stated earlier, the patent application contained, prior to the Final Action, claims directed to treating spasticity and claims directed to treating pain. In response to the Final Action, the claims were amended to focus on treatment of pain with the addition of a specific dosage range peculiar to the condition to be treated. In the response the Applicant stated, in relation to the Apain@ limitation:

> It is important to note that the claims are directed to treating pain. The claims are not directed to treating a spastic muscle. As stated in the specification, the pain treated is Aassociated with@ or Arelated to@ spasticity.
>
> .....
>
> It is well known that a muscle becomes spastic because of abnormal efferent signals from the central nervous system (CNS) which travel through motor neurons to the peripheral muscle. Contrarily, pain perceived as arising in a muscle is due to signals which travel from the periphery along sensory neurons to the CNS. Thus, not only is the direction of the neural traffic the opposite (from CNS to periphery for spasticity vs. from periphery to CNS for pain) but as well the pathways themselves differ (motor neurons for spasticity vs. sensory neurons for pain). Clearly therefore treating pain is not the same as or inherent in treating spasticity.

Based on the above arguments the Applicant contends that the claims are restricted to treating pain only and that the spastic muscle itself is not treated. This is consistent with the views expressed by the Applicant at the hearing. The relevant portions of its written submissions are reproduced below:

> Claims 1-7 are not directed to a functional improvement. That is the claims do not encompass relief of the spastic muscle condition. Relief of the spastic muscle by paralysis (i.e. muscle tone reduction) requires a high dose of the botulinum toxin. The inventors discovered that a low dose (i.e. 50-300 units) of a botulinum toxin can be used to treat the pain of post-stroke spasticity, separate from the muscle spasticity itself.
>
> The principle of the claimed invention is based upon a realization that for a patient with post-stroke spasticity the pain experienced by a patient and the muscles spasticity experienced by the patient are two distinct phenomena based upon separate underlying physiological mechanisms, which can be treated separately. Thus, a muscle becomes spastic because of abnormal signals from the central nervous system (CNS) which travel through *efferent motor* neurons to the peripheral muscle. On the other hand, pain perceived by the patient as arising from a muscle, is due to signals which travel from the periphery along *afferent sensory* neurons to the CNS. Thus, spasticity and pain can be distinguished not only in terms of the direction of the neural traffic (from CNS to periphery for spasticity versus from periphery to CNS for pain), but in terms of the pathways themselves, with motor neurons involved in spasticity and sensory neurons involved for pain. It was a realization of and application of these principles which permitted application of the present claimed invention. Prior to the claimed invention, it was not known that the pain (afferent sensory) neurons could be treated with a botulinum toxin separate from the treatment of motor (efferent muscle) neurons.

While the treatment of the pain associated with post-stroke spasticity separate from the treatment of the spasticity itself may be possible, the Board finds, for the reasons that follow, that such a principle is not present in the pending claims, having regard to the specification as a whole.

The claims themselves use the language Afor treating pain@. We would note that on its face this does not state Afor treating pain only@, which is the meaning the Applicant would have us use. However, we must have regard to the specification to determine if there is some other more specific meaning to be allocated to the claim language. In *Whirlpool Corp. v. Camco Inc.* (2000), 9 C.P.R. (4th) 129 (S.C.C.) at 153, Binnie J. repeated the caution of William L. Hayhurst, Q.C. in AThe Art of Claiming and Reading a Claim@ in *Patent Law of Canada* (1994) that:

> [t]erms must be read in context, and it is therefore unsafe in many instances to conclude that a term is plain and unambiguous without a careful review of the specification.

At the hearing the Examiner pointed to Example 10 of the present application as the most relevant to the claimed subject matter, with which the Board would agree. This Example is entitled AThe Use of Botulinum toxin types A-G in the Treatment of Muscle Spasms

and Control of Pain Associated with Muscle Spasms in Spasticity Conditions Secondary to Stroke, Traumatic Brain or Spinal Cord Injury@. Due to its importance in relation to the scope of the claims, we reproduce the passage from this Example below:

> A male, age 70, post-stroke or cerebral vascular event, is injected with 50 to 300 units of Botulinum toxin in the major muscles involved in severe closing of hand and curling of wrist and forearm or the muscles involved in the closing of the legs such that the patient and attendant have difficulty with hygiene. Relief of these symptoms occurs in 7 to 21 days.

There can be no doubt as to the relevance of this Example, as it is the only one dealing with post-stroke spasticity and pain, and discloses the dosage range of 50 to 300 units now claimed by the Applicant. Clearly Athese symptoms@ refers to the Asevere closing of hand and curling of wrist and forearm@ or Athe closing of the legs@. One can only deduce from this context that the treatment and relief of spasticity bring a concomitant control of the associated pain. That is, the pain is not treated separately from the spasticity, as the Applicant has suggested in their arguments. We also note that the title refers both to treatment of muscle spasms and control of pain. While there are numerous references in the description to Arelieving pain@, nowhere is there a suggestion that the pain is treated separately from spasticity for a condition Asecondary to a stroke or cerebral vascular event@ as in claim 1. We note that the specification fails to highlight the issues surrounding the separate treatment of pain as clearly as they were presented to the Board.

At page 8 we find one reference which might be said to allude to treatment only of pain. It is stated in relation to the dosages used in human therapeutic applications that the dosage is (our emphasis added):

> preferably in the ranges from about 80 to about 460 units per patient per treatment, although smaller or larger doses may be administered in appropriate circumstances such as up to about 50 units for the relief of pain and in controlling cholinergic secretions.

If it were possible to treat pain separately from spasticity, it would appear from the above passage that 50 units or thereabouts is the upper limit. Given that the claims specify 50 to 300 units, one must conclude that the claims indicate something other than the sole treatment of pain. Further, at page 10 there is a general discussion of the Examples and the procedure used. At lines 8-13 it is stated (our emphasis added):

> Following injection, it is noted that there are no systemic or local side effects and none of the patients are found to develop extensive local hypotonicity. The majority of patients show an improvement in function both subjectively and when measured objectively.

Clearly functional improvements are important overall, contrary to Applicant=s submissions.

In summary, the Board cannot accept Applicant=s contentions that pain is treated separately from spasticity. In view of the foregoing, the wording of the claims, namely, Afor treating pain@, in conjunction with the claimed range, cannot be interpreted to mean that pain only is treated. With this interpretation in mind, the Board will turn its attention to the outstanding issues.

OBVIOUSNESS

Examiner=s Position

Since the focus of the arguments has shifted significantly in response to the Final Action, the focus no longer being on the choice of particular serotypes, as was the case with former claims 1-34, the Board has endeavoured to extract from the Examiner=s arguments, the portions most relevant to the subject matter of the presently pending claims. In the Final Action the Examiner stated, in part:

> The prior art teaches botulinum toxin type A is effective at treating spasticity or involuntary muscle movement in a wide variety of muscle disorders and that this same treatment produces a concomitant reduction in the pain associated with said spasticity or movement suggesting that there is an association between muscle pain and spasticity.
>
> .....
>
> It is well known in the art that botulinum toxins comprise a family of pharmacologically related toxins (type A through G at the time of publication) that cause flaccid paralysis (see D3 and pages 2, 4 and 5 of the present application).
>
> .....
>
> D4 describes the use of botulinum toxin to treat disorders involving spastic sphincter smooth muscle and not the pain associated with such disorders.
>
> .....
>
> D3 suggests that botulinum toxin may be used to treat a variety of hyperkinetic movement and muscle disorders and the pain brought on by the resultant muscle spasms. D1, D2, D7 and D11 each teach the treatment of a wide variety of neuromuscular disorders/spastic muscles. The treatment disclosed in the teachings of these documents indicate that botulinum toxin is effective at treating the spasticity and pain associated with the neuromuscular disorder/spastic muscle. D11 specifically deals with a smooth muscle disorder with injection of the toxin near the deep part of the external anal sphincter. A skilled person reading such prior art would see that the treatment of muscle spasticity in a neuromuscular disorder/spastic muscle using botulinum toxin by known and established methods will provide a reasonable chance of success

> with respect to a concomitant and significant benefit to treat the pain associated with a given neuromuscular disorder/spastic muscle, including a smooth muscle.
>
> .....
>
> [T]he broad range of botulinum concentrations disclosed in the present application for the claimed uses also do not provide distinct and unobvious guidance to a person skilled in the art. This broad range falls within concentrations disclosed in prior art for botulinum toxin types A or F and their use to inhibit muscle spasticity and muscle pain relief for a variety of cholinergically influenced muscle disorders.

The Examiner, in the Final Action, brought up a point that claims relating to the use of botulinum toxin (particularly type A) to treat pain associated with stroke, cerebral event or brain injury, were previously deleted in response to an objection and therefore it is not appropriate that Applicant is still asserting such claims. However, upon a review of the prosecution it is clear that these claims were maintained in response to the Examiner=s objection, albeit focussing on serotypes other than A or F. Also, the presently pending claims contain the distinction of a particular dosage range. Given these facts, the Board does not consider that such subject matter as that of the present claims was abandoned by the Applicant.

Regarding former claims 35-38, which closely resemble the pending claims with the exception of the dosage range, the Examiner stated:

> D3 clearly establishes the therapeutic uses of botulinum toxin for a wide variety of cholinergically influenced muscle disorders (many of which are skeletal muscle disorders) and indicates that botulinum toxins may potentially be of some benefit to the relief of pain brought on by muscle spasms. However, D3 does not describe how botulinum toxin may be used to effect pain relief in a given muscle disorder. This problem is solved by the teachings of D1 or D2 wherein a method employing botulinum toxin A to treat muscle spasticity in stroke/head injury patients and spasmodic toritcollis patients resulted in significant pain relief. These teachings provide examples of several different muscle groups that can be treated by botulinum toxin A for pain relief. The teachings include details of the amount and mode of administration of botulinum toxin used, such teachings encompass the preferred embodiments of the instant application.
>
> .....
>
> [T]he Examiner argued in said Office action [the one preceding the Final Action] that D1, D2 and D11 each teach the concomitant relief of pain when botulinum toxin A was used to treat spasticity of a variety of different muscle disorders suggesting a link between the relief of muscle pain associated with relaxation of muscle spasticity with botulinum toxin treatment.
>
> .....
>
> [B]oth D1 (see e.g. Abstract, Results and Discussion) and D7 (see e.g. Tables 1-4) disclose the injection of botulinum toxin A into the muscles of the arm, hand and leg of patients who had a stroke for treating spasticity in said muscles with subsequent improvement in their movement/daily life activities.

.....

It is clear from page 3, for example that D7 discloses botulinum toxin A was effective at treating muscle spasticity and pain associated with ischemic injury, brain trauma, cervical myopathy with spastic spinal paralysis and multiple sclerosis in patients in need thereof.

In the brief submitted to the Board the Examiner had the following to say about the presently pending claims:

The examiner cited 8 prior art documents that support the following:

Botulinum toxin has utility in treating a wide variety of cholinergically influenced muscles disorders or spastic muscles conditions (D1-D4, D7, D11, D12 and D15) using claimed botulinum dosage

Botulinum toxin has utility in treating pain associated with a wide variety of cholinergically influenced muscle disorders or spastic muscle conditions (D1-D4, D7, D11, D12, and D15) using the claimed botulinum dosage.

Botulinum toxin has utility in treating spasticity and pain associated with a spastic muscle condition secondary to stroke or a vascular event (D1 and D7), including arm hand or leg i.e. present claimed invention.

Dosage disclosed in D1 and D7 appear to be within claimed dosage when one takes into account the ambiguous nature and lack of detail found in the Example on page 19 of the present application and Applicant=s misinterpretation of the disclosure of said two documents when one takes into account such things as potency of different botulinum toxins, severity of condition, total number of injection sites, etc.

Botulinum toxin serotypes other than serotype A has utility in treating muscle spasticity and pain associated therewith (D12 and D15).

Other important points:

claimed dosage, regardless of whether prior art disclosure is present, does not require inventiveness on the part of a skilled person in the art.

Regarding the dosage disclosed by reference D1, there was considerable debate at the hearing over what amount was disclosed. We will have more to say about this issue in the later analysis. As can be seen from the above comments by the Examiner, he has placed particular emphasis on documents D1 and D7 with respect to the issue of obviousness. This is consistent with the views of the Applicant regarding the most relevant documents.

Applicant=s Position

In the response to the Final Action, after a summary of the references applied, the Applicant had the following to say:

> The closest art cited by the Examiner with regard to the currently pending claims appears to be D1 and D7, and this is confirmed by page 8 of the Office Action. The present claims, in distinction to D1 and D7, are limited to treatment of pain and this limitation is supported by the specification.

The Applicant went on to discuss how the claims were not anticipated by D1 or D7. This is not relevant, as the Examiner objected to the claims as being obvious, not anticipated. The Applicant also commented on the inventiveness of the claims in relation to D1 and D7, stating in part that:

> The present claims are also inventive over D1 and D7 because these references are directed to methods for treating spasticity, alleviation of pain being only a side effect of the methods of D1 and D7. Additionally, the present claims set forth particular methods for treating pain which are not suggested by the spasticity treatment methods of D1 and/or D7. Thus, the present claims are limited to use of from 50 to 300 units of a botulinum toxin. Contrarily, D1 used the entire 50 ng vial to treat patients with post stroke spasticity. As disclosed by D7, 50 ng is 2000 units of toxin. Hence, the claims are limited to using from 2.5% (50/2000) to 15% (300/2000) of the amount of toxin D1 used. There is no motivation in D1 to use only from 2.5% to 15% of the dosage used in D1 because D1 has no interest to treat pain separately from the spasticity.
>
> Similarly, D7 discloses use of from 1000 units to 2000 units (25 ng to 50 ng) of BOTOX7. The claims pending in this application are limited to use of from 50-300 units. Thus, the present claims are limited to use of from 2.5% (50/2000) up to 30% (300/1000) of the dosages used in D7. Again, there is no motivation in D7 to use only from 2.5% to 30% of the dosage used in D7 because D7 (as well as a combination of D1 and D7) has no interest to treat pain separately from the spasticity.

In the submissions before the Board at the hearing, the Applicant summarized the teaching of the references other than D1 and D7, stating that:

> Thus D2, D12, and D14 disclose only treatment of spasmodic torticollis or certain dystonias, not any post-stroke spasticity treatment. D4 and D11 disclose only treatment of certain gastrointestinal (anismus) or urological (urethral) smooth muscle sphinctors. D3 has a brief mention of treating post stroke spasticity.

The Applicant then focussed on D1:

> D1 (Mémin) discloses treatment of eight patients having spasticity with a botulinum toxin. Seven of the eight patients had stroke related spasticity. Six of the eight patients suffered from pain. After treatment, five of the eight patients had pain relieved. It is important to note that D1 is all about functional (i.e. spasticity) improvement, and not at all about pain treatment. Thus, D1 does not disclose that any one of the eight spasticity patients had pain treated separate from their spasticity.

We would point out at this stage that, in view of our conclusion with respect to the scope of the pending claims, it is not necessary that a prior art reference teach that pain be treated separate from spasticity.

The Applicant goes on to discuss the specific dosages disclosed by D1:

> The dosage used in D1 is found in the Results section where it is reported that an average of 9.1 nanograms botulinum toxin was injected into each patient and that all patients, except one, received two sets of injections. It is reported under the Method Section that the botulinum toxin used was from Porton and as such 1 nanogram of the botulinum toxin used contained 40 units of botulinum toxin. D1 therefore teaches use of 364 (that is 9.1 ng X 40 units/ng) units of a botulinum toxin given twice, so that a minimum of 728 units of botulinum toxin was administered to each patient. D1 does mention that as little as 4 ng (or 160 units) of the botulinum toxin was administered, and that there was one patient who received only one set of injections. Significantly though it cannot be determined from D1 that a patient within the scope of present claim 1 (i.e. use of from 50 to 300 units to treat pain associated with spasticity) was treated.
>
> The claims are not obvious in view of D1 because D1 contains no hint for the skilled person to modify, let alone reduce, the administered dose of botulinum toxin for the treatment of pain, at least because D1 discloses that no side effect was observed (page 213, right hand side column, last sentence of D1: A*Aucun effet secondaire local, général, transitoire ou prolongé n=a été relevé.*@). With no side effect observed at the doses given in D1 there would be no motivation for the skilled person to reduce the dosage - because the dosage given in D1 was therapeutically successful and well tolerated.
>
> Finally, D1 teaches away from the present invention or presents a prejudice to lowering the dose of botulinum toxin in that it suggests that the analgesic effect of botulinum toxin could be linked to effects on the muscle tonus (page 214, left hand side column of D1: A*L=effet antalgique ... Il peut être attribué à la disparition de le tension musculaire.*@). Upon reading D1, the skilled person would therefore be unaware that the treatment of pain associated with muscle

spasm disorders could be achieved with doses different (i.e. low doses) from those required for the treatment of muscle spasms (i.e. the high doses used in D1). For these reasons the claims cannot be obvious over D1.

With respect to D7, the Applicant had the following to say:

D7 (Konstanzer) discloses a mixed group of patients treated with the Porton botulinum toxin of which only the three patients 1, 5 and 7 had suffered ischemic insult to the brain, which is a synonym for stroke. As shown by Table 2 on page 519 of D7 patients 1, 5 and 7 received, respectively, 3,000 units (25 ng + 50 ng), 1400 units (35 ng) and 720 units (18 ng) of botulinum toxin. D7 therefore is clearly not novelty destroying as these doses (720 to 3,000 units) are well outside the claimed range of 50 to 300 units.

With regard to obviousness, D7 does not contain any teaching or the slightest suggestion for the skilled person to alter or reduce the administered dose of botulinum toxin to treat pain. In fact, D7 teaches away or presents a prejudice to lowering the doses of botulinum toxin administered in D7 because the last sentence of the second paragraph on the right hand side column on page 520 of D7 states that no side effects were observed after administration of as much as 5,000 units of the botulinum toxin: A*...was aber weder den erwünschten Erfolg brachte, noch unerwünschte Nebenerscheinungen auslöste.*@ Hence D7 provides no motivation to use a low dose of a botulinum toxin (i.e. an amount less than the 720 units lowest dose used in D7 in a patient with post-stroke spasticity).

The lowest dose administered in D7 to any patient was 480 units, as can be determined from page 520, line 5 of D7 under Results (AErgebnisse@) which state that no less than 12 ng or 480 units was administered. Notably, this lowest dose of 480 units administered in D7 was given to Patient 2 who had spasticity due to brain tumor, not due to stroke, to which the present claims are all limited. Thus, according to Table 2 on page 519 of D7 read in conjunction with line 11 on page 518, right hand side column of D7 (A*...bei 1 Patienten ein operativ entfernter Hirntumor.*@) the lowest dose of 480 units in D7 was administered to patient 2 who had spasticity due to brain tumor removal, not a post stroke spasticity as in the present claims.

Furthermore, the entire objective of treatment in D7 was to lower muscle tonus and thereby treat the spasticity. Upon reading D7 the skilled person would be unaware that the treatment of pain associated with muscle spasm disorders could be achieved with doses different (i.e. low doses) from those required for the treatment of muscle spasms (i.e. the high doses of 720 to 5,000 units used in D7). Thus D7 provides no suggestion or motivation to use a dose of from 50-300 units to treat the pain associated with post-stroke spasticity.

We will have more to say about what the Applicant claims is disclosed by the prior art when we review the applied references, below.

In the summary submitted by the Applicant of their position on obviousness at para. 31, it was stated (our emphasis added):

> [I]t is important to note that both D1 and D7 are directed solely to the treatment of muscle spasticity, and that in D1 and D7 any pain relief is only ancillary to relief of the muscle spasm. Contrarily, the claimed invention is directed to relief of the pain, not to relief of the muscle spasm. That is why a low dose of botulinum toxin is claimed - a functional (muscle spasm) result is not claimed and is not within the scope of the claims.

Again, the Board cannot agree with the emphasized passage. To allocate such a meaning to the claims would be inconsistent with the rest of the specification.

Obviousness: Legal Principles [Note: This recommendation includes a supplemental analysis which was prepared as a result of the Supreme Court of Canada=s decision in *Sanofi-Synthelabo Canada Inc. v. Apotex Inc.* 2008 SCC 61, 69 C.P.R. (4th) 251. The supplemental analysis starts at para. 104].

Section 28.3 of the *Patent Act* sets out the conditions under which a claim may be found to be obvious:

> 28.3 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 more than one year before the filing 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.

The oft cited guide for assessing obviousness in Canada is the one recited by Hugessen J. in *Beloit Canada Ltd. v. Valmet Oy* (1986), 8 C.P.R. (3d) 289 at 294 (F.C.A.); rev=g (1984), 78 C.P.R. (2d) 1 (F.C.T.D.):

> The test for obviousness is not to ask what competent inventors did or would have done to solve the problem. Inventors are by definition inventive. The classical touchstone for obviousness is the technician skilled in the art but having no scintilla of inventiveness or imagination; a paragon of deduction and dexterity, wholly devoid of intuition; a triumph of the left hemisphere over the right. The question to be asked is whether this mythical creature (the man in the Clapham omnibus of patent law) would, in light of the state of the art and of common general knowledge as at the claimed date of the invention, have come directly and without difficulty to the solution taught by the patent. It is a very difficult test to satisfy.

In *Novopharm Limited v. Janssen-Ortho Inc.*, (2007), 59 C.P.R. (4th) 116 (F.C.A.), the Federal Court of Appeal, after identifying the previous quote from *Beloit* as the Aaccepted legal test@, endorsed an edited list of factors enunciated by Justice Hughes in the court below which would serve to guide the factual inquiry necessary in assessing obviousness. We will not repeat them here, but it is noted that Sharlow J. cautioned against slavishly following any rigid factual analysis in determining whether an invention would be obvious or not:

> There is no single factual question or a set of questions that will determine every case, or any particular case.

Applicant, in their submissions before the Board, has pointed out *Bayer Aktiengesellschaft v. Apotex Inc.* (1995), 60 C.P.R. (3d) 58 at 79 (Ont. Ct. Gen. Div.) as authority for the idea that obviousness in Canada has the connotation of Aplain as day@ or Acrystal clear@. While this case did put forth these expressions, in *Novopharm, supra*, Sharlow J. reiterated the caution of Justice Hughes that coined phrases or expressions from particular cases are not to be taken as though they are rules of law:

> In this regard phrases such as "worth a try" and "directly and without difficulty" and "routine testing" have been used by the courts. It is not useful to use

> such phrases as they tend to work their way into expressions of law or statements of expert witnesses. Sachs L.J. deprecated the coining of such phrases in *General Tire & Rubber Company v. Firestone Tyre & Rubber Company Limited*, [1972] R.P.C. 195 at pages 211-12.

With this guidance in mind, we turn to a review of the evidence before us and whether or not it renders the claims obvious.

Analysis

The Board must first determine what has been disclosed by the references cited by the Examiner. Like the Examiner and the Applicant, the Board believes it to be clear that D1 and D7 are the most relevant. However, given that it is permissible to look at the cumulative effect of the prior art (see *DeFrees and Betts Machine Co. v. Dominion Auto Accessories Ltd.* (1963), [1964] Ex. C.R. 331; *Windsurfing International Inc. v. Trilantic Corp.* (1985), 8 C.P.R. (3d) 241 (F.C.A.)), the Board would be remiss if it did not consider whether there was some applicable knowledge to be gained from the other references applied.

D2, published in 1986, describes a double-blind study of Botulinum toxin in which type A toxin was used to treat spasmodic torticollis, which is a disorder of the neck muscles causing pulling, turning, or jerking. According to the Summary section of the paper:

> [B]otulinum - A toxin produced both subjective and objective improvement, including significant pain relief in 14 of the 16 patients presenting with pain.

This paper also discloses that botulinum-A toxin has been used in the treatment of other disorders such as strabismus, endocrine orbital myopathy, lateral rectal paralysis, hemifacial spasm and blepharospasm. As for dosage, it is disclosed that each patient was given 100 mouse units (eq. to 40 ng) (50 mouse units (20 ng) per muscle). Each patient was given two treatments 3 months apart, one with toxin and one without. The results indicated both significant functional improvement and pain relief.

D3, published in 1992, is a review paper covering the general properties and use of botulinum toxin as well as other neurotoxins. It is disclosed that botulinum toxin type A was approved in 1989 in the US for the treatment of strabismus, hemi-facial spasm and

blepharospasm in patients 12 years of age and older by direct injection of the toxin into the hyperactive muscle. It was also being used experimentally for the treatment of a number of other dystonias. Dystonia is a term used to describe a neurological movement disorder with sustained muscle contractions, or spasms, causing twisting and repetitive movements. It is stated that botulinum neurotoxins comprise a family of pharmacologically similar toxins that block acetylcholine release from peripheral nerves and cause a flaccid paralysis. The paper focusses on type A as this was the one being used in therapeutic applications. It discloses information about the mechanism of action of the toxin, and its preparation.

At page 84 of this reference several focal dystonias and involuntary movement disorders which have been successfully treated with botulinum type A are listed. Among them is limb spasticity following stroke and other neurological disorders including cerebral palsy, although no specific dosages are given. For blepharospasm the paper points to one study with an average dose of 20 U with no long-term adverse effects. For hemi-facial spasm the authors point to injections of 10 to 20 U as providing relief in 90% of patients treated. With respect to spasmodic torticollis, in 1000 cases improvements have been reported in 50 to 90 % of patients. The authors point out, at the end of page 84, that:

> Botulinum toxin could potentially benefit humans who suffer from a variety of other hyperkinetic movement and muscle tone disorders including tics, tremors, bruxism, and pain brought on by muscle spasms.

The author reported at page 85 that:

> No adverse clinical effects of botulinum toxin have been found in patients who received low doses of botulinum toxin, e.g. 20 U. Single-fiber electromyography analysis has shown that injection of relatively large quantities of botulinum toxin (140 to 165 U) leads to toxin spread, weakening of distant muscles, and uncharacterized subclinical effects (116).

However, it is not clear which conditions or exactly which muscles were treated by using these dosages. Later, the use of 100 U is recommended to prevent dysphagia (inability to swallow), in association with eye muscles and those associated with spasmodic torticollis.

It is also reported that there is considerable concern that patients being treated with botulinum toxin will develop antibodies, particularly with high level injections over several years (see last full paragraph of page 85). However, there is no definite information on when this really becomes a concern. The author later points to the possible use of the other

serotypes, particularly in patients who develop immunity to type A. There is even a suggestion that combinations of botulinum toxins could be more effective in clinical practice than any one type alone (see p. 89, second full paragraph of right hand column).

D4, published in 1990, reports on a double-blind study of the effectiveness of botulinum A toxin in denervating and relaxing a spastic external urethral sphincter. The study involved five men with high spinal cord injuries and detrusor-sphincter dyssynergia. They were given either a low dose of botulinum A toxin or normal saline once per week for three weeks. The initial dose was 140 units of toxin or saline and all subsequent injections were 240 units. There were no significant side effects. Some patients experienced temporary upper extremity weakness.

D11, published in 1988, discloses information on the treatment of anismus with botulinum A toxin. Anismus is a condition where the anal sphinctors contract inappropriately (spasm) on straining with evacuation being attempted against a closed striated sphincter. The reference states that, being due to inappropriate muscle spasm, anismus seems to be a dystonic condition. The authors state that due to the success of the use of botulinum A toxin in the treatment of other dystonias, such as blepharospasm, strabismus, and spasmodic torticollis, they undertook the disclosed study to determine its effectiveness in treating anismus. Although this document refers to patients complaining of pain, the pain is abdominal pain which would result from the chronic severe constipation, and not pain due to the spasticity itself, contrary to the Examiner=s assertions in the Final Action.

As for dosage, it is stated that the first patient was injected with 10 ng of botulinum A toxin, which led to incontinence. It is also disclosed that this was chosen based on previous studies relating to strabismus and torticollis which required 3-5 and 40 ng respectively, since the puberectalis muscle is intermediate in size between the muscles treated previously. It was believed that the dose needed to be proportional to muscle mass. Later, the dose used was 3 ng when 1 ng failed to produce an improvement in 3 other patients, which dosage was used for the remaining patients. Four out of the seven had excellent results. It is not stated what type of toxin was used so it is not possible to equate the dosage to the units of the present claims.

D12, published in 1992, discloses the use of botulinum type F to treat several movement disorders. All of the patients treated had developed antibodies to type A toxin. Two patients suffered from torticollis, one from oromandibular dystonia and one from stuttering. The dosages used were 435 units (LD_{50}), 400 units, 120 units and 40 units

respectively. The authors noted that type A toxin is approximately nine times more toxic than type F toxin. It was found that type F toxin could safely be used at levels similar to those of type A toxin, but that the duration of action was shorter, consistent with previous animal studies.

D15, published in October 1993, relates to the use of botulinum toxin type F to treat torticollis in patients who had developed immunity to type A. It is reported that 10 of 15 patients improved after injection with type F and 6 of 9 with pain had reduction in pain. The same muscles were injected as were previously treated with type A. The authors report that in the past, 25-100 U (type A) of toxin was used to treat blepharospasm and 150-300 units (type A) for torticollis. The authors also refer to the D12 study of the use of type F. It is stated that most patients received a total of 250 U (mean dose 234.7; range 50-350 U) of type F.

Eleven had marked atrophy of the sternocleidmastoid muscle after injection of 25 to 50 U of type F. The authors acknowledge that it is unlikely that type F will prove an adequate therapy for many patients with torticollis. However, this is from a practical standpoint because of the brief duration of clinical effect. It is suggested that high doses of type F could be used in patients with severe torticollis in the post-laminectomy period since excessive neck weakness will be of a short duration.

It is useful at this point to summarize what may be gleaned from the above documents before reviewing D1 and D7. It seems clear enough that botulinum toxin, particularly type A, has been successful in treating a number of dystonias (i.e. neurological movement disorders) involving spastic muscles. D2 and D15 (which use type F toxin) further point to a concomitant relief of pain in treating the spastic condition. These documents also illustrate the variation in dosage which flows from the condition being treated, which may be, as is revealed in D11, partly due to the particular muscle mass, a factor which is influenced by the particular individual as well. This is in agreement with Applicant=s own disclosure which at page 8 states: AThe dosages used in human therapeutic applications are roughly proportional to the mass of muscle being injected.@ Applicant also states at page 8 that :

> The dose of toxin administered to the patient will depend upon the severity of the condition; e.g., the number of muscles groups requiring treatment, the age and size of the patient and the potency of the toxin.

We can see from the references the differences in dosages when treating the muscles of the eye as opposed to the neck for example. In D11 it is reported that 3-5 ng was appropriate for

strabismus and 40 ng was appropriate for torticollis. D12 indicates similar variation in dosage with condition in the use of types A and F. In relation to the present claims the only document which mentions treatment of spasticity secondary to stroke is D3 , but no dosages are specified. As Applicant has contended, there is no specific disclosure of the claimed dosage in treating post-stroke spasticity.

D1 (Mémin et al. - 1992)

This reference is undoubtedly the closest piece of prior art. This document, which was published in French, discusses the use of botulinum toxin in treating spasticity. At the hearing, the Applicant provided a translation of this document to the Board. The paper discusses the past uses of botulinum toxin as well, to treat various spastic disorders. The study included 8 patients, 7 men and 1 woman. Seven of them suffered a cerebrovascular accident, or stroke (6 infarctions, 1 hematoma), and 1 experienced a crainio-cerebral trauma with right temporaparietal lesion. Symptoms were dominant in the upper limbs in 6 cases (4 left, 3 right) and in the lower left limb in 1 case. Two cases involved the entrapment of the thumb in the hand. For the case of the lower limb, there was partial paralysis of the anterior leg muscle with a dystonia in the bending of the toes. Botulinum toxin A from the Porton Down Laboratory was used in the study. As per Applicant=s submissions before the Board and in accordance with their own description, 1 ng of such a toxin contains 40 units (U) of the toxin. In the absence of any evidence to the contrary, we will accept this conversion formula.

Injections were made into the long supernator muscle and the biceps of the arm, to the flexors of the fingers and toes, and to the anterior leg muscle. It is stated that because the spasticity and muscle volume was different for each case, the dosage was also different (in a ratio of 4:1). The average dose per patient and per series was 9.1 ng (364 U) with a range of from 4 ng (160 U) to 16 ng (640 U). It is also stated that every patient except one received two series of injections:

Tous, sauf un cas ont reçu deux séries d=injections.

It is also stated that 5 out of the 6 people who experienced pain improved. There was general functional improvement without any adverse side effects. Seven had improvement in relation to stiffness.

There was considerable debate at the hearing regarding the amount of toxin used disclosed by this document. The Applicant contended that because it was stated that two series of

injections were administered, they were administered in quick succession, meaning that the actual dosage per treatment was double the value stated, which would put the 4 ng (160 U) dosage outside the claimed range of 50-300 units. The Applicant also contends that it cannot be ascertained that a patient was given a dosage within the claimed range to treat pain associated with spasticity. The Examiner, on the other hand, at the hearing, contended that there was no teaching that a dose as low as 4 ng was not used to treat pain associated with spasticity.

When the Board looks at the D1 reference, we realize that it is true that one cannot ascertain with absolute certainty which patient received a 4 ng dosage. However, there is nothing in this document which would suggest that dosages this low were not effective at treating pain and spasticity. It is also noted that the range given is 4 ng to 16 ng, so even a higher dosage of 7 ng (280 U) would still fall within Applicant=s claimed range.

It is stated that 5 out of 6 patients who received treatment and had symptoms of pain were improved. There is no exclusion in the document of the 4 ng dosage in relation to these patients, so the Board must conclude that even the minimum dosage in the claimed range, 4 ng, would be effective at treating pain associated with spasticity resulting from stroke, since there was only one patient who did not have a stroke. This is what we believe the skilled person would take from this document when reviewing it in an objective manner. The Applicant has argued that there was no motivation to use a low dosage of toxin in the treatment of pain. We note that the authors state at page 214, that despite the use of low dosages in comparison with previous studies using botulinum toxin, the improvement in comfort of the patient, in relation to both pain and hypertonia is capable of reducing the indications of neurosurgical techniques:

> *Malgré l=utilisation de doses relativement faibles en comparaison avec les groupes musculaires déjà concernés par la toxine, l=amélioration apportée au confort du malade tant sur le plan de la douleur que de l=hypertonie est susceptible de réduire les indications des techniques neurochirurgicales.*

Clearly then, there is an indication that doses lower than those typically used for other conditions can be effective for treating pain and spasticity. This would direct the skilled person towards a lower dosage in an attempt to treat pain and spasticity resulting from stroke or cerebral vascular event.

In relation to the issue of the two series of injections, the Board believes that the document taken at face value discloses that 4 ng was used as a dosage for a particular treatment. If this was not the case we believe that the authors would have stated that the dosage was 8 ng,

rather than mislead the reader. This view is reinforced by the Summary published in English with this document. It is stated in the Summary that:

> The beneficial effects of one injection lasted more than 5 months. Seven patients received a second course of treatment.

When read in conjunction with the earlier quotation that all except one patient received two series of injections one must assume that after a period of time (i.e. 5 months) patients received their second course (i.e. series) of treatment. This makes it clear to the Board that 4 ng should be taken as a treatment dosage. The Board also notes that this Summary cannot be a third party translation of the earlier A*Résumé*@ given in this document. It is in fact written in the first person and also contains information not found in the rest of the document, namely, the statement that the beneficial effects of one injection lasted more than 5 months. The Applicant did not challenge the validity of the information contained in this Summary and reproduced it as appears in their translation provided to the Board.

Based on Mémin, the Board is left with the fact that it was previously disclosed that a range of 160 units to 640 units, which overlaps the claimed range, was useful in treating the pain associated with spasticity, which spasticity resulted from a stroke. Based on this reference alone the Board would conclude that Applicant=s claimed range of 50-300 units was at least obvious, since it encompasses dosages which were known before the claim date. Given the fact that the claimed range encompasses known dosages, the claim would normally fall for anticipation, for no one may claim so broadly as to encompass known subject matter (see *Diversified Products Corp. v. Tye-Sil Corp.* (1991), 35 C.P.R. (3d) 350 at 362 (F.C.A.); *Minerals Separation North American Corp. v. Noranda Mines Ltd.* (1947) 12 C.P.R. 99 at 146 (Ex. Ct.)).

However, we are faced with the question of obviousness. The Mémin reference itself indicates, as noted, that based on the spasticity and particular muscle volume, the dosage would need to be adjusted. Therefore, we see no inventive merit in Applicant=s particular variation from the known range. It appears to us to be no more than the inherent variation in using botulinum toxin to treat a particular patient. If there was some other reason why a dose as low as 50 units should be used to treat post-stroke spasticity pain, it is not evident from Applicant=s disclosure, particularly with respect to Example 10 which is the most closely related to the claimed subject matter. Therefore, given the known dosage range and the guidance offered to the skilled person by the Mémin reference, we believe the person skilled in the art would have come directly and without difficulty to the claimed invention.

Applicant has argued that because of the lack of side effects, there was no motivation to reduce the dosage further. However, as we have found from the Mémin reference, the dosage is very much dependent on the particular patient and their condition, so there certainly was motivation to change the dosage based on these criteria. We would also note that the Mémin reference, as specified in the *Résumé*, discloses the results of a preliminary study and does not claim to have established hard limits on the effective dosage range of botulinum toxin in the treatment of pain associated with post-stroke spasticity. Applicant has also argued that D1 does not make the claimed invention obvious since it suggests that the analgesic effect could be linked to effects on the muscle tonus and therefore the skilled person would be unaware that the treatment of pain could be achieved with dosages different from those required for muscle spasms. These arguments are not persuasive, as we have found that dosages within the claimed range were used to treat both pain and spasticity, and due to our interpretation of the scope of the claims, it is not necessary that the prior art teach that only pain be treated to the exclusion of spasticity. Our interpretation of the claims also leads to the realization that there is significant overlap in the ranges claimed by the Applicant and those disclosed by Mémin (50-300 U and 160-640 U, respectively). Variation in dosage is expected in view of individual physiology and condition as per the Mémin reference which, as stated earlier, used dosages in the rage of 4:1 due to variation in muscle volume and spasiticity.

In relation to the dependent claims, there is not much to add. Mémin, as noted earlier, discloses human intra-muscular treatment and deals with injection into the arms, hand, and leg. The recitation of the seven serotypes in claim 3 and 6 adds nothing to the patentability of claims 1 and 5 since there are in fact only seven serotypes known, all of which are already encompassed within the scope of the independent claims. If the particular use of any one of them were found to be obvious then claims 3 and 5, which claim the use of any one of them, must fall as well. With respect to the particular claim to the use of type A in claim 7, we note that Mémin used type A toxin.

D7 (Konstanzer et al. - 1993)

The Board would like to make another point on the obviousness of the claims, but before we do, we will look to the D7 reference cited by the Examiner. This reference was published in German in 1993 and again the Applicant has supplied the Board with a translation which we will use in the following discussion. While the exact date of publication is not specified, the Applicant has not disputed its applicability. D7 discloses a study in which eleven patients with protracted focal and painful spasticity were treated with botulinum toxin A injected into individual muscles of the arms and legs including the hands and

feet. Of note is a statement by the authors that pronounced spastic increase in tone leads, as a rule, to pain, deformation of joints, and difficulties in patient care. Such a statement would support the Examiner=s contention that there is a general link between spasticity and pain, which is also consistent with Applicant=s disclosure and our own interpretation of the claims. As the Applicant pointed out in their arguments before the Board, the objective of the trial in D7 was to lower muscle hypertonia caused by spasticity, and to reduce functional impairments. However, this does not change the fact that if pain relief accompanied this treatment of spasticity related symptoms, this would put the treatment within the scope of the claims.

In D7 there were only three patients (1, 5, 7) who suffered a stroke, but all suffered from severe local problems as a consequence of local spasticity, and all experienced pain in connection with the spasticity. The toxin used was Porton Down botulinum type A (1 ng = 40 mouse units). It is stated that the dosage depended on prior experience in the cervical region and height/body weight of the patient. There were no local or general adverse side effects. Five patients felt the decreasing tension in the muscle affected as being favourable and experienced an alleviation of the pain in the treated region. The authors also state that single-time or repeated administration of botulinum type A will prevail for the pain therapy of fixed contractures and that if antibodies begin to develop, type F might be a viable alternative. The authors stated that the clinical impression made by the patient group being presented in the study showed a uniform reduction of the muscle tone and spasm, whose extent appeared to be dose dependent.

Of the three patients who suffered from stroke, two (Patients no. 1, 5) suffered from pain and both patients indicated a reduction in pain as a result of treatment (see Table 4). Patient no. 1 received 25 ng (1000 U) of toxin in the flexor muscles of the hand and 50 ng (2000 U) in the muscles associated with footdrop. The Applicant in their submissions suggested that these two values should be added to give 3000 U for patient no. 1. However, these values were used to treat very separate muscles groups and cannot be looked upon as being directed to a total single dosage, as there is nothing to suggest that the treatment of one group would influence the other. Other prior art documents such as D1, D2, D4, D11, D12 and D15 specified dosage amounts for a specific spasticity and therefore for a specific muscle group as well. Patient no. 5 had 35 ng (1400 U) injected into the flexor muscles of the hand. Patient no. 7, although not indicating pain as a symptom in Table 1, was reported as experiencing a reduction in pain as well in Table 4.

Applicant contends that D7, due to the use of higher doses, with no adverse side-effects, teaches away from the claimed invention. However, the Board does not agree.

D7 discloses a study in which the combination of muscles treated for each stroke patient varied as did the dosage for each combination (see Table 2 of this reference). Applicant=s claims specify no particular groups of muscles to be treated, with the exception of claim 5, which specifies an arm, hand or leg, but even this does not specify the precise muscles. The variation in dosage in D7 was to be expected given the different patients and the different targeted muscles. In comparison with D1, it is unclear whether or not the same combination of muscles were treated. Likewise, it is difficult to compare the data of D7 with the present claims which specify no particular muscles, or level of spasticity. Therefore, we do not see D7 as teaching away from the invention, but merely disclosing particular dosages which were useful in treating spasticity associated with a specific combination of muscles. We believe this to be true of D1 as well, although what dosage corresponds to what muscle or muscles is unclear.

Further Conclusions on Obviousness

As we have stated, the collection of prior art applied by the Examiner establishes that botulinum toxin has been useful in treating various spastic conditions with the relief of both pain and spasticity. They also establish that the dosage will vary with the particular condition and individual. D1 and D7 also support these conclusions with D1 disclosing that dosage depends on muscle volume and level of spasticity. D7 discloses that the particular amount of toxin used depended on the extent of the spasticity and the height/body weight of the patient, along with some guidance from past experience with other muscles.

Given that from D1 and D7, it was known to use botulinum toxin to treat spasticity due to stroke, we can see no invention in determining the appropriate dosage for a given spastic muscle. The prior art provides the skilled person with the basic guidance they need to determine an amount appropriate to the situation. We have summarized the various factors that need to be considered when determining that amount. This leaves the skilled person with the task of determining, through their own knowledge of anatomy, the patient=s condition, and the guidance of past treatments, what the appropriate amount would be, just as was done in the prior art references. Therefore, we believe that based on their own common general knowledge and the guidance provided by the prior art, which for our purposes represents the state of the art, a skilled person would have come directly and without difficulty to an appropriate dosage of botulinum toxin (such as 50-300 units) needed to treat the pain/spasticity secondary to stroke. Our previous conclusions regarding the patentability of the dependent claims apply equally in this case.

Therefore the Board is of the opinion that claims 1-7 would have been obvious in view of the D1 reference to Mémin taken alone, or in view of the prior art references D1 through D15 taken as a whole.

SECTION 2 - METHOD OF MEDICAL TREATMENT

Examiner=s Position

The issue of non-patentable subject matter was only raised by the Examiner in the Summary submitted to the Board. The reason for this, as we understand, is that the amendments made to the claims in response to the Final Action by the Applicant emphasized the particular dosage range by adding it to the independent claims. In the Summary the Examiner had the following to say:

> The introduction of a dosage regimen in the present use claims appears to have introduced a new objection, namely an objection under section 2 of the *Patent Act* because they are merely claims directed to a method of medical treatment disguised as use claims. In support of this view, the PAB is referred to unpublished Commissioner=s decision 1252.

Applicant=s Position

The Applicant requested a copy of the aforementioned unpublished decision from the Board. However due to confidentiality requirements, unpublished Commissioner=s decisions, in the same manner as unpublished patent applications, cannot be released to the public. The Applicant pointed out that if the Board were to rely on such a decision and the Applicant did not have access to the decision:

> it would deprive the applicant of its right to know the case it needs to meet and make the necessary representations in response

thereby violating basic principles of natural justice. The Board agrees that the Applicant must Aknow the case it needs to meet@ and so will not refer to this unpublished decision. This case will be viewed on its own merits as would any other. We would also note that, in any case, the Commissioner is not bound by any past Commissioner=s decisions, so such a case cannot form a binding precedent on her. Further, as will be apparent from the later review of the relevant case law, the courts have provided us with their own guidance on the matter of patentability of dosage ranges.

In support of the present claims, the Applicant, in their submissions before the Board, pointed to issued patents which contained use claims including specific dosage ranges. However, such patents do not represent any kind of binding precedent. We do not know the

circumstances under which these patents were granted, and so they cannot be compared to the present case.

The Applicant pointed to various other authorities in support of the pending claims, stating:

> The decision of *Tennessee Eastman Co. v. Commissioner of Patents* (1972), 62 C.P.R. 1176 (S.C.C.) stands for the proposition that a method of medical treatment is not patentable. However, subsequent to *Tennessee Eastman*, the Court and the Patent Office have gone on to recognize that use claims are patentable. The provision of a dosage within the use claims does not transform a previously acceptable use claim into a method of medical treatment claim.
>
> Methods of medical treatment claims have been held not to be patentable subject-matter because they require the exercise of a specialized skill. The Courts have been called upon to consider use claims with dosages and have held such claims to be patentable. In *Merck & Co v. Apotex Inc.* (2005), 41 C.P.R. (4th) 35, in dealing with an objection to the claims on the ground that they were directed to a method of medical treatment because they contained a dosage form, the Court held that such an allegation was to be dismissed since the claims were taken out of the reach of Tennessee Eastman as they were Adistinguishable from the work of a physician, which requires the exercise of specialized skill@ and because the patent was Afor a vendible product having real economic value, as demonstrated by its immediate success in the market, and was therefore, not for a non patentable method of treatment@.
>
> Furthermore, the Manual of Patent Office Practice clearly provides that use claims are acceptable. Section 11.10.02 reads as follows:
>
> > *Guidelines for use claims*
> >
> > *(I) Use claims are permitted. Moreover, use claims incorporating method steps are acceptable as long as the use has been clearly identified and it is not a method of medical treatment. If the claim is complete and understandable without the method steps, then the claim as a whole is acceptable. The method steps merely provide a restriction to the previously recited use.*

The Board realizes that claims in the form of AUse of x for y@ are generally accepted by the Patent Office. However, the mere fact that a claim is in this form does not automatically bestow patentability on the claim. The section from the Manual of Patent Office Practice quoted by the Applicant even points out that if a use claim is directed to a method of medical treatment, it is not permitted. For example, if a use claim includes a treatment step, it will still be objectionable on its face.

Section 2 and Methods of Medical Treatment: Legal Principles

Section 2 of the *Patent Act* defines Ainvention@ as:

> any new and useful art, process, machine, manufacture or composition of matter, or any new and useful improvement in any art, process, machine, manufacture or composition of matter.

To be patentable, an invention must not only be Anew and useful@ it must fall into one of the five recognized categories of subject matter. In *Tennessee Eastman Co. v. Commissioner of Patents* (1970), 62 C.P.R. 117 at 154 (Ex. Ct.) Kerr J. stated, in relation to a claim for a method of surgical bonding of tissue:

> In my view the method here does not lay in the field of the manual or productive arts nor, when applied to the human body, does it produce a result in relation to trade, commerce or industry or a result that is essentially economic. The adhesive itself may enter into commerce, and the patent for the process, if granted, may also be sold and its use licensed for financial considerations, but it does not follow that the method and its result are related to commerce or are essentially economic in the sense that those expressions have been used in patent case judgments. The method lies essentially in the professional field of surgery and medical treatment of the human body, even although it may be applied at times by persons not in that field. Consequently, it is my conclusion that in the present state of the patent law of Canada and the scope of subject-matter for patent, as indicated by authoritative judgments that I have cited, the method is not an art or process or an improvement of an art or process within the meaning of s. 2(d) of the *Patent Act*.

This decision was upheld by the Supreme Court of Canada (*Tennessee Eastman Co. et al. v. Commissioner of Patents* (1972), 8 C.P.R. (2d) 202 (S.C.C)), although the court seemed to rely on former s. 41 which related to Asubstances prepared or produced by chemical processes and intended for food or medicine@. However, Mr. Justice Pigeon did state that:

> Having come to the conclusion that methods of medical treatment are not contemplated in the definition of Ainvention@ as a kind of Aprocess@, the same must, on the same basis, be true of a method of surgical treatment.

Later, in *Imperial Chemical Industries Ltd. v. Commissioner of Patents* (1986), 9 C.P.R. (3d) 289 (F.C.A.), Heald J., in dealing with an argument that only Amedical methods which utilize materials prohibited pursuant to s-s. 41(1) of the Act, namely, materials produced by chemical processes@, should be prohibited in accordance with *Tennessee Eastman, supra*, referred to the previous quotation of Pigeon J. and stated:

> In my opinion, this is a clear and unequivocal statement that A... methods of medical treatment are not contemplated in the definition of Ainvention@ as a kind of process ...@. That was the sole issue before the court and it is here answered in unmistakable and unambiguous language. Accordingly, in my view, the force of that pronouncement cannot be restricted merely to factual situations where s-s 41(1) of the Act applies.

The above case dealt with a method of cleaning teeth by the application of a composition consisting of an unbound lanthanum cation. We therefore have the present situation where methods of medical treatment are not patentable, even when not practised by a medical professional. The Applicant submitted that methods of medical treatment were not patentable because they required the exercise of professional skill. In view of the *ICI* case, *supra*, a claim is not taken outside of the method of medical treatment exclusion by the fact that it can also be practised by a non-professional.

The Applicant also pointed to *Merck & Co. v. Apotex Inc.* (2005), 41 C.P.R. (4th) 35 (F.C.) as support for the patentability of a use claim incorporating a dosage. This case involved claims to the use of alendronate for treating osteoporosis where a once weekly dose of 70 mg was specified. It was agreed by the parties that novelty resided only in the larger once weekly dosage. Justice Mosley found, contrary to the decision of the U.K. courts on the same matter, that:

> the patent is for a vendible product having real economic value, as demonstrated by its immediate success in the market, and is, therefore, not for an unpatentable method of treatment.

At the hearing, another case relating to use claims incorporating dosages was brought to the attention of the Applicant by the Board, namely *Axcan Pharma Inc. v. Pharmascience Inc.* (2006), 50 C.P.R. (4th) 321 (F.C.). In this case the contentious claim was directed to

a pharmaceutical composition which included a dosage range. It was found that the claim was not defeated by the prior art because of the different dosage range used:

> the said composition being processed in a form allowing for the said treatment of primary billary cirrohosis based on a dose of 13 to 14 mg/kg/day.

In the course of his reasons, Justice Harrington referred to the reasons of Mr. Justice Binnie in *Apotex Inc. v. Wellcome Foundation Ltd.*, [2002] 4 S.C.R. 153, where he stated:

> Tennessee Eastman was concerned with the patentability of a surgical method for joining incisions or wounds by applying certain compounds. The decision was based on former s. 41 of the *Patent Act*, now repealed. The Court concluded that the method (apart from the compounds) was not patentable. The policy rationale, as explained by Wilson J. in Shell Oil, supra, at p. 554, was that the unpatentable claim was
>
> > essentially non-economic and unrelated to trade, industry, or commerce. It was related rather to the area of professional skills.
>
> The AZT patent does not seek to Afence in@ an area of medical treatment. It seeks the exclusive right to provide AZT as a commercial offering. How and when, if at all, AZT is employed is left to the professional skilled judgement of the medical profession.

Justice Harringtion noted, following the reasoning of Binnie J., that Aan invention relating to the area of professional skill is not patentable@. He also referred to *Visx Inc. v. Nidek Co. et al.* (1999), 3 C.P.R. (4th) 417 (F.C.T.D.) in which Mr. Justice Dubé stated:

> In my view, the Professional Skill Defence is not availabl e to attack the validity of the three patents in issue. These patents do not teach professi

onal skills to surgeons. They deal with an apparatus, a machine, a combination of several components. In that sense, the apparatus is similar to other medical equipment, as x-ray machines, dentist drills, scalpels, all of which are patentable if they teach an invention. The invention in the Visx patents does not pose a limitation upon

the
surgeons
' skills.

In comparing the *Visx* situation with the one before him, Justice Harrington stated (our emphasis added):

> The invention claimed here is quite different. It is up to the physician based on his or her knowledge of the patient=s rate of metabolism and other factors to determine the appropriate daily dosage.

Justice Harrington also referred back to the *Merck* case, pointed out by the present Applicant, and in comparing that case with his own, stated (our emphasis added):

> Contrary to the position taken by the U.K. Courts, Mr. Justice Mosley found that the patent was for a vendible product having real economic value, and was not for an unpatentable method of treatment. However, in this case the number of capsules to prescribe is a matter between the patient and her doctor, and does not form part of a monopoly protected by Letters Patent. Therefore, the patent is invalid because it claims a method of medical treatment

and later stated (our emphasis added):

> There is a distinction between the dosage in a capsule and a dosage range based on the patient=s weight. As I read the claim, the emphasis is on the dosage range, and a dosage range is not a vendible product.

From this limited jurisprudence we may take that, if a dosage is claimed as part of the patent monopoly it must not be in the form of a range, such that in order to determine the appropriate dosage for a particular patient, specific knowledge of that patient is required, and judgement is required based on that knowledge, matters which fall within the skills of the physician, and are therefore unpatentable. As Mr. Justice Harrington put it, the dosage must be in Avendible product@ form, and not in the form of a guideline to physicians. This would seem to accord with the previous quote from Mr. Justice Binnie in *Apotex, supra*. If what is claimed can no longer be considered a Acommercial offering@, then it may fall within the exclusion. This is of course, not to say that a claim, in order to be patentable, must be directed to a Avendible product@ or a Acommercial offering@. The above guidance is restricted to the case where a dosage range is found in a claim.

Analysis

In the present case, the Applicant in response to the Final Action amended the use claims previously on file to include a particular dosage range of from 50 to 300 units of botulinum toxin. It has already been shown by the prior art that it was known to use botulinum toxin to treat pain associated with spasticity secondary to a stroke. The Board has also concluded that the claimed range would have been obvious. Nevertheless we still have the issue of whether inclusion of the claimed dosage range causes the claim, on its face, to fall within the method of medical treatment exclusion as particularly characterized by the Federal Court in *Axcan* and *Merck*, *supra*. At page 8 of the present application it is stated:

> The dose of toxin administered to the patient will depend upon the severity of the condition: e.g., the number of muscle groups requiring treatment, the age and size of the patient and the potency of the toxin.
> .....
> The dosages used in human therapeutic applications are roughly proportional to the mass of muscle being injected.

and on page 9:

> Ultimately, however, both the quantity of toxin administered and the frequency of its administration will be at the discretion of the physician responsible for the treatment and will be commensurate with questions of safety and the effects produced by the toxin.

We believe it to be clear from the above passages that the particular dosage to be administered to a patient, in the present case, is based on the physician=s professional judgement and the particular physiology of the patient. While a dosage range is claimed, it is the physician who must decide in any given case where in that range a particular use will fall. Whereas in the AZT case (*Apotex, supra*), the claims did not seek to fence in an area of medical treatment, the claims in the present case do. The claim seeks to fence in a range within which physicians must exercise their professional skill and judgement in any given case, and therefore the claims are directed to an unpatentable method of medical treatment.

Applicability of NOC Decisions

At the hearing, a point was raised regarding the applicability of case law under the *Patented Medicines (Notice of Compliance) Regulations* (NOC). As previously discussed, the Applicant pointed to the *Merck* case, an NOC case, as support for the contention that use claims incorporating dosage forms are patentable. At the hearing the *Axcan* case was

brought to the attention of the Applicant as the other case involving dosages and their validity under section 2 of the *Patent Act*.

The Applicant, in response, pointed to a recent decision of the Federal Court of Appeal in which there was allegedly a ruling which established that NOC cases "have no precedential basis" and "should not be relied upon". The Applicant also, in view of this position, agreed that the *Merck* case would also be disregarded in such a case. The exact reference was not known at the time but was later identified by the Applicant as *Eli Lilly v. Novopharm* (2007), 62 C.P.R. (4th) 161 (F.C.A.), where Sexton J.A. stated (our emphasis added):

> NOC proceedings were never intended to be substitutes for an infringement action:
>
> > *Merck Frosst Canada Inc. v. Canada (Minister of National Health and Welfare)* (1994), 55 C.P.R. (3d) 302 (F.C.A.) at 319 (leave to appeal to the S.C.C. dismissed [1994] S.C.C.A. 330); *Pfizer, supra* at paragraph 17. Similarly it is inappropriate to rely on NOC proceedings to set binding precedent on controversial and uncertain questions in patent law (see *Sanofi-Aventis, supra*, at paragraph 49). NOC proceedings are supposed to be summary in nature and do not lend themselves to such determinations. Rather Eli Lilly can seek resolution of these questions in the infringement proceedings which it has already commenced. The decision in Sanofi-Aventis , supra , affirms this point at paragraph 40:
> >
> > While it is important in each case to ensure the application of the doctrine of abuse of process does not give rise to unfairness in the circumstances, in my view, no such unfairness would result in the present case. Prohibition proceedings under the NOC Regulations do not prevent patentees from enforcing their patent rights through actions for patent infringement in accordance with the Patent Act . Moreover, the findings from any such prohibition proceedings have no bearing on patent infringement actions. [emphasis added]

The passage highlighted by the Board in the main paragraph, taken out of context, could be construed as expressing the view that principles of patent law established in NOC cases should not be taken as authoritative. However, the Board does not believe that this was what was meant by the Federal Court of Appeal. The passage above does not stand on its own, but refers to *Sanofi-Aventis Canada Inc. v. Novopharm Limited* (2007), 59 C.P.R. (4th) 416 (F.C.A.) at para. 49, as authority for such a statement. Paragraph 49 of that case states (our emphasis added):

> Sanofi-Aventis and Schering also emphasize that proceedings under the NOC Regulations are of a preliminary nature and are accompanied by limited procedural safeguards. While this argument may be sufficient to establish that decisions made in the context of the NOC Regulations should not be binding on judges adjudicating actions for patent infringement or declarations of patent

> invalidity, it does not change the fact that relitigation by a first person of an issue already decided against it within the context of the NOC Regulations is generally not permissible. As I have already said, the possibility of different judges adjudicating equivalent proceedings concerning the same issue reaching different results threatens the integrity of the adjudicative process. The nature of the proceedings does not change this reality.

which reveals that what the Federal Court of Appeal was referring to was the idea that decisions in NOC cases are not determinative of issues of validity and infringement. What this means is that a court in a full blown impeachment or infringement proceeding could end up with a different result from another court presiding over an NOC case, with the same parties involved. We believe this interpretation to be reinforced by the above passage from *Sanofi-Aventis* emphasized by Sexton J. A. himself in the quotation from *Eli Lilly*. Such a situation has already occurred in the cases of *Janssen-Ortho Inc. v. Novopharm Ltd.* (2005), 35 C.P.R. (4th) 353 (F.C.) and *Janssen-Ortho Inc. v. Novopharm Ltd.* (2006), 59 C.P.R. (4th) 116 (F.C.), where contrary to the findings by Mr. Justice Mosley in the NOC proceeding, Mr. Justice Hughes, in an infringement and validity action, found the patent valid and infringed. Nevertheless, the same principles of patent law would apply in both situations.

In view of the above, we do not interpret the *Eli Lilly* case *supra*, as the Applicant would have us interpret it. Points of law established in NOC cases must be taken as expressing the views of the court, which views, to the extent that they have not been overturned by, or are inconsistent with, those of a higher court, or are inconsistent with those expressed in another decision of the same court, should be taken as authoritative. As such, we have found the claims of the present application to not comply with s. 2 of the *Patent Act* in accordance with the principles of *Merck* and *Axcan*.

OTHER ISSUES

Prophetic/Hypothetical Examples

In the Summary of Reasons submitted to the Board, the Examiner stated:

> Example allegedly in support of the claimed invention on page 19 of the present application does not appear to solve the objective problem. This example is hypothetical. No data is presented which indicates the problem is actually solved. In fact, it relates not to treatment of pain but rather to treating a different symptom i.e. spasticity.

A review of Example 10 on page 19 reveals that the above contention is not entirely accurate. Example 10 does indicate treatment of muscle spasm, but also indicates control of pain. It was in response to this statement that the Applicant took issue with such an objection, on the grounds, as previously stated, that such an objection was not made in the Final Action, and that it was not a new problem which resulted from the Applicant=s amendments. The Board notes that in the Final Action at page 4, the Examiner stated:

> The Examples disclosed in the instant application deal with prophetic or hypothetical treatments/patients as opposed to actual experimental/clinical data. This argument was made by the Examiner in the Office action dated June 12, 2001 (pages 2-4).

The Board also notes that this statement was made in the context of an objection that the claims are obvious, which we find to be inappropriate, since issues such as claim support (which was the original basis for this objection, see below), must be dealt with separately from considerations of obviousness, novelty, etc.

The Examiner points to the Office Action of June 12, 2001, where the Board notes that an objection was made under subsection 138(2) of the *Patent Rules*, alleging that the claims (1-36 at the time) lacked Asubstantive support in the present description@. Within this objection, the Examiner outlined his concerns regarding AExperimental vs. hypothetical data@. In the response to this action the Applicant addressed the Examiner=s concerns through argument and even suggested that the objection would have been better founded on inoperability. What is important is that in the subsequent actions, including the Final Action, this objection is not to be found. While there are allusions to such an objection in the context of obviousness in the Final Action, we do not see this as proper. If the Examiner wished to maintain such an objection, then a proper detailed argument should have been consistently presented during prosecution, including in the Final Action. The fact that this was not done would imply, from the Applicant=s viewpoint, a concession on the part of the Examiner that such an objection was unfounded. In any case, given our findings above as to obviousness and patentable subject matter it is unnecessary to further review this issue.

POSTSCRIPT

Prior to the finalization of a decision for this case the Supreme Court of Canada released its decision in *Sanofi-Synthelabo Canada Inc. v. Apotex Inc.,*

2008 SCC 61, 69 C.P.R. (4th) 251, which outlined a four-step approach to be followed when assessing the obviousness of a claim, and which included the possibility of considering whether the invention was Aobvious to try@. Recognizing that this decision was now the authoritative approach to assessing the obviousness of a claim, and in the interest of fairness to the Applicant, the Applicant was invited by the Board to make any submissions that it deemed necessary to address any effect that the *Sanofi* decision may have on the pending obviousness rejection. The Applicant provided such submissions on February 17, 2009. We provide below, in conjunction with a supplemental obviousness analysis under *Sanofi*, a review of those submissions, as well as our conclusions on the effect of *Sanofi* on our earlier findings as to obviousness. We have also, in view of *Sanofi*, made additional comments on the applicability of NOC cases.

Analysis under *Sanofi*

In the submissions of February 17, 2009, the Applicant chose not to address the effect of the basic four-step approach set out in *Sanofi*, *supra*. However, for the sake of completeness we provide a brief breakdown below following the approach.

(1) (a) *The Aperson skilled in the art@*

Given the context of the invention we would attempt to characterize the person skilled in the art as a researcher working in the field of neurotoxins and neuromuscular disorders. This person may comprise a collection of individuals from the fields of neurology, pharmacology, toxicology and bacteriology, for example.

(1) (b) *The Common General Knowledge*

The person skilled in the art would be expected to possess the common general knowledge relating to such a researcher, such as known experimentation techniques, knowledge of neurotoxins, their function and effect, particularly as related to botulinum toxin. The person would also possess knowledge of neuromuscular disorders and conditions relating to muscle spasms.

In outlining the Aperson skilled in the art@, we acknowledge that we do not have the benefit of expert testimony, as the courts would, in assessing who this person would be and what common general knowledge they would possess, but we believe what we have said is a fair assessment based on the subject matter of the description and claims. The knowledge of the person skilled in the art for our purposes will be dictated by the evidence before us, namely the prior art documents applied.

(2) *The Inventive Concept*

In this case we see no reason to attempt to summarize the claims beyond their form as we have interpreted them. The inventive concept is succinctly expressed by the claim.

(3) *The differences between the state of the art and the inventive concept*

These have already been discussed in our earlier analysis. We would simply point out that with respect to the D1 Mémin et al. reference, there are no differences. This piece of prior art discloses dosages of botulinum toxin which fall within the claimed range when the toxin was used to treat pain associated with post-stroke spasticity. Assuming though, as we did earlier, that there were differences, those differences would be (as per our earlier separate conclusions on obviousness) (I) the variation in the claimed range and that of the prior art with overlapping values, and (ii) the absence of values disclosed by the prior art which fall within the claimed range.

(4) *Were these differences obvious?*

For this, we would again refer to our previous analysis which we believe still applies here. Although our conclusions were stated in relation to the test outlined in *Beloit*, we believe they would stand in view of more recent case law as well, whether the test was Avery plain@ or Amore-or-less self-evident@ (See *Pfizer Canada Inc. v. Apotex*, 2009 FCA 8 at paras. 27 - 29 and *Bristol-Myers Squibb Canada Co. v. Apotex Inc.*, 2009 FC 137 at para. 150, especially given that the claims would have been at least obvious in view of the range disclosed in Mémin et al. In our analysis which excluded the disclosure of values within the claimed range, while some experimentation would be needed to determine the proper dosage of botulinum toxin for a specific individual post-stroke spasticity, we believe, as we stated earlier, that the factors to be considered were known in view of the state of the art. We would in such a case consider the experimentation to be routine, rather than inventive. The guidance provided by the prior art would make the determination of a suitable dosage Amore-or-less self-evident@.

In their submissions, the Applicant briefly addressed the Aobvious to try@ test set out in *Sanofi*, *supra*. As the applicant points out, it is difficult for the Board to assess all of the factors to be considered under Aobvious to try@, given the lack of evidence in relation to them.

> *Is it more or less self-evident that what is being tried ought to work?*
> The Applicant believes, as stated in their submissions, that:
> The use of a lower dose or subtherapeutic dose (i.e. less than the amount which results in muscle paralysis) in order to treat the pain of spasticity, as opposed to treating the muscle spasticity cannot be obvious to try because all of the art taught use of higher doses of botulinum toxin.

As presented under our analysis of obviousness in the main part of this review, we have found not only that the prior art disclosed ranges which fall within the claimed range, but also that, collectively, it provided sufficient guidance to the person skilled in the art to arrive at a suitable dosage. Admittedly, some non-inventive experimentation may be needed to determine the optimal dosage for a particular individual case of pain/spasticity secondary to stroke. Again, we determined that the claim is not limited to treatment of pain only.

What is the extent, nature and amount of effort required to achieve the invention?
The Applicant did not adduce any evidence in relation to this question, but did comment that:

> Suffice it to say however, that as stated above, given that the claimed invention has three variables and that the skilled person would have had to experiment to find the right combination as claimed, extensive experimentation would have been required.
> .....
> For example, to arrive at the claimed invention, the person of ordinary skill would first carry out animal experiments (to begin to titrate the correct dose to use in human clinical trials). When experiments on humans then begin, one must keep in mind that the subjects (usually elderly) are already in a compromised and weakened state (all having post-stroke spasticity) which mandates not only careful patient selection and observation but a careful series of graduated dose injections, with results typically being assessed in conjunction with the patient=s caregiver. As such, the extent, nature and amount of effort required to achieve the invention would be significant.

Given that there is no evidence relating to how the invention was arrived at, we cannot say one way or the other whether it would be Aextensive@. We are also not convinced that the Applicant=s comments regarding the type of experimentation that would be necessary in order to determine the appropriate dosage are correct. The prior art applied

discusses studies already conducted on humans and reports the effects of the dosages used. In the absence of any specific evidence, we therefore give such comments little weight in the determination of obviousness.

Is there a motive provided in the prior art to find the solution the patent addresses?
The Applicant submitted that there is nothing in the prior art that suggests the claimed invention. However, as we have found, the prior art did disclose the treatment of pain/spasticity secondary to a stroke. In one case (Mémin et al.), dosages were disclosed which fell within the claimed range, and collectively, even absent such disclosure, the art provided sufficient guidance to arrive at the invention. There was definitely, as evident from our discussion of the prior art, a motive to find suitable dosages of toxin for treating various spasticities, including those secondary to stroke.

The course of conduct which culminated in the making of the invention.
As the Applicant stated in their submissions, there was no evidence presented in relation to this factor.

In light of the above, our conclusions on the obviousness of the claims are not affected by the approach set out in *Sanofi*, including the application of an Aobvious to try@ test.

Applicability of NOC Decisions in view of *Sanofi*

We had previously stated our views on the general applicability of decisions made in relation to the *Patented Medicines (Notice of Compliance) Regulations*, namely that the points of law established in such cases should be taken as authoritative. With the release of the Supreme Court of Canada=s decision in *Sanofi, supra*, we believe it necessary to point out that this decision was one made under the *NOC Regulations*. In this case Rothstein J. outlined the requirements necessary to establish anticipation of a claim, namely disclosure and enablement, as well as the approach to be followed in assessing the obviousness of a claim. We do not see why these broad principles established by the Court in *Sanofi, supra,* should be ignored simply because the case related to a Notice of Allegation under the *NOC Regulations*. Likewise, earlier points of law established by lower courts in dealing with cases under the *NOC Regulations* are authoritative to the extent that they have not been overturned by, or are inconsistent with, those of a higher court, or are inconsistent with those expressed in another decision of the same court.

Further, we point out that subsequent to the Supreme Court decision in *Sanofi*, lower courts have felt bound by and applied the principles established by that case in non-NOC cases (See

Uview Ultraviolet Systems Inc. v. Brasscorp Ltd., 2009 FC 58 and *Bridgeview Manufacturing Inc. v. 931409 Alberta Ltd.*, 2009 FC 50).

Related Commissioner=s Decisions

In a very recent decision of the Commissioner of Patents, (2009) C.D. no. 1290 (P.A.B. and Commissioner of Patents), the Board proposed an approach to assessing patentable subject matter. According to this approach, a claimed invention is unpatentable if the claim, either in form or in substance:

- does not fit into the definition of one of the five categories of invention,
- is directed to excluded subject matter (i.e., subject matter that has been excluded by judicial interpretation of section 2 and subsection 27(8) of the *Patent Act*), or
- relates to non-technological subject matter.

According to this approach, if a claim is determined to be unpatentable according to one ground, it is unnecessary to further assess the claim with respect to the other grounds. In the present case, having found that claims 1 to 7, on their face, are directed to excluded subject matter, the Board finds that it is unnecessary to address the further grounds set out in the approach.

RECOMMENDATIONS

Accordingly, the Board recommends that:

(1) the Examiner=s objection to claims 1-7 as being obvious be upheld, and

(2) the Examiner=s objection to claims 1-7 as being directed to an unpatentable method of medical treatment be upheld.

Stephen MacNeil	Mark Couture	Paul Fitzner
Member	Member	Member

I concur with the findings and recommendation of the Patent Appeal Board. Accordingly, I refuse to grant a patent on this application. Under Section 41 of the *Patent Act*, the applicant has six months within which to appeal my decision to the Federal Court of Canada.

Mary Carman
Commissioner of Patents

Dated at Gatineau, Quebec,
this 5 day of June, 2009