



US00RE36547F1

(12) **EX PARTE REEXAMINATION CERTIFICATE (5087th)**

United States Patent

Crain et al.

(10) **Number: US RE36,547 F1**

(45) **Certificate Issued: Mar. 22, 2005**

(54) **METHOD OF SIMULTANEOUSLY ENHANCING ANALGESIC POTENCY AND ATTENUATING DEPENDENCE LIABILITY CAUSED BY EXOGENOUS AND ENDOGENOUS OPIOID AGONISTS**

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Reexamination Request:

No. 90/006,471, Dec. 2, 2002

Reexamination Certificate for:

Patent No.: **Re. 36,547**
Issued: **Feb. 1, 2000**
Appl. No.: **08/782,452**
Filed: **Jan. 13, 1996**

Related U.S. Patent Documents

Reissue of:

(64) Patent No.: **5,512,578**
Issued: **Apr. 30, 1996**
Appl. No.: **08/276,966**
Filed: **Jul. 19, 1994**

Related U.S. Application Data

(63) Continuation-in-part of application No. 08/097,460, filed on Jul. 27, 1993, now Pat. No. 5,472,943, which is a continuation-in-part of application No. 07/947,690, filed on Sep. 19, 1992, now abandoned.

(51) **Int. Cl.** 7 **A61K 31/44**
(52) **U.S. Cl.** **514/282; 514/811; 514/812**
(58) **Field of Search** **514/282, 811, 514/812**

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Primary Examiner—Raymond J Henley, III

(57) **ABSTRACT**

This invention relates to a method of selectively enhancing the analgesic potency of morphine and other clinically used bimodally-acting opioid agonists and simultaneously attenuating development of physical dependence, tolerance and other undesirable side effects caused by the chronic administration of said bimodally-acting opioid agonists comprising the co-administration of a bimodally-acting opioid agonist which activates both inhibitory and excitatory opioid receptor-mediated functions of neurons in the nociceptive (pain) pathways of the nervous system and an opioid receptor antagonist which selectively inactivates excitatory opioid receptor-mediated side effects. This invention also relates to a method of using excitatory opioid receptor antagonists alone to block the undesirable excitatory side effects of endogenous bimodally-acting opioid agonists which may be markedly elevated during chronic pain. This invention further relates to a method of long-term treatment of previously detoxified opiate, cocaine and alcohol addicts utilizing said excitatory opioid receptor antagonists, either alone or in combination with low-dose methadone, to prevent protracted physical dependence, and to compositions comprising an excitatory opioid receptor antagonist of the invention and a bimodally-acting opioid agonist.