PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61K 31/47, C07D 401/12, 215/48, 417/12, 409/12, 401/14 — A1

(11) International Publication Number: WO 97/44036

(43) International Publication Date: 27 November 1997 (27.11.97)

(21) International Application Number: PCT/GB97/01359

(22) International Filing Date: 20 May 1997 (20.05.97)

(30) Priority Data:

9610506.9	20 May 1996 (20.05.96)	GB
9623234.3	7 November 1996 (07.11.96)	GB
9626883.4	24 December 1996 (24.12.96)	GB
9708072.5	22 April 1997 (22.04.97)	GB

(71) Applicant *(for all designated States except US)*: CHIROSCIENCE LIMITED [GB/GB]; Cambridge Science Park, Milton Road, Cambridge CB4 4WE (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: DYKE, Hazel, Joan [GB/GB]; Chiroscience Limited, Cambridge Science Park, Milton Road, Cambridge CB4 4WE (GB). MONTANA, John, Gary [GB/GB]; Chiroscience Limited, Cambridge Science Park, Milton Road, Cambridge CB4 4WE (GB). LOWE, Christopher [GB/GB]; Chiroscience Limited, Cambridge Science Park, Milton Road, Cambridge CB4 4WE (GB). KENDALL, Hannah, Jayne [GB/GB]; Chiroscience Limited, Cambridge Science Park, Milton Road, Cambridge CB4 4WE (GB). SABIN, Verity, Margaret [GB/GB]; Chiroscience Limited, Cambridge Science Park, Milton Road, Cambridge CB4 4WE (GB).

(74) Agent: GILL JENNINGS & EVERY; Broadgate House, 7 Eldon Street, London EC2M 7LH (GB).

(81) Designated States: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published

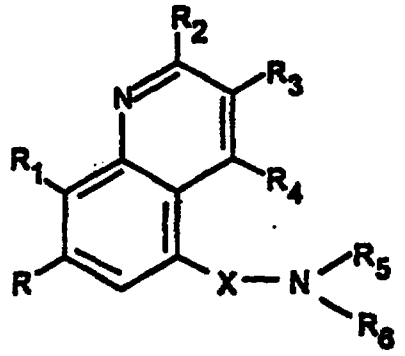
With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: QUINOLINE CARBOXAMIDES AS TNF INHIBITORS AND AS PDE-IV INHIBITORS

(57) Abstract

A compound of general formula (i), wherein X is CO or CS; R is H, halogen or alkyl; R_1 represents OH, alkoxy optionally substituted with one or more halogens, or thioalkyl; R_2, R_3 and R_4 are the same or different and are each H, R_7, OR_{11}, COR_7, $C(=NOR_7)R_7$, alkyl-$C(=NOR_7)R_7$, halogen CF_3, alkyl-$C(=NOH)R_7$, $C(=NOH)R_7$, CN, CO_2H, CO_2R_{11}, $CONH_2$, $CONHR_7$, $CON(R_7)_2$, NR_9R_{10} or $CONR_{12}R_{13}$ where $NR_{12}R_{13}$ is a heterocyclic ring optionally substituted with one or more R_{15}; R_5 represents H, arylalkyl, heteroarylalkyl, heterocycloalkyl, $S(O)_mR_{11}$ or alkyl optionally substituted with one or more substituents chosen from hydroxy, alkoxy, CO_2R_8, $SO_2NR_{12}R_{13}$, $CONR_{12}R_{13}$, CN, carbonyl oxygen, NR_9R_{10}, COR_{11} and $S(O)_nR_{11}$; R_6 represents aryl, heteroaryl, heterocyclo, arylalkyl, heteroarylalkyl or heterocycloalkyl; in R_5 and/or R_6, the aryl/heteroaryl/heterocyclo portion is optionally substituted with one or more substituents alkyl-R_{14} or R_{14}. The compounds can be used to treat disease states, for example disease states associated with proteins that mediate cellular activity, for example by inhibiting tumour necrosis factor and/or by inhibiting phosphodiesterase IV.



(I)