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**Declarations under Rule 4.17:**

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations 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, EG, 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, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)*
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(54) Title: SUSTAINED-RELEASE TRAMADOL FORMULATIONS WITH 24-HOUR EFFICACY

(57) Abstract: A sustained-release tramadol formulation oral administration is provided which, upon initial administration of one dose, provides an analgesic effect within 2 hours, which analgesic effect continues for at least 24 hours after administration.

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# INTERNATIONAL SEARCH REPORT

Internal	Application No
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**A. CLASSIFICATION OF SUBJECT MATTER**  
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According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
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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)

EPO-Internal, WPI Data, PAJ, BIOSIS

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, P	BHAVESH BODALIA ET AL.: "A Comparison of the Pharmacokinetics, Clinical Efficacy, and Tolerability of Once-Daily Tramadol Tablets with Normal Release Tramadol Capsules" JOURNAL OF PAIN AND SYMPTOM MANAGEMENT, vol. 25, no. 2, February 2003 (2003-02), pages 142-149, XP001180925 cited in the application Abstract page 145; figure 1; table 1  <div style="text-align: center;">-/--</div>	1-32

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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Date of the actual completion of the international search

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## INTERNATIONAL SEARCH REPORT

Intern 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	L. ADLER ET AL.: "A Comparison of Once-Daily Tramadol with Normal Release Tramadol in the Treatment of Pain in Osteoarthritis" THE JOURNAL OF RHEUMATOLOGY, vol. 29, no. 10, 2002, pages 2196-2199, XP009029330 cited in the application Abstract	1-32
X	US 5 776 492 A (BETZING JUERGEN ET AL) 7 July 1998 (1998-07-07) column 1; claims 1,5; examples 2-5	1-32
X	WO 99/01111 A (EURO CELTIQUE SA ;CHASIN MARK (US); HUANG HUA PIN (US); GOLDENHEIM) 14 January 1999 (1999-01-14) claims 1,15; examples 1-8	1-32
X	EP 0 624 366 A (EURO CELTIQUE SA) 17 November 1994 (1994-11-17) page 6, line 54 -page 7, line 5; claims 1,7,13	1-32

## INTERNATIONAL SEARCH REPORT

Information on patent family members

Internation application No  
PCT/CA 03/01638

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5776492	A	07-07-1998	DE 19530575 A1	20-02-1997
			AT 205708 T	15-10-2001
			AU 703310 B2	25-03-1999
			AU 6194196 A	27-02-1997
			BR 9604034 A	09-06-1998
			CA 2182939 A1	20-02-1997
			CN 1145780 A ,B	26-03-1997
			CZ 9602359 A3	12-02-1997
			DE 59607710 D1	25-10-2001
			DK 759296 T3	26-11-2001
			EP 0759296 A1	26-02-1997
			ES 2164198 T3	16-02-2002
			GR 3036720 T3	31-12-2001
			HK 1010100 A1	12-04-2002
			HU 9602266 A2	29-12-1997
			IL 119080 A	24-07-2001
			JP 9110684 A	28-04-1997
			NO 963430 A	20-02-1997
			NZ 299141 A	19-12-1997
			PL 315749 A1	03-03-1997
			PT 759296 T	28-03-2002
			RU 2174837 C2	20-10-2001
			SI 759296 T1	31-12-2001
			SK 104296 A3	07-05-1997
			ZA 9606985 A	24-02-1997
			WO 9901111	A
CA 2270975 A1	14-01-1999			
EP 1009387 A1	21-06-2000			
JP 2000510487 T	15-08-2000			
JP 2004002419 A	08-01-2004			
US 2002102302 A1	01-08-2002			
WO 9901111 A1	14-01-1999			
US 6306438 B1	23-10-2001			
EP 0624366	A	17-11-1994		
			GB 2284760 A	21-06-1995
			GB 2287880 A	04-10-1995
			AT 3413 U2	27-03-2000
			AT 138566 T	15-06-1996
			AT 201989 T	15-06-2001
			AU 3995797 A	18-12-1997
			AU 6196394 A	17-11-1994
			CA 2123160 A1	11-11-1994
			CN 1099262 A ,B	01-03-1995
			CZ 9401093 A3	16-11-1994
			DE 9422335 U1	13-04-2000
			DE 69400215 D1	04-07-1996
			DE 69400215 T2	31-10-1996
			DE 69427472 D1	19-07-2001
			DE 69427472 T2	08-11-2001
			DE 699436 T1	10-04-1997
			DE 729751 T1	13-03-1997
			DK 624366 T3	01-07-1996
			DK 699436 T3	23-07-2001
			EG 20577 A	30-08-1999
EP 0624366 A1	17-11-1994			
EP 0699436 A1	06-03-1996			

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Internal Application No  
PCT/CA 03/01638

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0624366	A	EP 0729751 A1	04-09-1996
		ES 2088312 T3	01-08-1996
		ES 2159591 T3	16-10-2001
		FI 942092 A	11-11-1994
		FI 20030560 A	14-04-2003
		GR 3020084 T3	31-08-1996
		GR 3036565 T3	31-12-2001
		HU 75703 A2	28-05-1997
		ID 25988 A	10-11-1994
		IL 109460 A	10-03-1998
		IL 119660 A	12-09-2002
		IN 182370 A1	27-03-1999
		IN 182556 A1	01-05-1999
		JP 3045924 B2	29-05-2000
		JP 7053361 A	28-02-1995
		JP 3267561 B2	18-03-2002
		JP 11124327 A	11-05-1999
		JP 3443574 B2	02-09-2003
		JP 2002154954 A	28-05-2002
		NO 941719 A	11-11-1994
		NO 993484 A	11-11-1994
		NO 20013566 A	11-11-1994
		NZ 260408 A	28-05-1996
		PL 176474 B1	30-06-1999
		PT 699436 T	30-10-2001
		SG 67347 A1	21-09-1999
		SK 54194 A3	07-12-1994