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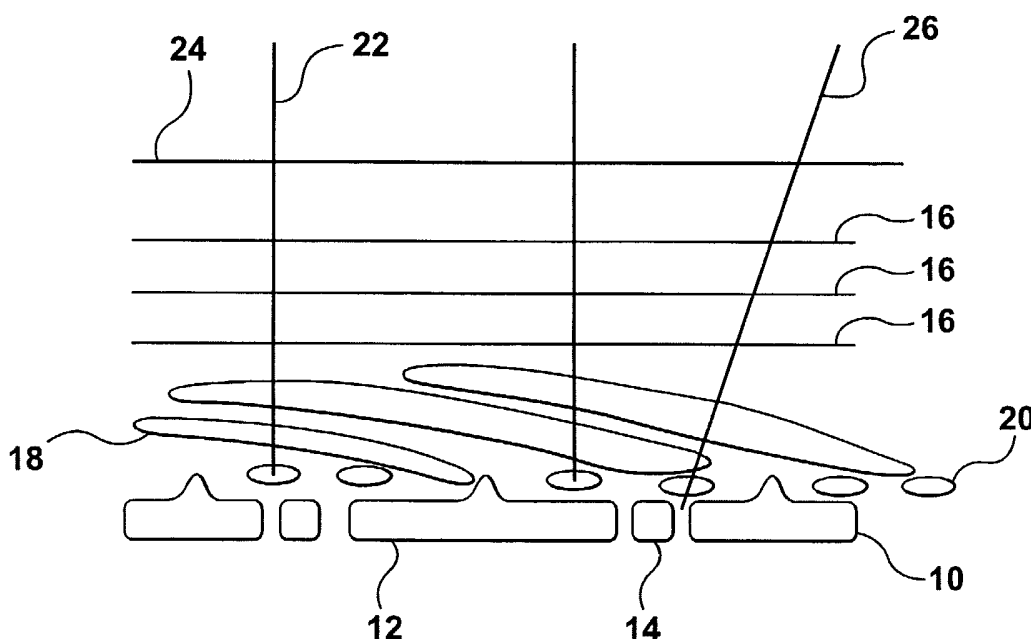
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2,369,810 30 January 2002 (30.01.2002) CA
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- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
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[Continued on next page]

(54) Title: METHOD OF TREATING PAIN WITH BOTULINUM TOXIN



(57) Abstract: A method of treating pain is provided. The method comprises administering to the intrinsic spinal muscles of a mammal an amount of a toxin sufficient to paralyze the muscles. This prevents the muscles from shortening and can allow healing to occur. The paralyzing agent may be used in combination with a growth factor to treat spinal compression. A kit for the treatment of pain by injection of the intrinsic spinal muscles is also provided. The kit comprises a paralyzing agent, an injection syringe with needle, and an acupuncture needle with injector system.



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*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

## INTERNATIONAL SEARCH REPORT

Inter national Application No  
PCT/CA 03/00127

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 7 A61K38/48 A61P29/00 A61P23/02 //(A61K38/48, 38:18), (A61K38/48, 38:18, 31:445), (A61K38/48, 38:18, 31:167), (A61K38/48, 31:445), (A61K38/48, 31:167) According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) IPC 7 A61K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) MEDLINE, EPO-Internal, PAJ, WPI Data, BIOSIS, CHEM ABS Data		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DAVIS D ET AL: "Significant improvement of stiff-person syndrome after paraspinal injection of botulinum toxin A." MOVEMENT DISORDERS: OFFICIAL JOURNAL OF THE MOVEMENT DISORDER SOCIETY. UNITED STATES JUL 1993, vol. 8, no. 3, July 1993 (1993-07), pages 371-373, XP008016910 ISSN: 0885-3185	1-4, 6, 8, 20, 21
Y	page 372, right-hand column, paragraphs 1, 2  page 373, left-hand column, paragraph 1  ---	1-6, 8, 10-15, 19-23
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<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.		
<input checked="" type="checkbox"/> Patent family members are listed in annex.		
° Special categories of cited documents :		
*A* document defining the general state of the art which is not considered to be of particular relevance *E* earlier document but published on or after the international filing date *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) *O* document referring to an oral disclosure, use, exhibition or other means *P* document published prior to the international filing date but later than the priority date claimed		*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. *&* document member of the same patent family
Date of the actual completion of the international search  <p style="text-align: center;">31 July 2003</p>		Date of mailing of the international search report  <p style="text-align: center;">07/08/2003</p>
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer  <p style="text-align: center;">Lechner, O</p>

## INTERNATIONAL SEARCH REPORT

Inter national Application No  
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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FOSTER L ET AL: "Botulinum toxin A and chronic low back pain: a randomized, double-blind study." NEUROLOGY. UNITED STATES 22 MAY 2001, vol. 56, no. 10, 22 May 2001 (2001-05-22), pages 1290-1293, XP008016926 ISSN: 0028-3878	1-3,6,8, 20-23
Y	page 1291, left-hand column, paragraph 3  page 1291, right-hand column, paragraph 4 page 1292, right-hand column, paragraph 3 ---	1-6, 10-15, 19-23
X	COMELLA C L ET AL: "Extensor truncal dystonia: successful treatment with botulinum toxin injections." MOVEMENT DISORDERS: OFFICIAL JOURNAL OF THE MOVEMENT DISORDER SOCIETY. UNITED STATES MAY 1998, vol. 13, no. 3, May 1998 (1998-05), pages 552-555, XP008016909 ISSN: 0885-3185 abstract page 553, left-hand column, paragraph 3 page 554, left-hand column, paragraph 5 page 553, left-hand column, paragraph 3 ---	1-4,6,8, 20-23
Y	BURG D ET AL: "Effective treatment of a large muscle hernia by local botulinum toxin administration!" HANDCHIRURGIE, MIKROCHIRURGIE, PLASTISCHE CHIRURGIE: ORGAN DER DEUTSCHSPRACHIGEN ARBEITSGEMEINSCHAFT FUR HANDCHIRURGIE: ORGAN DER DEUTSCHSPRACHIGEN ARBEITSGEMEINSCHAFT FUR MIKROCHIRURGIE DER PERIPHEREN NERVEN UND GEFASSE: ORGAN DER.. GERMANY MAR 1999, vol. 31, no. 2, March 1999 (1999-03), pages 75-78, XP008016908 ISSN: 0722-1819 the whole document ---	1-6,8, 10-15, 19-23
Y	US 5 053 005 A (BORODIC GARY E) 1 October 1991 (1991-10-01) cited in the application column 3, line 25,46-54 column 4, line 64-66 ---	1-6,8, 10-15, 19-23
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## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/CA 03/00127

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>GASSNER H G ET AL: "Addition of an anesthetic agent to enhance the predictability of the effects of botulinum toxin type A injections: a randomized controlled study." MAYO CLINIC PROCEEDINGS. UNITED STATES JUL 2000, vol. 75, no. 7, July 2000 (2000-07), pages 701-704, XP008017126 ISSN: 0025-6196 the whole document -----</p>	15

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/CA 03/00127

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claims 1-9 and 21-23 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2.  Claims Nos.: 1, 7-10, 16, 20, 21, 23  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
  
see FURTHER INFORMATION sheet PCT/ISA/210
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1,7-10,16,20,21,23

Present claims 1, 7, 9, 10, 16 and 20 relate to an extremely large number of possible compounds, partially defined by reference to a desirable characteristic or property, namely (muscle) paralyzing agent(s) and tissue growth factor. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Claims 8, 9, 20, 21, 23 relate to pathologic conditions/diseases/therapeutic uses vaguely defined by reference to pathophysiological mechanisms or desirable result, i.e. neuropathies of the spine and complications thereof, paralyzing intrinsic spinal muscles, spinal compression disorder and relaxation of an intrinsic spinal muscle. The claims cover all pathologic conditions/diseases having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the use of botulinum toxin alone or in combination with the specific tissue growth factors mentioned in the application (c.f. page 12, line 22-27) and/or a local anaesthetic selected from Naropin, Xylocaine and Marcaine, for treating pain and especially pain caused by disc herniation, facet joint disease and spinal stenosis.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 03/00127

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5053005	A	NONE	