



INTELLECTUAL PROPERTY INSTITUTE OF CANADA
INSTITUT DE LA PROPRIÉTÉ INTELLECTUELLE DU CANADA

TOO MUCH? TOO LITTLE? JUST RIGHT?

INCREASED SCRUTINY OF THE DESCRIPTION AND THE GOLDILOCKS SYNDROME

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Overview

- **Origin of the promise doctrine**
- **Chronic disease**
- **Advantages & goals**
- **Selection patents**
- **Patents with no explicit promise**
- **Eurocopter**
- **Viagra**
- **Conclusions**

Evolution of the utility test

Canadian patent law has tremendously changed over the last decade

In the 1990s very few patents were found to lack utility

Lack of utility is nowadays one of the 1st ground of invalidity of patents in Canada

Utility - Yes

Evolution or regression?

Utility - No

Quinapril 2005 (ACE inhibitor): FC & FCA
Nefazodone 2005 (depression): FC & FCA
Omeprazole 2007 (gastric ulcer): FC
Atorvastatin 2008 (cholesterol): FCA rev'g
Perindopril 2008 (blood pressure): FC & FCA
Metamine 2009 (Alzheimer's): FC
Escitalopram I 2009 (antidepressant): FC, FCA
Latanoprost I 2009 (glaucoma): FC & FCA
Atomoxetine I 2010 (ADHD): FC
Escitalopram II 2010 (antidepressant): FC
Olanzapine 2010 (schizophrenia): FCA, rev'g in part
Lovastatin 2010 (cholesterol): FC & FCA
Replinigade 2010 (diabetes): FC
Latanoprost II 2011 (glaucoma): FC
Rosiglitazone 2011 (diabetes): FC
Anastrozole 2011 (cancer): FC & FCA
Donepezil 2011 (Alzheimer's): FC & FCA
Fenofibrate 2012 (cholesterol): FC
Efavirenz 2012 (HIV): FC
Imatinib 2013 (leukemia): FC
clopidogrel 2013 (platelet aggregation): FCA rev'g
Zelendroic acid 2013 (bone resorption): FC (for '937)
Bauer 2010 (skate quarter): FC & FCA

Ramipril I 2005 (blood pressure) FC & FCA [sound prediction]

Atorvastatin 2007 (cholesterol): FC
Modafinil 2008 (narcolepsy): FC
Rampril II 2009 (blood pressure): FC & FCA [sound prediction]
Amlodipine 2009 (blood pressure): FC & FCA
Olanzapine 2009, 2011 (schizophrenia): FC 2x's

Atomoxetine II 2010 (ADHD): FC & FCA
Esomeprazole 2010 (acid reflux): FC
Irbesartan 2010 (blood pressure) FC

Latanoprost II 2011 (glaucoma): FCA rev'g
clopidogrel 2011 (platelet aggregation): FC

Zelendroic acid 2013 (bone resorption): FC (for '895)

Eurocopter 2012 (landing gear): FC (partial)

Why?

The appearance of «the promise doctrine»

The disclosure necessary for sound prediction

Of a factual basis

Of a sound line of reasoning

Or of both

We do not draft in a vacuum

Clients are interested in non-Canadian markets

Evolving requirements in US, Europe and Canada:

- written description; sufficiency
- utility requirement; promise of the patent;
- consideration of statutory subject matter
- prosecution strategies:
 - e.g. obviousness & KSR
- increasing need for a proper priority application
 - avoiding self collision in Europe

United States Patent and Trademark Office

An Agency of the Department of Commerce

Director's Forum: David Kappos' Public Blog

Posted at [10:14AM Dec 03, 2009](#) in [ip](#) | [Comments\[4\]](#)

Tuesday Nov 24, 2009

The Impact of KSR



As you all know, the Supreme Court's April 2007 decision in KSR v. Teleflex was a landmark case in the law of obviousness. Although the KSR Court reaffirmed the well-known Graham v. John Deere inquiries as the appropriate framework for evaluating claims under 35 U.S.C. 103, the Court's emphasis on a flexible approach clearly calls for new thinking about obviousness by patent examiners and practitioners alike.

KSR has unquestionably refocused the obviousness inquiry by reinvigorating the fundamental questions of Graham. Because the Supreme Court clarified that teaching-suggestion-motivation was not the sole test of obviousness, the Graham analysis is not to be carried out in a rigid manner. As a result, some claims that may have been found to be non-obvious before KSR will now correctly be found to be obvious.

Inventors and practitioners will need to take these developments into account when preparing and prosecuting applications. For example, it may be necessary to review a broader cross-section of prior art than was previously necessary, or to consider filing evidence of unexpected results earlier rather than later in the course of prosecution. By being proactive, practitioners will expedite prosecution and avoid unnecessary fees and RCE filings.

2013 Special 301 Report



Acting United States Trade Representative Demetrios Marantis
Office of the United States Trade Representative

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goods in-transit. With respect to pharmaceuticals, the United States continues to have serious concerns about the availability of rights of appeal in Canada's administrative process for reviewing regulatory approval of pharmaceutical products and also has serious concerns about the impact of the heightened utility requirements for patents that Canadian courts have been adopting recently. The United States looks forward to continuing its close cooperation with Canada on IPR issues, including through the TPP negotiations.

Eli Lilly sues Canada for \$500 million

Lilly: Canada unfairly shortened life of patents

September 13, 2013
ABC News

re:
STRATTERA - atomoxetine
and
ZYPREXA - olanzipine

Posted: 09/13/2013
Last Updated: 19 hours ago



[TheIndyChannel.com Staff](#) | [Email Me](#)

INDIANAPOLIS - Eli Lilly and Company has filed a \$500 million international lawsuit against the Canadian government.

Lilly says Canada unfairly shortened the life of patents for its best-selling drugs.

The case was filed Thursday under the rules of the North American Free Trade Agreement.

Lilly says Canadian courts unfairly threw out the patents when challenged by the generic drug manufacturers.

The legal fight will move to the next stage after the two sides failed to settle their differences during a 90-day consultation process which ends Friday.

Doug Norman, general patent counsel for Lilly, released the following statement Thursday:

"Patent decisions in Canada over the last decade not only fly in the face of long-established international standards, but they're subjective and completely unpredictable. The standard seems to be that there is no standard. The Notice of Arbitration (NOA) is the next natural step in Lilly's continuing efforts to address financial losses from improper invalidation of our Strattera® and Zyprexa® patents under Canada's 'promise utility doctrine.'

"The promise doctrine is a creation woven from federal court decisions made since 2005. It's impossible to know what specific "promise" can be implied from an application, and how much data are needed to support it. If this pattern persists, the already challenging business of medical innovation will become all the more difficult in Canada, producing painful consequences for Canadian patients and the economy at a time when its domestic biopharmaceutical industry is suffering job losses and undergoing extensive restructuring. The NOA is a necessary step in this important process."

How did it all start?

Consolboard

Question was whether s. 36 (1) required an indication of the utility in the patent

Resulted in this very famous quote :

Consolboard v. MacMillan (Sask.), 1 S.C.R. 504

Consolboard v MacMillan Bloedel [1981] 1 SCR 504 (pg525)

References Halsbury's Laws of England:

“...on the meaning of "not useful" ... It means "that the invention will not work, either in the sense that it will not operate at all or, more broadly, that it will not do what the specification promises that it will do"... the practical usefulness of the invention does not matter, nor does its commercial utility, unless the specification promises commercial utility, nor does it matter whether the invention is of any real benefit to the public, or particularly suitable for the purposes suggested... it is sufficient utility to support a patent that the invention gives either a new article, or a better article, or a cheaper article, or affords the public a useful choice...”

Consolboard v MacMillan Bloedel [1981] 1 SCR 504 (pg 526)

Although (i) s. 36(1) requires the inventor to indicate and distinctly claim the part, improvement or combination which he claims as his invention and (ii) to be entitled to an invention must be

invented it (s. 28(1)(a)), I do not read the concluding words of s. 36(1) as obligating the inventor in his disclosure or claims to describe in what respect the invention is new or in what way it is useful. He

the invention is new or in what way it is useful. He must say what it is he claims to have invented. He is not obliged to extol the effect or advantage of his discovery, if he describes his invention so as to produce it.

What is the test according to Consolboard?

Patent must describe completely and fully the invention

And the methods for producing or reconstructing it

For the POSA

No need to disclose the real utility of the invention

olanzapine

Long saga

FC- FCA-FC

According to the Court the olanzapine patent promises advantages over the prior art patent

The patent boasts the superiority of olanzapine so there is a promise of superiority

Part based on a dog study but dogs are not a good model to predict cholesterol levels in humans

Prediction not sound, no evidence of clinical superiority

Surprisingly the same patent was found to be valid in the NOC case against Apotex (2007 FC 455)

Sanofi v. Apotex (clopidogrel)

Recently the Federal Court of Appeal set the promise test

A promise in a patent is an explicit promise of specific results

Courts should not try to read a promise between the lines

Sanofi-Aventis v. Apotex 2013 FCA 186, rev'g 2011 FC 1486

Drafting questions to consider

- Is the evaluation of the promise limited to selection patents, or does it apply to any patent?
- What language may be considered a promise?
- Is the promise determined by the claims, the specification, or both?
- What information is required to support a promise?
- Can we “control” what the promise is, or is this determination open to interpretation by experts?

Chronic disease patents

Latanoprost

Apotex

- Promise is that the compound is efficient in the treatment of glaucoma on a chronic basis without side effects
- The data in the patent is not a chronic use study
- Single dose may not predict long term
- Need to disclose the factual basis and the prediction

Pharmascience

- Promise is that compound will be useful in the treatment of glaucoma
- Tests results in three animal models and in humans is sufficient to demonstrate the utility

Apotex v. Pfizer (NOC) 2011 FCA 236, rev'g 2010 FC 447

Pfizer v. Pharmascience (NOC) 2009 FC 1294; aff'd 2011 FCA 102

CA 1,339,132 (latanoprost) FD: 1989

latanoprost I FC & FCA: utility shown; latanoprost II FC utility shown, FCA rev'g

PROSTAGLANDIN DERIVATIVES FOR THE TREATMENT OF GLAUCOMA OR OCULAR HYPERTENSION

The invention is concerned with the use of prostaglandin derivatives of PGA, PGB, PGD, PGE and PGF, in which the omega chain has been modified with the common feature of containing a ring structure, for the treatment of glaucoma or ocular hypertension. The invention relates also to ophthalmic compositions, containing an active amount of these prostaglandin derivatives, and the manufacture of such compositions.

CA 1,339,132 (latanoprost) specification

Pg 3: Prostaglandins (PGs) were known to reduce intraocular pressure

- Use of PGs and their derivatives for treatment of ocular hypertension or glaucoma known**
- Problem in causing superficial irritation, corneal irritation, and vasodilation in the conjunctiva (covering of the white of the eyes)**

Pg 4: PG application leads to feeling of grittiness

CA 1,339,132 (latanoprost) specification

We have now found that a solution to the problems discussed above is the use of certain derivatives of prostaglandins A, B, D, E and F, in which the omega chain has been modified with the common feature of containing a ring structure, for the treatment of glaucoma or ocular hypertension.

Examples 1-12 – synthesis of compounds

Pg 18: Ocular discomfort evaluated in cats (after 60 min)

- Conjunctival hyperemia (enlarged blood vessels; red-eye) evaluated in rabbits
- Intraocular pressure determined using monkeys and humans (up to a 9 hr period)

CA 1,339,132 (latanoprost) specification

Pg 19 : 14 compounds tested over 60 min period (initial screening) in Table III

It is evident from Table III that modification of the omega chain of the prostaglandin skeleton introduced new and unexpected features to the prostaglandins with respect to ocular irritation (discomfort). Particularly 17-phenyl,18,19,20-trinor-PGF_{2α}-IE and analogs were unique in exhibiting a complete loss of ocular irritation with retained IOP lowering effect in monkeys. Whereas the 17-phenyl,18,19,20-trinor-PGF_{2α} derivatives were extremely well tolerated, 16-phenyl-17,18,19,20-tetranor-PGF_{2α}-IE caused clear ocular discomfort although to a lesser degree than PGF_{2α}-IE or 15-propionate-

CA 1,339,132 (latanoprost) specification

In addition to the lack of ocular discomfort the omega chain modified analogs also exhibited an advantage over naturally occurring prostaglandins in that they caused considerably less conjunctival hyperemia as studied in the rabbit eye

The intraocular pressure lowering effect of omega chain modified and ring-substituted prostaglandin analogs is demonstrated in Table V. It can be seen that particularly 16-phenyl-tetranor and 17-phenyl-trinor prostaglandin analogs significantly reduced IOP in animal eyes (Table V).

Pfizer v Pharmascience (2009 FC 1294; aff'd 2011 FCA 102)

latanoprost II

[Claim 1: A therapeutic composition for topical treatment of glaucoma or ocular hypertension, containing a prostaglandin PGA, PGB, PGD, PGE or PGF in an amount sufficient to reduce intraocular pressure without causing substantial ocular irritation and an ophthalmologically compatible vehicle, which the omega chain of the prostaglandin has the formula...]

Claims 12, 19, 31, 37 and 38 at issue

Claim 12 (depends from claim 1) composition, claim 19 directed to compound

Claims 31, 37, 38 directed to use of different compounds for “the treatment of glaucoma or ocular hypertension”

Held: Claims not obvious, have utility and are not overbroad

Pfizer v Apotex (2011 FCA 236; rev'g 2010 FC 447) latanoprost I

FC held: Claims not obvious, have utility and are not overbroad

FCA did not agree:

[13] According to Apotex, this claimed utility, correctly construed, means that chronic use of latanoprost “will reduce intraocular pressure without causing substantial ocular irritation”: glaucoma is a chronic disease, the management of which requires chronic treatment.

Pfizer v Apotex (2011 FCA 236) latanoprost I

[5] ...I agree with Apotex that the Applications Judge erred in her construction of the promise of the '132 patent, an error which affected the rest of her analysis.

[14]...at the time of the filing of the '132 patent, the inventors had only conducted single dose studies, yet promising that the compounds can be used chronically without eliciting unwanted side effects...the '132 patent is not based on demonstrated utility, but rather on a prediction of chronic treatment without substantial side effects.

Pfizer v Apotex (2011 FCA 236) latanoprost I

Can reference to prior art documents to support line of reasoning be made?

[43] At the hearing, counsel for Pfizer argued that the line of reasoning was to be found in the studies listed in the “References” section of the patent... Pfizer also took the position that a POSITA, taking the prior art as a whole, would be able to infer that multiple doses of latanoprost would give the same results as the single dose studies.

[44] This position seems at odds with the concept of disclosure in patent law [citing AZT 2002 4 SCR 153, para 70]... a patent that provides no more disclosure than is available in the prior art does not provide a sound basis for the prediction [citing raloxifene 2009 FCA 97 para 17].

Drafting points: latanoprost

- **How much data is required to support long term/chronic use?**
 - Is claiming a chronic condition feasible?
 - How many illnesses are chronic?
- **If the data supporting utility falls short, is there an argument for sound prediction?**
- **Could different language have been used to avoid the promise of chronic treatment?**
 - would use claims directed to only ocular hypertension been challenged?
 - no use defined in product claims (18, 19), yet claims held invalid:
 18. 13,14-dihydro-17-phenyl-18,19,20-trinor-PGF₂ -alkyl-ester, in which the alkyl group has 1-10 carbon atoms.
 19. Compound of claim 18, wherein the alkyl group is isopropyl.

Novopharm v Lilly (atomoxetine)

Atomoxetine ADHD

Novopharm

- Not sufficient evidence that atomoxetine was clinically useful in treating ADHD
- 7 weeks trial on 21 adults is not enough to meet the promise of treating ADHD since ADHD is a chronic disease.

Novopharm v. Eli Lilly 2010 FC 915, aff'd *Eli Lilly v. Teva* 2011 FCA 220

CA 2,220,735 atomoxetine FD:1996

atomoxetine I FC utility shown; atomoxetine II FC & FCA no utility

TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

Tomoxetine is a well-known drug, the chemical name of which is (R)-(-)-N-methyl-3-(2-methylphenoxy)-3-phenylpropylamine. It is regularly used as a salt, and salts are included in the term tomoxetine as used here. See, for

...

Tomoxetine is a notably safe drug, and its use in ADHD, in both adults and children, is a superior treatment for that disorder because of its improved safety. Further, tomoxetine is effective at relatively low doses, as discussed below, and may safely and effectively be administered once per day. Thus, difficulties created by the multiple dosing of patients, particularly children and disorganized adults, are completely avoided.

old & known
compound

CA 2,209,735 atomoxetine

Pg 3: dosage range; oral administration; utility:

The method of the present invention is effective in the treatment of patients who are children, adolescents or adults, and there is no significant difference in the symptoms or the details of the manner of treatment among patients of different ages. In general terms, however, for

16 claims – directed to new use for old and known compound:

1. The use of tomoxetine for treating attention-deficit/hyperactivity disorder in a patient in need thereof.

Novopharm v Lilly 2010 FC 915 atomoxetine

Is data to support utility required in specification?

[36] ... the '735 Patent offers no information about the nature or sources of the evidence relied upon by the inventors to support the promise of atomoxetine's utility to treat ADHD by demonstration or by sound prediction.

[94] ... there is no reference to the MGH [Massachusetts General Hospital] Study in the '735 Patent...

[20] – MGH results considered preliminary

Novopharm v Lilly 2010 FC 915 atomoxetine

[32] There is no dispute about the inventive promise of the '735 Patent. The 16 patent claims involve the use of atomoxetine for treating ADHD... The patent does not claim the compound atomoxetine but only its use to treat ADHD...

Novopharm v Lilly 2010 FC 915 atomoxetine

[77] – use of atomoxetine to treat ADHD not obvious

[79] – use not anticipated: “..the ‘430 Patent refers specifically to atomoxetine as an NRI [norepinephrine reuptake inhibitor] but only to treat depression...”

[88] – not a selection patent: “... by limiting the claim in the ‘735 Patent to the use of atomoxetine to treat ADHD, there is no requirement that Lilly disclose any special advantage that atomoxetine might enjoy over the compounds claimed by the ‘009 Patent...”

Novopharm v Lilly 2010 FC 915 atomoxetine

[94] Even though there is no reference to the MGH Study in the '735 Patent, Lilly relies upon it to demonstrate the utility of atomoxetine to treat ADHD at the time of the Canadian filing date of January 4, 1996.

[112]...In the case of the '735 Patent, the inventors claimed a new use for atomoxetine to effectively treat humans with ADHD. What is implicit in this promise is that atomoxetine will work in the longer term.

Novopharm v Lilly 2010 FC 915 atomoxetine

[112]...I do not, however, agree... that if a single case [the MGH] study involving one patient showed a clinical benefit, this “scintilla of utility” would, as a matter of course, be sufficient to establish utility... The evidence to demonstrate utility must be sufficient to support the promise that atomoxetine works to treat ADHD in some patients.

(emphasis added)

Novopharm v Lilly 2010 FC 915 atomoxetine

[120]... to the extent that the '735 Patent is based on a sound prediction from the MGH Study that atomoxetine is useful in the treatment of ADHD, the patent fails for want of disclosure because some reference to those findings was required to be set out in the patent.

Similar to conclusion in raloxifene (2009 FCA 97):

“[15]...when a patent is based on a sound prediction, the disclosure must include the prediction. As the prediction was made sound by the Hong Kong study, this study had to be disclosed.”

Novopharm v Lilly 2011 FCA 220 atomoxetine

[21]... [the Judge was] interpreting what “treatment” means in this patent in the context of ADHD, a chronic disorder requiring sustained treatment. He was not adding a promise above and beyond that already expressed in the words of the patent, namely that atomoxetine is an effective treatment of ADHD.

Novopharm v Lilly 2011 FCA 220 atomoxetine

[32]...The utility of the patent is thus determined by examining whether atomoxetine will do what Lilly promised that it would do.

[34] The question is whether Lilly had sufficient evidence in 1996 to establish that atomoxetine would deliver on the promise of the patent.

Novopharm v Lilly 2011 FCA 220 atomoxetine

[35]...the Judge concluded that the clinical trial had serious methodological limitations, particularly its short duration and small sample, shortcomings that were also acknowledged by the authors of the MGH Study.

[36] The Judge agreed that the data from this pilot study were promising... Nonetheless, the patent promised that atomoxetine was an effective treatment of ADHD, that is, it would alleviate manifestations of the disorder in some patients to such a degree that a doctor would consider prescribing it.

(emphasis added)

Novopharm v Lilly 2011 FCA 220 atomoxetine

[39] It is also relevant that, on the basis of the MGH Study, Lilly did not immediately proceed with the development of atomoxetine. Rather, atomoxetine was one of three compounds which Lilly considered as possible treatments of ADHD, before finally selecting atomoxetine. Lilly's contemporaneous conduct does not suggest that it viewed the MGH Study as demonstrating that atomoxetine was an effective treatment of ADHD. (emphasis added)

- implying Lilly may have had doubt's about compound's use

Drafting points: atomoxetine

- **Comments about utility without specific support, not sufficient to support a utility or a promise**
 - Is a commercial utility required to satisfy utility requirement?
- **Include data and line of reasoning in specification**
 - both required for sound prediction
- **How much evidence is required to support utility?**
- **If the MGH study was included would this be enough?**
 - is there a diligence requirement in Canada?
 - do we need to inquire with inventors re: diligence?

Advantages and goals

Donepezil (Pfizer v. Mylan)

Promise is an effective treatment for Alzheimer, potential advantages (lack of side effects, better toxicity and better duration compared to the prior art) should not be construed as a promise

Pfizer v. Mylan (NOC) 2011 FC 547, aff'd 2012 FCA 103

CA 1,338,808 donepezil FD: 1988

FC & FCA – utility shown

Cyclic Amine Compound

The invention relates to a cyclic amine compound,
a therapeutical composition and medical treatment of
senile dementia. . . .

In view of the above situation, the present
inventors have made extensive and intensive studies
on various compounds for many years with a view to
developing a drug which has a persistent activity
and a high safety.

As a result, the present inventors have found
that a piperidine derivative represented by the
following general formula (I) can attain the desired
object.



CA 1,338,808 donepazil

Specifically, the compound of the present invention represented by the following general formula (I) has great advantages of having strong and highly selective antiacetylcholinesterase activity, increasing the amount of acetylcholine present in the brain, exhibiting an excellent effect on a model with respect to disturbance of memory, and having a persistent activity and a high safety when compared with physostigmine which is a conventional popular drug in the art, which renders the compound of the present invention very valuable.

CA 1,338,808 donepazil

Pg 2-21: description of compounds

Pg 22-48: synthesis of compounds

Experimental examples: 1, 2 – mouse and rat brain assays (esterase inhibitory activity)

Experimental example 3: learning impairment assay – rats (Tables 2, 3 pgs 52, 52)

Pgs 55-56: administration; dosage ranges

Examples 1-249: synthesis of compounds

Pg 147: Table 10 -inhibitory effect in esterase assay

CA 1,338,808 donepezil

Following experimental example 3 (pg 54):

Therefore, the objects of the present invention are to provide a novel compound effective for various kinds of dementia and the sequelae of cerebrovascular diseases, to provide a process for preparing the same, and to provide a novel pharmaceutical comprising the same as an effective ingredient.

CA 1,338,808 donepezil

The compound of the present invention is effective for treatment, prevention, remission, improvement, etc. of various kinds of senile dementia, particularly senile dementia of the Alzheimer type; cerebrovascular diseases accompanying cerebral apoplexy, e.g. cerebral hemorrhage or cerebral infarcts, cerebral arteriosclerosis, head injury, etc.; and aprosexia, disturbance of speech, hypobulia, emotional changes, recent memory disturbance, hallucinatory-paranoid syndrome, behavioral changes, etc. accompanying encephalitis, cerebral palsy, etc.

CA 1,338,808 donepezil

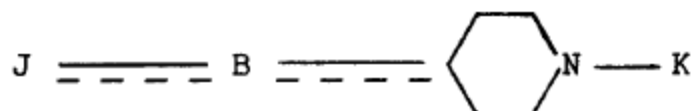
Further, the compound of the present invention has a strong and highly selective anticholinesterase action, which renders the compound of the present invention useful also as a pharmaceutical based on this kind of action.

Specifically, the compound of the present invention is effective for, for example, Huntington's chorea, Pick's disease and delayed ataxia or tardive dyskinesia other than senile dementia of the Alzheimer type.

Pfizer v Mylan 2012 FCA 103 donepezil

[14]...“Is the ‘808 Patent, and in particular, claim 6 and claim 18, invalid because it is based upon an unsound prediction of the promised utility?”

1. A piperidine compound having the following formula:



6. The compound 1-benzyl-4-[(5,6-dimethoxy-1-indanon)-2-yl]methylpiperidine or a pharmaceutically acceptable acid addition salt thereof.

18. A therapeutical composition for treating senile dementia, which comprises an acetylcholinesterase inhibitory effective amount of the compound or salt as defined in any one of claims 1 through 17 and a pharmaceutically acceptable carrier.

Pfizer v Mylan 2012 FCA 103 donepezil

[18] The application judge concluded “that the ‘promise’ or stated utility of the ‘808 Patent” was “that a new class of compounds has been discovered (donepezil being one) which, having regard to the cholinergic function theory of AChE inhibition, is effective for the treatment of Alzheimer’s”: Reasons at para. 232

Pfizer v Mylan 2012 FCA 103 donepezil

[19] The application judge further found that even though donepezil's utility had not been demonstrated through testing on humans, its promised utility could be soundly predicted as of the filing date of the '808 Patent (June 21, 1988)...- the application judge found that a factual basis existed in that "donepezil was made and was tested in various ways in both mice and rats" (Reasons at para. 241);

Pfizer v Mylan 2012 FCA 103 donepazil

[55]...Mylan argues that where a patentee promises that a compound will be free from negative side effects or has better toxicity and duration than prior art compounds, the patentee will be held to that promise...cites *Apotex Inc. v. Pfizer Canada Inc.*, 2011 FCA 236, 95 C.P.R. (4th) 193 (“*Latanoprost*”)

Pfizer v Mylan 2012 FCA 103 donepazil

Distinguishing Latanoprost:

[56] The patent in *Latanoprost* claimed a “therapeutic composition for topical treatment of glaucoma or ocular hypertension, containing a prostaglandin...in an amount sufficient to reduce intraocular pressure without causing substantial ocular irritation...”...this Court construed the patent considered in *Latanoprost* as promising the avoidance of side effects. In contrast, claim 18 of the ‘808 Patent simply refers to a “therapeutical composition for treating senile dementia...” without any further promise relating to side effects or toxicity.

Pfizer v Mylan 2012 FCA 103 donepezil

[57] Though some references are made in the ‘808 Patent to potential toxicity and efficacy benefits of donepezil, and to its potential advantages over prior art compounds, the application judge, on the basis of the expert evidence before him, rightly concluded that these references are not to be construed as promises. He noted that the use of the specification of a patent in order to construe its promise “is not to serve as an invitation to a zealous lawyer to read a patent specification in such a way as to persuade a Court, one way or the other, as to what the promise is”...

(emphasis added)

Drafting points: donepazil

- **When is a reference not a promise?**
 - Are comments made in passing a reference?
- **Reference to Alzheimer's, but promise is for AChe inhibition**
- **Promise determined from specification and claims:**
 - in latanoprost “promising the avoidance of side effects” not satisfied (even though data re: irritation provided in spec):
 - claim 1 (latanoprost) included a promise: “in an amount sufficient to reduce intraocular pressure without causing substantial ocular irritation...”;
 - But: claim 19 compound claim – no promise in claim; invalid

Advantages and goals

Anastrozole (AstraZeneca v. Mylan)

Promise is only that the compound has inhibitory effects on aromatase

No specific promise of fewer side effects compared to the prior art

Patent that only mentions that its aim is to solve a problem without promising that it had would be valid

A compound that is not commercially or clinically useful could be valid as an aromatase inhibitor

Astrazeneca v. Mylan (NOC) 2011 FC 1023, aff'd 2012 FCA 109

CA 1337420 anastrozole FC: 1988

FC & FCA utility shown

TITLE – (SUBSTITUTED-ARALKYL)HETEROCYCLIC COMPOUNDS

This invention relates to (substituted-aralkyl)-heterocyclic compounds, and in particular relates to such compounds which are useful as inhibitors of the enzyme aromatase.

A variety of compounds possessing aromatase inhibitory activity is known, of which the most important clinically is aminoglutethimide. Aminoglutethimide, however, has the drawback that it affects other aspects of steroid metabolism, with the consequence that its use is often associated with undesirable side-effects. It is a particular object of the present invention to provide aromatase inhibitory compounds with fewer undesirable side effects than aminoglutethimide.

CA 1337420 anastrozole

Pg's 2-8 description of compounds

Pg's 9-11 synthesis of compounds

Pg 11:

As indicated above, the compounds of the invention of the formula I are useful as aromatase inhibitors. Aromatase inhibition may be demonstrated by the following tests:—

Pg 12 - in vitro activity aromatase inhibitory activity

Pg's 12-13 in-vivo activity ovulation inhibition in rats

Pg 13 formulations; administration

Examples 1- 70: synthesis of compounds

Astrazeneca v Mylan 2011 FC 1023 anastrozole

[29] ... claims 13, 14 and 15 ...are at issue in this proceeding.

13. The compound 2,2'-[5-(1H-1,2,4-triazol-1-ylmethyl)-1,3-phenylene]di(2-methylpropiononitrile).

14. A pharmaceutical or veterinary composition which comprises an effective amount of the compound 2,2'-[5-(1H-1,2,4-triazol-1-ylmethyl)-1,3-phenylene]di(2-methylpropiononitrile) together with a pharmaceutically or veterinarily acceptable diluent or carrier.

15. The use of the compound 2,2'-[5-(1H-1,2,4-triazol-1-ylmethyl)-1,3-phenylene]di(2-methylpropiononitrile) as an inhibitor of the enzyme aromatase.

Astrazeneca v Mylan 2011 FC 1023 anastrozole

[92] AstraZeneca's position is that the patent only promises aromatase inhibition.

[93] Mylan's position is that the patent contains a threefold promise: (1) the inhibition of aromatase; (2) its therapeutic utility against estrogen dependent cancers; and (3) fewer side effects than AG.

Astrazeneca v Mylan 2011 FC 1023 anastrozole

Aromatase is an enzyme which effects aromatisation of ring A in the metabolic formation of various steroid hormones. Various cancers, for example breast cancer, are dependent upon circulating steroid hormones which have an aromatic ring A. Such cancers can be treated by removing the source of ring A aromatised steroid hormones, for example by the combination of oophorectomy and adrenalectomy. An alternative way of obtaining the same effect is by administering a chemical compound which inhibits the aromatisation of the steroid ring A, and the compounds of the invention are useful for this purpose.

Does the phrase (2nd para) “useful for this purpose” refer to:

- treatment of breast cancer or**
- inhibiting the aromatization of steroid ring A?**

Astrazeneca v Mylan 2011 FC 1023 anastrozole

[107] ...a skilled person would read the 420 Patent with the knowledge that aromatase inhibitors can be used in the treatment of breast cancer...

however

[108] ... the experts' understanding of the relevant scientific context is one factor to consider when construing the promise of the patent, but it is not necessarily determinative. The Court must also consider the plain language of the claims and the disclosure.

Astrazeneca v Mylan 2011 FC 1023 anastrozole

[109] ...[while] the second paragraph of the 420 Patent ... does refer to cancer treatment, the language focuses on the pharmacological action of the invention. The purpose of the invention is to inhibit the aromatisation of steroid ring A. While it may be common general knowledge that aromatase inhibition can be used in the treatment of breast cancer, I do not read an explicit promise of therapeutic utility into this paragraph.

Astrazeneca v Mylan 2011 FC 1023 anastrozole

[113] The language of the 420 Patent also does not approach the degree of clarity or specificity of other patents in which this Court has read a promise of therapeutic utility.

[..examples of specific promises provided..]

[117] These are just a few examples of the type of language that has supported a finding of therapeutic utility. In each case, there is clear language promising that the pharmacological compound will be effective or useful in the treatment of a disease. Such language cannot be found in the 420 Patent.

(Emphasis added)

Astrazeneca v Mylan 2011 FC 1023 anastrolzole

Donepezil - supporting a finding of therapeutic utility:

“The invention relates to a cyclic amine compound, a therapeutical composition and medical treatment of senile dementia.”

“The compound of the present invention was found based on the acetylcholinesterase inhibitory action and, therefore, is effective for treatment and prevention of various diseases which are thought to be derived from the deficiency of acetylcholine”

“Examples of such diseases include various kinds of dementia including Alzheimer senile dementia...”

“Therefore, the objects of the present invention are to provide a novel piperidine derivative effective as a pharmaceutical, particularly for treatment and prevention of central nervous system diseases,”

(emphasis in original) FC & FCA utility shown

Astrazeneca v Mylan 2011 FC 1023 anastrolzole

Ramipril - supporting a finding of therapeutic utility:

“The present invention relates to carboxyalkyl dipeptides which are useful as inhibitors of angiotensin-converting enzyme and as antihypertensive agents. [Emphasis added]”

“The compounds of this invention have useful pharmacological properties. They are useful in the treatment of high blood pressure.”

“...suitable for oral or parental administration to provide compositions useful in the treatment of cardiovascular disorders and particularly mammalian hypertension”

(emphasis in original) FC & FCA no utility (in both ramipril I & II)

Astrazeneca v Mylan 2011 FC 1023 anastrolzole

Lovastatin - supporting a finding of therapeutic utility:

“These new compounds have excellent properties of inhibiting cholesterol biosynthesis and are useful against hypercholesteremia and hyperlipemia.”

“The compounds of this invention are highly useful as antihypercholesteremic agents for the treatment of atherosclerosis, hyperlipemia and like diseases in humans”

FC & FCA utility shown

Astrazeneca v Mylan 2011 FC 1023 anastrozole

Object clause: a “hope or wish”, or a promise?

“It is a particular object of the present invention to provide aromatase inhibitory compounds with fewer undesirable side effects than aminoglutethimide.”

[132] A plain reading of the word ‘object’ suggests that it is an aim to be fulfilled...A goal, purpose, or aim... [based on dictionary definition]

[133] Goals and objectives are by definition forward looking. They refer to potential, possibility or contingent events or consequences.

Astrazeneca v Mylan 2011 FC 1023 anastrozole

Was utility (aromatase inhibitor useful in treatment of breast cancer) soundly predicted?

[166] There is no doubt that further and better testing could have been done, but scientific perfection is not required to demonstrate utility.

Inhibitor (in vitro) assays: details of test not described;

- data compared to known values of AG & not directly assayed**
- test still considered adequate**

Ovulation inhibition (in vivo) assays: ovulation inhibition may not be a result of aromatase inhibition; but

- data between two tests consistent**

Astrazeneca v Mylan 2011 FC 1023 anastrozole

Can reference to a study support the line of reasoning?

[180] In both *Novopharm sildenafil FCA [2010 FCA 242 para 90]* and *Pfizer latanoprost [2011 FCA 236 para 30]*, the Federal Court of Appeal speaks of the need to refer to a study in the patent disclosure to demonstrate utility. Both of these cases dealt with patents that promised therapeutic utility, while I have found that the 420 Patent only promises pharmacological action. The scope of the disclosure requirement is informed by or takes its colour from the nature of the claim. While a full study might be necessary to demonstrate therapeutic utility, I find that the two laboratory tests disclosed in the 420 Patent are adequate to demonstrate pharmacological action as aromatase inhibitors.

See also [188]

Astrazeneca v Mylan 2012 FCA 109 anastrozole

[8] The question in dispute in this appeal concerns the construction of the underlined sentence in the following paragraph from the patent specification...

It is a particular object of the present invention to provide aromatase inhibitory compounds with fewer undesirable side effects than [AG].

[25] Mylan ...[argued] the Judge put undue weight on the dictionary definition of “object”, rather than considering its meaning in the context of patent law... *Amfac Foods Inc. v. Irving Pulp & Paper, Ltd. (1986), 12 C.P.R. (3d) 193 (F.C.A.)* at 199 ...an “object clause” [was used] to define the scope of the invention...

Astrazeneca v Mylan 2012 FCA 109 anastrolzole

[26] I do not agree. Patents are not required to contain a clause describing the object of the invention. When they do, the meaning of the object clause depends on the specific context, including the wording of the particular clause in question and its relationship to the rest of the patent.

Para's [28] – [29] - Meaning of the word “object” is determined by expert evidence and patent as a whole

- only one reference to fewer side effects in specification**
- claims 13, 15 reference inhibiting aromatase activity**

Drafting points: anastrolzole

- Promise based on claims and disclosure
- Expert's opinions one factor to construe promise of the patent “but not necessarily determinative”
- Lower degree of clarity or specificity of the promise may be beneficial(!):
 - i.e. avoid a promise of therapeutic utility, but
 - will likely cause trouble in the US and Europe
- Selection of assays and models important for predicting utility; reference to study required for therapeutic utility
- In some contexts object clauses are non limiting
 - ...really?

Selection patents

A selection patent is a special beast

Since the compound claimed in the selection patent has never been made but has already been disclosed, enabled and/or claimed in a prior publication the invention in the selection patent is the discovery of special properties that are new, unobvious and useful

Often the Courts will construe the promise as being the existence of these special properties

The novelty of the selection and its advantages over the genus patent is the invention

Selection patents (Sanofi 2008 SCC 61) *Plavix*

“In re I. G. Farbenindustrie A. G.'s Patents (1930), 47 R.P.C. 289 (Ch. D.). ...in the field of chemical patents,...there are often two "sharply divided classes". The first class of patents,... are based on an originating invention, namely, the discovery of a new reaction or a new compound. The second class comprises patents based on a selection of compounds from those described in general terms and claimed in the originating patent. ...the selected compounds cannot have been made before, or the selection patent "would fail for want of novelty". But if the selected compound is "novel" and "possess[es] a special property of an unexpected character", the required "inventive" step would be satisfied...” (emphasis added)

Sanofi-Aventis v. Apotex (clopidogrel)

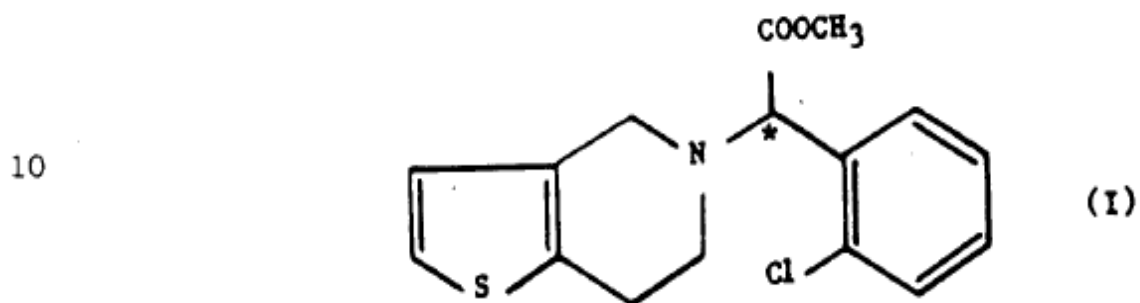
- The most recent judgment about selection patent is the CA judgment concerning clopidogrel
- In this case the Court construed the inventive concept as being the special properties of clopidogrel over the genus patent
 - More active
 - Less toxic
- The Court refused to accept that the patent promised use in humans, the patent only refer to a possible use in human
- The patent does not promise anything

CA 1,336,777 clopidogrel FD: 1988

FC no utility; FCA rev'g utility shown

The present invention relates to the dextro-rotatory enantiomer of methyl alpha-5 (4,5,6,7-tetrahydro (3,2-c) thieno pyridyl) (2-chlorophenyl)-acetate, a process for its preparation and pharmaceutical compositions containing it.

5 The compound of the invention corresponds to the following formula (I):



CA 1,336,777 clopidogrel

25 In an unexpected manner only the dextro-rotatory enantiomer I_d exhibits a platelet aggregation inhibiting activity, the levo-rotatory enantiomer I_l being inactive. Moreover, the inactive levo-rotatory enantiomer I_l is the less well tolerated of the two enantiomers.

10 Among the mineral and organic acid salts of the dextro-rotatory isomer of the compound of Formula (I_d) salts have been found which crystallize easily, are not hygroscopic and are sufficiently water-soluble as to make their use as active medicinal principles particularly advantageous.

15 The present invention thus relates more particularly to the hydrogen sulfate, the taurocholate and the hydrobromide of the dextro-rotatory enantiomer of methyl alpha-5 (4,5,6,7-tetrahydro (3,2-c) thieno pyridyl) (2-chlorophenyl)-acetate.

CA 1,336,777 clopidogrel

Pg 2-7 stereoisomer discussion; reaction scheme to produce dextro-rotary compound

Example 1 – synthesis of dextro-rotary compound

Example 2 – synthesis levo-rotary compound

Pg 11 – pharmacological study - rat

PHARMACOLOGICAL STUDY

The platelet aggregation inhibiting activity and the toxicity of these new compounds was compared to those of the racemic mixture described
35 in the French patent No. 82.12599 (Publication No. 2 530 247), published on January 20, 1984.

CA 1,336,777 clopidogrel

- 12 -

1336777

A description will now be given of the results of this study which demonstrates another advantage of the invention, namely that the salts of the dextro-rotatory isomer have a better therapeutic index than the salt of the racemic mixture; in fact, the levo-rotatory isomer exhibits almost no platelet aggregation inhibiting activity and its toxicity is markedly higher than that of its dextro-rotatory homologue.

CA 1,336,777 clopidogrel

Pg 14 - aggregation with ADP - Table 1 demonstrates the levo-rotary (1l) isomer is inactive, the dextro-rotary isomer (1d) as active as racemate

Pg 15 - aggregation of collagen - Table II

Pg 17 - antithrombic activity; rats - Table III

Pg 18 - toxicology study; rats - Table IV

Pg 20 - inhibitory properties to platelet aggregation found with 1d, not 1l

- dosage forms; administration methods

CA 1,336,777 clopidogrel

Pg 21:

On account of its interesting inhibitory properties towards platelet aggregation and its interference in the mechanism of formation of arterial and venous thromboses, the medicine of the invention can be usefully administered in the treatment and prevention of platelet disorders due to extracorporeal blood circuits or the consequence of complications in atheroma.

- Section “H” (para [119] – [132]) of FC & [50] – [71], & [124] – 135] of FCA decision reviewed meaning of 5 words “...medicine of the invention can be...”
 - Does this statement promise a use of compound in humans?

Sanofi v Apotex 2011 FC 1486 clopidogrel

[109] Where there are technical terms in a patent, the Court is assisted by experts as to the meaning of such terms. The term the “medicine of the invention” as referred to in the ‘777 Patent is one such technical phrase that must be interpreted by the Court... Indeed, **the meaning of the phrase “medicine of the invention” informs the promise of the patent and must be ascertained at this stage of the analysis before the promise of the patent can be determined.**

Sanofi v Apotex 2011 FC 1486 clopidogrel

[121] The positions of the parties regarding the above could not be further apart...Apotex' position is that page 21 of the '777 Patent guarantees treatment in humans ... Sanofi's position is that page 21 of the '777 Patent does not in any way make reference to treatment in humans or, if it does, only to the "potential" for use in humans.

[123] Whilst the '777 Patent does not refer to a guarantee, it does refer to more than a remote "potential" in humans. Unable to accept either of the two extreme interpretations of page 21 urged by the parties, the Court finds that the '777 Patent makes reference to use in humans.

Sanofi v Apotex 2011 FC 1486 clopidogrel

[382] As the promise of the patent is the use of the invention for treatment in humans, and the invention only specifies “greater” or “lesser” values, the Court will not scrutinize the degree of difference as argued by Apotex, but it will inquire into whether there was a sound prediction that there would be some degree of activity, tolerability and toxicity difference that would occur in humans.

Sanofi v Apotex 2011 FC 1486 clopidogrel

[533]... clopidogrel falls in the third category. Its formation of metabolites was essential in order to understand its activity... it automatically creates an “unbreachable fire wall” and, thus, any prediction from animal to human is unknown.

[541] The Court finds that, based on the evidence, there is no question that a pro-drug compound like clopidogrel has to be metabolized. It was thus critical for Sanofi’s scientists to recognize that metabolism was a significant hurdle in the line of reasoning to predict that the invention could be used in humans.

Sanofi v Apotex 2011 FC 1486 clopidogrel

[570] However, the Court is of the opinion that upon reading the '777 Patent, it does not instruct the POSITA that there was a factual basis and a line of reasoning for the prediction that the animal studies conducted on rat models could be extrapolated to the prediction that the compound – clopidogrel – had a use in humans. The disclosure in the '777 Patent is insufficient.

Sanofi v Apotex 2011 FC 1486 clopidogrel

[572] The tests disclosed in the '777 Patent are with respect to only one strain of animal, in one gender (female), using only a single time point. There was no disclosure of the factual basis or the line of reasoning for the prediction. There was no basis for the POSITA to make “the leap” to predict use in humans.

Invention also held to be obvious (v SCC)

Sanofi v Apotex 2013 FCA 186 clopidogrel

[50] When this Court said at paragraph 80 of Olanzapine, cited above, that the promise of the patent must be ascertained, it should not be taken to have assumed that every patent contains an explicit promise of a specific result since, subject to what is said below with respect to selection patents, there is no obligation on the part of the inventor to disclose the utility of his invention in the patent....

(Emphasis added)

Sanofi v Apotex 2013 FCA 186 clopidogrel

[66] While these “indications” are consistent with human use, they are not inconsistent with other uses. Although Dr. Hirsh was entitled to form an opinion on the basis of the inference which he drew, the Trial Judge was held to a higher standard. He erred in law in reading into the ‘777 patent a promise for use in humans on the basis of inferences, in the absence of language at least as clear and unambiguous as that used to establish the advantages of the selection over the compounds of the genus patent.

(emphasis added)

Sanofi v Apotex 2013 FCA 186 clopidogrel

[67]...As Dr. Byrn made clear, the inventive step was in the differential activity and tolerability of clopidogrel as demonstrated in rats. The pharmaceutical industry's interest of the invention obviously lay in its potential use in humans which the invention foreshadowed. The person skilled in the art would understand that in alluding to this possibility, the inventors were not promising that this result had been or would be achieved.

Sanofi v Apotex 2013 FCA 186 clopidogrel

[70]...A selection patent describes a compound which has an unexpected advantage over the compounds of the genus patent. That unexpected advantage need not be an improvement on every aspect of the invention described in the genus patent, though it may be. It is sufficient that it is a new and useful improvement on some aspect of that invention.

Sanofi v Apotex 2013 FCA 186 clopidogrel

Concurring reasons:

[124]...one may wonder why an inventor would include comments relating to a practical purpose to which an invention may be applied when such statements are not necessary under Canadian law.

[125]...there are other cases where the reasons for including them have little to do with an intent to promise a result within the meaning of *Consolboard*... when Canadian applications are filed on the basis of European applications (priority date), it is useful to know that under European Union patent law, an invention must be capable of industrial application, which is a wide concept. Because of this, European applications will often contain some statements in that respect. In this context, and considering that no such requirement exists in our law, one must be careful not to treat each reference to a practical purpose as a promise of a specific result within the meaning of *Consolboard*.

(emphasis added)

Sanofi v Apotex 2013 FCA 186 clopidogrel

[127] Thus, even if I were to assume that the Trial Judge was correct to construe the last part of the long sentence on page 21 of the '777 patent as referring to human use (“...the medicine of the invention *can* be usefully administered in the treatment and prevention of platelet disorders due to extracorporeal blood circuits or the consequence of complications in artheroma [Emphasis added].”), I could not construe this statement as a promise of a specific result within the meaning of *Consolboard*.

Drafting points: clopidrogrel

- **FC: If promise determined to be something not disclosed – still need to have supporting data**
 - promise determined to be use in humans; no human data
 - rat model not predictive “creating an unbreachable firewall”
- **FCA: Explicit promise not required**
- **Need to consider context of promise-like statements**
 - that something “can be” used, is not necessarily a promise
- **Selection patents describe unexpected advantage**
 - but no need for improvement to be in every aspect of invention described in genus

Eli Lilly v. Novopharm (olanzapine)

Apply Consolboard

Promise is key to utility analysis

Where the specification does not promise a specific result, no particular level of utility is required; a mere scintilla of utility suffice. However, where the specification sets out an explicit «promise, utility will be measured against that promise»

Need first to construe the patent to determine if it contains a promise or not

- Question of law to be determined with experts

Is the promise demonstrated or soundly predicted?

Eli Lilly v. Novopharm 2010 FCA 197, rev'g 2009 FC 1018; sent back, resulting in 2012 FCA 232, aff'g 2011 FC 1288

Eli Lilly v. Novopharm Olanzapine

The patent promise utility in humans

The animal model was not predictive of such utility

CA 2,041,113 (olanzapine) FD: 1991

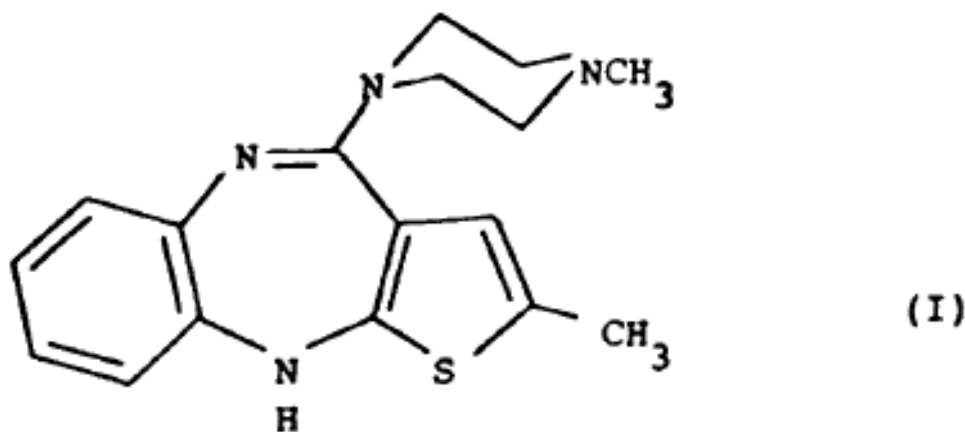
FC no utility; FCA questioning; FC no utility

- Olanzapine (Zyprexa): medicine for treating schizophrenia
- Haloperidol (widely used)
 - problem: high incidence of extra pyramidal symptoms
- Clozapine (on market)
 - resulted in lower white blood cell count; life threatening
- Prior genus patent CA 1,075,687 to “thienobenzodiazapines”
 - olanzapine included in genus; but not disclosed
- Prior candidate drug from '687 – flumezapine
- Human trial with flumezapine terminated after consultation with US FDA due to side effects

CA 2,041,113 (olanzapine) FD: 1991

We have now discovered a compound which possesses surprising and unexpected properties by comparison with flumezapine and other related compounds.

The compound of the invention is of the formula



CA 2,041,113 (olanzapine) specification

The results of pharmacological tests show that the compound of the invention is an antagonist of dopamine at D-1 and D-2 receptors, and in addition has antimuscarinic anticholinergic properties and antagonist activity at 5HT-2 receptor sites. It also has antagonist activity at noradrenergic α -receptors. These properties indicate that the compound is a potential neuroleptic with relaxant, anxiolytic or anti-emetic properties, and is useful in treating psychotic conditions such as schizophrenia, schizophreniform diseases and acute mania. At lower doses the compound is indicated for use in the treatment of mild anxiety states.

As mentioned above, the compound of the invention has shown a high level of activity in the clinical evaluation of psychiatric patients suffering from schizophrenia, and it exhibits this high activity at surprisingly low dosage levels.

- antagonist activity
- neuroleptic (anti-psychotic),
- anxiolytic (anti-panic/anxiety)

- high level of activity in clinical evaluation
- high activity at surprisingly low dosage

CA 2,041,113 (olanzapine) specification

- Open trial in schizophrenic patients:
 - 6 out of 8 patients showed 66-87% improvement at 4 weeks
- Three ongoing human trials
 - preliminary results confirm efficacy at lower dosage
 - mild and transient elevation of liver enzymes (CPK) v. flumezapine; less adverse effect on muscle tissue
- Lower elevation of prolactin levels
 - “than other currently used neuroleptic drugs”
- No alteration of white blood cell count
 - clozapine noted in background to lower white blood cell count
- Dog studies - no rise in cholesterol levels
 - v. ethyl flumezapine which showed a significant rise

CA 2,041,113 (olanzapine) specification

Overall, therefore, in clinical situations, the compound of the invention shows marked superiority, and a better side effects profile than prior known antipsychotic agents, and has a highly advantageous activity level.

- Compound exhibits useful central nervous system activity
- Compound assessed using standard behavioural tests predictive of antipsychotic activity in mouse and rat models

This profile of activity in in vitro receptor binding assays, like that observed in the behavioural tests, would indicate that the compound is effective in the treatment of psychotic conditions but is less likely to induce extra pyramidal side-effects.

CA 2,041,113 (olanzapine) specification

Pg 15-16 - Dosage ranges provided; methods of administration, formulations

Pg 17 Examples 1 & 2: synthesis of compounds

Pg 22 Examples 3 & 7, capsule preparation

Example 4 tablet preparation

Pg 23 Examples 5 & 6 injectable preparations

CA 2,041,113 (olanzapine) claims

3. 2-Methyl-10-(4-methyl-1-piperazinyl)-4H-thieno-[2,3-b][1,5] benzodiazepine. (olanzapine)

6. The use of olanzapine for the manufacture of a drug for the treatment of schizophrenia.

13. A pharmaceutical composition comprising olanzapine and a pharmaceutically acceptable diluent or carrier

14-16. A pharmaceutical composition in capsule or tablet form containing 0.1 to 20 mg (or 0.5 to 10mg, or 2.5 to 5 mg) of olanzapine.

adapted from 2009 FC 1018 (para.[46])

Lilly v Novopharm 2009 FC 1018 olanzapine

“[33] The ‘113 patent proclaims a number of advantageous qualities for olanzapine. These can be grouped into two main categories. First, the ‘113 patent identifies certain advantages of olanzapine over the other compounds from the ‘687 patent. Second, the ‘113 patent boasts the superiority of olanzapine over other known antipsychotic drugs used in the treatment of schizophrenia and related conditions.”

Lilly v Novopharm 2009 FC 1018 olanzapine

Overall, therefore, in clinical situations, the compound of the invention shows marked superiority, and a better side effects profile than prior known antipsychotic agents, and has a highly advantageous activity level.

“[42] Because of its placement – just after a description of particular side effects and olanzapine’s comparative advantages – and because of the introductory words of the sentence (“overall, therefore”), I interpret this assertion as being a general contention about the advantages of olanzapine in respect both of its efficacy and the particular side effects discussed in the preceding passages...” (emphasis added)

Lilly v Novopharm 2009 FC 1018 olanzapine

Superior to what?

[52] As mentioned, there is a general assertion in the '113 patent that olanzapine is superior to the class of compounds covered by the '687 patent. It says that olanzapine displays “surprising and unexpected properties” as compared to flumezapine and other related compounds...

Lilly v Novopharm 2009 FC 1018 olanzapine

[53]... However, in my view, the comparisons in the ‘113 patent between olanzapine and “prior known antipsychotic agents” are also relevant here... the skilled reader, aware of the ‘687 patent, would interpret the alleged superiority of olanzapine over other antipsychotic drugs on the market as being another major advantage of olanzapine over the other ‘687 compounds...” (emphasis added)

- No direct comparative data provided

Prior art compounds: CA '113 pg 2

A widely-used antipsychotic, haloperidol, is one such drug, which has been reported as causing a high incidence of extra pyramidal symptoms and may also cause tardive dyskinesia. More recently, clozapine, one of a large group of tricyclic antipsychotics, has been introduced with the claim that it is free from extra pyramidal effects. However, the compound was found to cause agranulocytosis in some patients, a condition resulting in a lowered white blood cell count which can be life-threatening, and it may now only be employed under very strict medical observation and supervision.

Two commercial products discussed in '113 patent: haloperidol and clozapine
Problems with these compounds addressed in the '113 patent

Lilly v Novopharm 2009 FC 1018 olanzapine

[119] Clearly, it is not enough for a selected compound merely to achieve what was promised in the genus patent... a valid selection patent involves a “discovery that the selected members possess qualities, hitherto undiscovered, particular to themselves and not attributable to them by virtue of the fact that they are belonging to a class specified by an earlier invention”... The advantage must be something better and different than what the general class is supposed to be able to do.

(emphasis added)

Lilly v Novopharm 2009 FC 1018 olanzapine

“[127] In my view, the alleged advantages of olanzapine over flumezapine and ethyl olanzapine are not substantial... there is no evidence that olanzapine was superior to any other compounds in the ‘687 class in respect of the characteristics described in the ‘113 patent. The comparisons did not relate to the class as a whole and I have no evidence that any advantage was peculiar to olanzapine.”

(emphasis added)

“[26] Lilly halted its clinical trials on flumezapine in April 1982 after receiving reports of elevated liver enzymes and a muscle enzyme called creatine phosphokinase (CPK) in some patients.”

“[30]... Ethyl flumezapine had been an abject failure.”

“[147] I would not conclude that the selection of olanzapine as a development compound was an obvious choice... olanzapine was not the only candidate under consideration, and did not even appear to be particularly active. It was not “more or less self-evident” that olanzapine would work”

Lilly v Novopharm 2010 FCA 197 olanzapine

“[20].... selection patents exist to encourage researchers to further use their inventive skills so as to discover new advantages for compounds within the known class”

Olanzapine is novel – not made or specifically disclosed in genus patent (para [50])

Advantages could not be ascertained until made

Not obvious – novel compound with advantages

Lilly v Novopharm 2010 FCA 197 olanzapine

[78] With respect to selection patents, the inventiveness lies in the making of the selected compound, coupled with its advantage or advantages, over the genus patent... The advantage or the nature of the characteristic possessed by the selection must be stated in the specification in clear terms (Sanofi, para. 114)...

[79] However, no specific number of advantages is required. One advantage may be enough or any number of seemingly less significant advantages (when considered separately) may suffice... (emphasis added)

Lilly v Novopharm 2010 FCA 197 olanzapine

[82]...Summary:

- 1) the promise is ascertained using expert evidence;
- 2) requires either sufficient information upon which to base the promise on; or if insufficient,
- 3) sufficient information to make a sound prediction (“more than mere speculation”);
- 4) promise is determined at the time of filing; or
- 5) if based on sound prediction, “it must ultimately be born out”

Lilly v Novopharm 2011 FC 1288 olanzapine

Utility and sufficiency referred back to FC:

[67]...I found there to be a general assertion that the ‘113 patent that olanzapine is superior to the class of compounds covered by the ‘687 patent. The patent states that olanzapine displays “surprising and unexpected properties” as compared to flumezapine and other related compounds...

- (i) Olanzapine has lower elevations of liver enzymes than flumezapine;**
- (ii) Olanzapine has lower elevations of CPK than flumezapine;**
- (iii) Olanzapine has less EPS liability than flumezapine; and**
- (iv) Olanzapine does not elevate cholesterol, but ethyl olanzapine does.**

Lilly v Novopharm 2011 FC 1288 olanzapine

[70] While the '113 patent refers only to two of the '687 compounds and their disadvantages, it is clear that neither of them had been used for the treatment of schizophrenia or any other condition. By contrast, according to the '113 patent, not only could olanzapine be used for that purpose, it was, “overall”, markedly superior to, and had a better side effects profile than, other drugs on the market.

(emphasis added)

Lilly v Novopharm 2011 FC 1288 olanzapine

Overall, therefore, in clinical situations, the compound of the invention shows marked superiority, and a better side effects profile than prior known antipsychotic agents, and has a highly advantageous activity level.

Drafters nightmare: statement became a magnet for interpretation – e.g. mentioned in para's

[45], [46], [51], [60], [70], [96], [97], [98], [99], [101], [107], [109], [120], [121], [122], [123], [124], [203], [206], [248]

Effect of expert opinion (2011 FC 1288)

[207] I would summarize the factual basis for the '113 patent's promise as follows:

- preclinical tests showed that olanzapine had antipsychotic potential and might have relatively low liability for some forms of EPS;
- olanzapine showed a liability to elevate liver enzymes, just as flumezapine had done;
- olanzapine's tendency to raise CPK appeared to be similar to flumezapine's at therapeutic doses;
- olanzapine's EPS liability appeared to be comparable to flumezapine's, perhaps somewhat lower than conventional antipsychotics;
- olanzapine's prolactin liability appeared to be relatively mild;
- olanzapine was just as toxic as ethyl olanzapine except in respect of an irrelevant parameter – causing an elevation of cholesterol in female dogs;
- olanzapine appeared to have had some antipsychotic effect on some schizophrenia patients in a magnitude comparable to conventional antipsychotics;
- olanzapine's therapeutic effect appeared at fairly low doses, but not lower than flumezapine's;
- olanzapine did not affect white blood cells in the few human subjects who had taken olanzapine for a short period of time.

Drafting points: olanzapine

- **Access to expert opinions to evaluate strength of data provided while drafting is likely restricted**
- **Stated advantages need to be included in specification; advantages need to be relevant**
 - selection of control/reference data important
 - care required when making broad comparative statements
 - they may include commercial products; and
 - may require direct comparison with products in market
 - sound line of reasoning required
- **May need more than one advantage(?)**

Patent with no specific promise

Escitalopram (Lundbeck vs Apotex)

Patent on the active enantiomer of citalopram

Not considered a selection patent since the enantiomers of that drug were never disclosed before.

- Implicit disclosure does not exist in patent law

Patent only states that the active enantiomer was useful as an antidepressant

Patent was found valid since it provided to the public a new compound, never disclosed before and useful as an antidepressant

- It afforded the public a choice

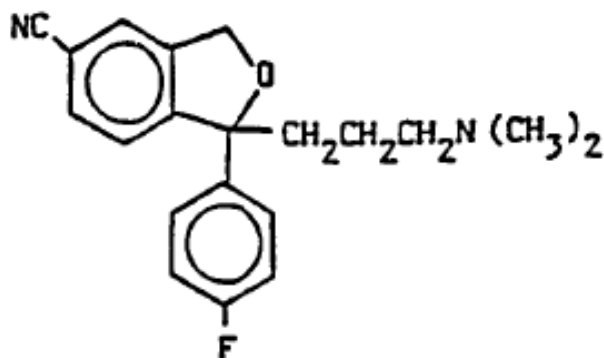
Lundbeck v. Apotex 2009 FC 146, aff'd 2010 FCA 320 (NOC), 2013 FC 192

CA 1,339,452 es/citalopram FD: 1989

FC & FCA utility shown

ENANTIOMERS OF CITALOPRAM AND DERIVATIVES THEREOF

The present invention relates to the two novel enantiomers of the antidepressant drug 1-(3-dimethylaminopropyl)-1-(4'-fluorophenyl)-1,3-dihydroisobenzofuran-5-carbonitrile (citalopram) of the following formula I:



I

CA 1,339,452 escitalopram

Pg 2:

Racemate old and known;

Citalopram disclosed and claimed in US 4,136,193

Antidepressant activity known

**Previous attempts to isolate enantiomers of
citalopram failed (i.e. enantiomers known):**

CA 1,339,452 escitalopram

Surprisingly, it has now proven possible to resolve the intermediate 4-[4-(dimethylamino)-1-(4'-fluorophenyl)-1-hydroxy-1-butyl]-3-(hydroxymethyl)-benzonitrile II, into its enantiomers and finally in a stereoselective way to convert these enantiomers to the corresponding citalopram enantiomers. Likewise, monoesters of II formed by optical-

...

Furthermore, it was shown to our surprise that almost the entire 5-HT uptake inhibition resided in the (+)-citalopram enantiomer.

CA 1,339,452 escitalopram

Pg 3: synthesis of compound (+)-citalopram (escitalopram)

Example's 1-3: compound preparation

Pg 9: mouse assay for measuring inhibition of 5-HTP uptake

- rat assay for measuring inhibition of ^3H -seotonin uptake

Pg's 12-14: dosage forms; formulations

Pg 13: solutions for injection. - Results upon administration to human beings have been very gratifying.

No human data provided

CA 1,339,452 escitalopram

Pg 14:

The invention also comprises a method for the alleviation, palliation, mitigation or inhibition of the manifestations of certain physiological-psychological abnormalities of animals, especially depressions by administering to a living animal body, including human beings, an adequate quantity of (+)-citalopram or a non-toxic acid addition salt thereof. An adequate quantity would be from about 0.001

Claims under challenge:

Claim 1: (+)-citalopram and non-toxic addition salts

Claim 3: composition useful as an antidepressant comprising compound of claim 1 (claim 5: at an amount from ...)

Lundbeck v Apotex 2009 FC 146 escitalopram I

- **US 4,136,193 discloses a formula >200 compounds**
- **Citalopram disclosed and claimed in US patent [42]**
 - (+)-citalopram (escitalopram) was not prepared

[43]...There is no indication that escitalopram has other desirable or surprising traits such as less toxicity or an unexpected and substantial increase in solubility, stability, handling properties, processability or in its side effects profile. Consequently, if escitalopram is a selection patent, it is invalid.

Lundbeck v Apotex 2009 FC 146 escitalopram I

[44] However, I am satisfied that escitalopram is not a selection patent.

[46] ... if the subject matter of either prior U.S. patent were worked, the result would be a racemate, not an enantiomer. Consequently it cannot be said that patent '452 formed part of either U.S. patent, and so the selection patent argument falls for lack of prior disclosure.

Lundbeck v Apotex 2009 FC 146 escitalopram I

[48] ... the utility of escitalopram could not be determined until citalopram was resolved in sufficient quantities to allow for suitable testing.

[133]... the inventor did not promise that escitalopram was better than citalopram as an antidepressant, although there are now indications that it is indeed the case.

Lundbeck v Apotex 2009 FC 146 escitalopram I

[133]...Although there is no evidence that escitalopram had been tested on humans that is not a condition precedent to obtaining a patent... The testing disclosed was on rodents, the same testing which had been done on citalopram. Since citalopram was a useful antidepressant and escitalopram was more potent with no indication of adverse side effects, it follows that the prediction was a sound one...

escitalopram

not a selection patent

- Generic compound disclosed
- Several hundred compounds
- Racemate (citalopram) disclosed (and claimed) in US 4,136,193
- Problems producing enantiomers in prior art;
- Enantiomers *not disclosed or claimed in CA*
- Working of '193 produces racemate
- In CA 1,339,452 (+)-citalopram separated
 - (+)-citalopram exhibits activity

v

clopidogrel

selection patent

- Generic compound disclosed
- Over 250,000 compounds
- Racemate (L- and D-rotary isomers) disclosed and claimed in CA 1,194, 875
- Problems producing enantiomers in prior art;
- Enantiomers *disclosed & claimed in CA*
- Working of '875 produces racemate
- In CA 1,336,777 D-rotary isomer separated
 - D-rotary isomer exhibits activity and less toxicity

Lundbeck v Apotex 2013 FC 192 escitalopram II

243 ...Apotex submits that Lundbeck promised in the disclosure that (+)-Citalopram had greater therapeutic effect than Citalopram. This promise could only be demonstrated by testing upon humans, and so the patent falls unless there was a sound basis for making it. I agree that if such a promise was made it was not based on a sound prediction. However, the real question is whether Lundbeck made such a promise. I find that it did not.

solutions for injection. - Results upon administration to human beings have been very gratifying.

Drafting points: escitalopram

- **Disclosure and claiming of compound in parent patent required to be considered selection patent**
 - enantiomer not disclosed (or tested) until produced
- **Utility of escitalopram disclosed not a promise**
 - no promise made that was better than citalopram
- **For selections (and improvements) use the same models as in the parent patent**
- **Re - promise: claims take precedence over disclosure**
- **Results that are “very gratifying” (even if not done) not considered a promise**

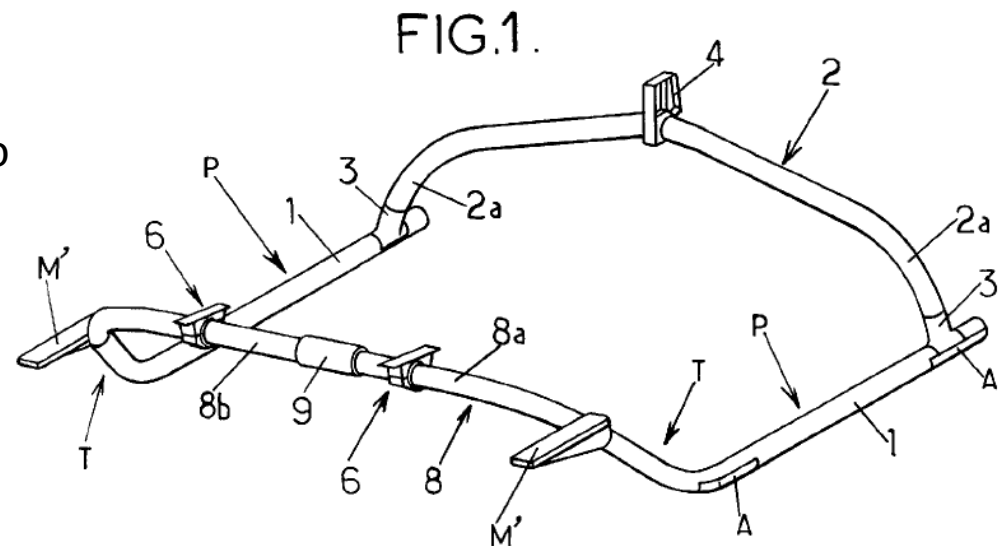
Eurocopter v. Bell

- **Patent concerns an helicopter landing gear where the front cross piece is integrated, inclined and offset**
- **Compared to the prior art where the front cross piece is substantially perpendicular to the skid**
- **Patent says that this new configuration has advantages over the prior art**

CA 2,207,787 (FR) Eurocopter US 5,860,621

A helicopter landing gear;

... each of said skids has at the front an inclined transition zone with double curvature orienting itself transversely in relation to said longitudinal ground support surfaces, above the plane of the latter; the two transition zones together constitute, in this way, an integrated front cross piece; and the integrated front cross piece is offset in relation to the front delimitation of the plane of contact of the longitudinal support surfaces of the skids on the ground



Promise of the patent

- **Claim 1 includes any inclination, forward or backward**
- **Claim 15 covers inclination forward and claim 16 inclination backward**
- **The patent promises that the inclined cross piece provides certain advantages**

CA 2,207,787 (FR) Eurocopter

The purpose of the present invention is to overcome these disadvantages of the prior art and to obtain helicopter landing gear with a new design making it possible to reduce the said disadvantages significantly:

approximately 20% reduction in mass,
simplification of the manufacturing and approximately 10% cost reduction,
approximately 10% reduction in the load factor on landing,
elimination of mechanical anti-ground resonance systems.

For this purpose, landing gear according to the invention, of the type defined at the beginning, is characterized in that each of the said skids has at the front an inclined transition zone with double curvature orienting itself transversely with respect to the said longitudinal support stretches which stand on the ground, above the plane of the latter, the two transition zones together constituting in this way an integrated front cross-piece offset either forwards or backwards with respect to the front delimitation of the plane of contact of the said longitudinal support stretches of the skids on the ground.

- Reduce disadvantages significantly
- Reduce mass of landing gear
- Eliminate anti-ground resonance
- Front inclined transition zone with double curvature, front cross piece offset forwards or backwards

CA 2,207,787 (FR) Eurocopter

The ground resonance behaviour is characterized in particular by the landing gear's roll stiffness. As the landing gear is fixed to the structure, for example by means of a single rear point and two front points, the torsional stiffness with respect to the pitch axis is principally obtained by the flexion of the front cross-piece. The variant according to which the points at which the front cross-piece stands on the ground are offset longitudinally towards the front of the aircraft with respect to the points of attachment to the structure of the latter has the advantage of allowing the roll functioning of the assembly to cause the front cross-piece to work both in torsion and in flexion instead of in pure flexion. A reduced roll stiffness results from this, which improves the ground resonance behaviour of the helicopter in the roll mode and this avoids any divergent phenomenon which would risk causing an accident.

Inclining the front cross piece plays an important role in the roll and pitch mode of the landing gear

Ground resonance behavior is improved

CA 2,207,787 (FR) Eurocopter

These various compromises make it possible to meet the size requirements of the landing gear and to satisfy the following three criteria:

- absorption of energy corresponding to normal vertical impact speeds,
- critical landing speed resulting in residual deformation situated outside of the normal operating range, and
- sufficient flexibility to avoid the use of an additional anti-resonance system.

Landing gear:

Absorbs energy at landing speeds

At high landing speed – there is residual deformation

Flexible – no need for anti-resonance system

Eurocopter v Bell 2012 FC 113 landing gear

[296] Claim 15 covers the variant whereby the integrated front cross piece is offset forwards in relation to the front delimitation of the plane of contact of the longitudinal support surfaces of the skids on the ground. Conversely, claim 16 covers the variant whereby the integrated front cross piece is offset backwards in relation to the front delimitation of the plane of contact of the longitudinal support surfaces of the skids on the ground. Both variants are covered by claim 1.

(emphasis added)

Eurocopter v Bell 2012 FC 113 landing gear

[215] ...an explicit promise to reduce drawbacks of prior art “significantly” is made by the inventors in the specification, and more particularly:

- (a) Elevated acceleration factors upon landing (load factors);**
- (b) Difficult frequency adaptation with respect to ground resonance; and**
- (c) High landing gear weight.**

**[216] This is the promised utility of the disclosed invention.
Restated para [338] & [339]**

Eurocopter v Bell 2012 FC 113 landing gear

[350] On a balance of probabilities, Bell has not proven that the invention will not work, or that it will not do what the specification promises it will do. However, Bell nevertheless submits that it has met its burden of proving that, at the Canadian filing date, there was no evidence or data to support a prediction made in the specification with respect to the promised utility of particular embodiments (such as Figures 1 and 11e) included in claims 15 and 16 of the '787 Patent. Absent such evidence or data, Bell submits that the presumption of validity is not enough to save one or more embodiments.

Eurocopter v Bell 2012 FC 113 landing gear

The promise of the '787 Patent was only delivered in claim 15 (front cross piece inclined & offset forward).

The utility of skid-type landing gear of claim 15 was demonstrated as of the filing date.

Claims 1 to 14, and 16, covering landing gear with the front cross piece offset backwards were not demonstrated or soundly predicted at the time of filing and invalid.

**Judgment by the Court puts on Eurocopter the
burden of proving that the invention is useful
Appeal was argued last May, outcome to follow**



Drafting points: landing gear

- **Mechanical inventions involving combinations of interactive elements may lack predictability**
- **For complex mechanical inventions consider providing data in support of variants**
 - Is computer modeling sufficient if a line of reasoning established?

Teva v. Pfizer (sildenafil) 2012 SCC 60

- **Patent as filed included 260 quintillion compounds**
- **Specifications referred to nine preferred compounds**
- **And to two most preferred compounds**
- **Patent disclosed tests performed to show that sildenafil was useful to treat ED**
- **The patent did not mention on which compound the tests were performed**

Teva v. Pfizer (sildenafil)

- The patentee disclaimed claims 1, 8-17, 19-27
- Sildenafil is covered by claim 7
- Claim 6 covers another compound

CA 2,163,446 sildenafil

FC & FCA utility; sufficient disclosure; not obvious; SCC rev'g

PYRAZOLOPYRIMIDINONES FOR THE TREATMENT OF IMPOTENCE

This invention relates to the use of a series of pyrazolo[4,3-d]pyrimidin-7-ones for the treatment of impotence.

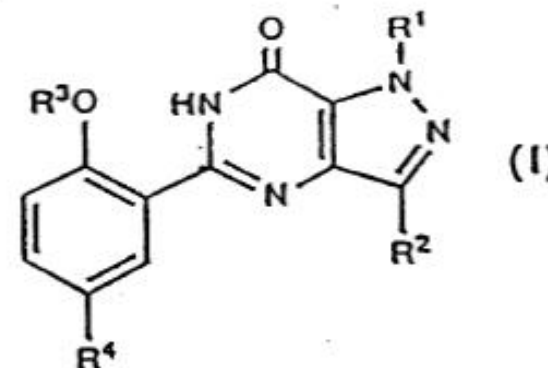
The compounds of the invention are potent inhibitors of cyclic guanosine 3',5'-monophosphate phosphodiesterases (cGMP PDEs) in contrast to their inhibition of cyclic adenosine 3',5'-monophosphate phosphodiesterases (cAMP PDEs). This selective enzyme inhibition leads to elevated cGMP levels which, in turn, provides the basis for the utilities already disclosed for the said compounds in EP-A-0463756 and EP-A-0526004, namely in the treatment of stable, unstable and variant (Prinzmetal) angina, hypertension, pulmonary hypertension, congestive heart failure, atherosclerosis, conditions of reduced blood vessel patency e.g. post-percutaneous transluminal coronary

Invention directed to a group of compounds with activity



CA 2,163,446 sildenafil

Unexpectedly, it has now been found that these disclosed compounds are useful in the treatment of erectile dysfunction. Furthermore the compounds may be administered orally, thereby obviating the disadvantages associated with i.c. administration. Thus the present invention concerns the use of a compound of formula (I):



- All compounds active to treat ED

...

for the manufacture of a medicament for the curative or prophylactic treatment of erectile dysfunction in a male animal, including man.

- and use of all compounds to treat ED

CA 2,163,446 sildenafil

Pg's 6-7:

Especially preferred individual compounds of the invention include:

5-(2-ethoxy-5-morpholinoacetylphenyl)-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-(5-morpholinoacetyl-2-n-propoxyphenyl)-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-[2-ethoxy-5-(4-methyl-1-piperazinylsulphonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-[2-allyloxy-5-(4-methyl-1-piperazinylsulphonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-{2-ethoxy-5-[4-(2-propyl)-1-piperazinylsulphonyl]phenyl}-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-{2-ethoxy-5-[4-(2-hydroxyethyl)-1-piperazinylsulphonyl]phenyl}-1-methyl-3-n-propyl-1,6-dihydro-7H-

- 9 compounds listed as especially preferred
- compound of claim 6
- Claim 5 (within a group)
- compound of claim 7
- Claim 5 (within a group)
- Claim 5 (within a group)
- Claim 5 (within a group)...



CA 2,163,446 sildenafil

- Pg 7: methods for determining cGMP PDE and cAMP PDE activity & pharmaceutical compositions as described in EP 0463756 & EP 0526004
- Pg 8: methods for inhibition studies
 - specific compounds that were tested not identified:

Inhibition studies were performed using a substrate concentration of 500nM throughout. All inhibitors were dissolved in DMSO and concentration-response curves were constructed over the range 3×10^{-10} to 1×10^{-4} M in half log increments. IC_{50} values were calculated using the sigmoidal curve fitting algorithm of biostat.

CA 2,163,446 sildenafil

The compounds of the invention have been tested in vitro and found to be potent and selective inhibitors of the cGMP-specific PDE_v. For example, one of the especially preferred compounds of the invention has an IC₅₀ = 6.8 nM v. the PDE_v enzyme, but demonstrates only weak inhibitory activity against the PDE_{II} and PDE_{III} enzymes with IC₅₀ = >100 µM and 34 µM respectively.

In man, certain especially preferred compounds have been tested orally in both single dose and multiple dose volunteer studies. Moreover, patient studies conducted thus far have confirmed that one of the especially preferred compounds induces penile erection in impotent males.

- Generic ref to compounds tested, all active in vitro

- one compound (X) exhibits selective inhibitory activity

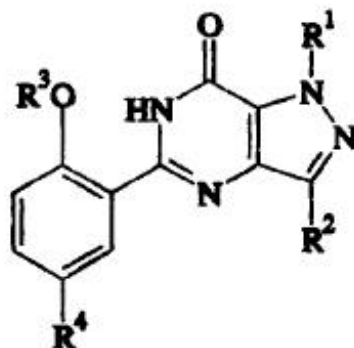
- compound X active in ED

CA 2,163,446 sildenafil

Disclaimer - Renonciation

1.

The use of a compound of formula (I):



(I)

Claim 1 -
Swiss style
use claim

...

or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition containing either entity, for the manufacture of a medicament for the curative or prophylactic treatment of an erectile dysfunction in a male animal or sexual dysfunction in a female animal.

CA 2,163,446 sildenafil

Claim 1: “produces 260 quintillion possible compounds” (para 4; 2012 SCC 60)

Claim 6: activity of compound not known

Claim 7 = sildenafil (use as defined in claim 1); is sildenafil clearly described?

Disclaimer submitted re: claims 1, 8-17, 19-27;

6. The use according to claim 4 wherein the compound of formula (I) is 5-(2-ethoxy-5-morpholinoacetylphenyl)-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one or a pharmaceutically acceptable salt thereof.

7. The use according to claim 4 wherein the compound of formula (I) is 5-[2-ethoxy-5-(4-methyl-1-piperazinylsulphonyl)-phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one or a pharmaceutically acceptable salt thereof.

Teva v Pfizer 2012 SCC 60 sildenafil

5 At the time of Pfizer's patent application, Pfizer had conducted tests that demonstrated that sildenafil was effective in treating ED. None of the other compounds in Patent '446 had been shown to be effective in doing so. Although Patent '446 includes the statement that "one of the especially preferred compounds induces penile erection in impotent males" ... neither the disclosure—the descriptive portion of the patent application—nor the claims specify that sildenafil is the compound that works.

(emphasis added)

Teva v Pfizer 2012 SCC 60 sildenafil

73 Although Patent '446 includes the statement that “one of the especially preferred compounds induces penile erection in impotent males” ... the specification does not indicate that sildenafil is the effective compound, that Claim 7 contains the compound that works, or that the remaining compounds in the patent had been found not to be effective in treating ED. The claims were structured as “cascading claims”, with Claim 1 involving over 260 quintillion compounds, Claims 2 to 5 concerning progressively smaller groups of compounds, and Claims 6 and 7 each relating to an individual compound.

Teva v Pfizer 2012 SCC 60 sildenafil

74 ... even if a skilled reader could have narrowed the effective compound down to the ones in Claim 6 and Claim 7, further testing would have been required to determine which of those two compounds was actually effective in treating ... “the skilled reader must undertake a minor research project to determine which claim is the true invention”.

80... the public’s right to proper disclosure was denied in this case, since the claims ended with two individually claimed compounds, thereby obscuring the true invention The disclosure failed to state in clear terms what the invention was....

Bad facts make bad law

- The Court was very troubled by the fact that Pfizer did not disclosed on which compound the tests were done
- The Court saw in this behavior a clear attempt to hide something to the public in order to keep a competitive advantage
- Nobody from Pfizer explained why the compound on which the tests were done was not mentioned in the patent
- When the story of the invention is not a good one to tell it can lead to invalidity

Drafting points: sildenafil

- **Disclosure and claiming of a specific active compound may not be enough to satisfy disclosure requirement**
 - need to also state in clear terms what the invention is
- **If:**
 - a genus of compounds is disclosed,
 - activity only associated with one compound, and
 - linking the compound to activity is not “easily” determined (“minor research project”)
- **Then:**
 - associating the compound with activity is required

Drafting questions re-considered

- Is the evaluation of the promise limited to selection patents, or does it apply to any patent?
- What language may be considered a promise?
- Is the promise determined by the claims, the specification, or both?
- What information is required to support a promise?
- Can we “control” what the promise is, or is this determination open to interpretation by experts?