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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
90/009,474	06/01/2009	4847265	03023.000100.36	5871

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EXAMINER

ART UNIT                      PAPER NUMBER

DATE MAILED: 03/26/2010

Please find below and/or attached an Office communication concerning this application or proceeding.



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(THIRD PARTY REQUESTER'S CORRESPONDENCE ADDRESS)

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**MAILED**

**MAR 26 2010**

**CENTRAL REEXAMINATION UNIT**

**EX PARTE REEXAMINATION COMMUNICATION TRANSMITTAL FORM**

REEXAMINATION CONTROL NO. 90/009,474.

PATENT NO. 4847265.

ART UNIT 3991.

Enclosed is a copy of the latest communication from the United States Patent and Trademark Office in the above identified *ex parte* reexamination proceeding (37 CFR 1.550(f)).

Where this copy is supplied after the reply by requester, 37 CFR 1.535, or the time for filing a reply has passed, no submission on behalf of the *ex parte* reexamination requester will be acknowledged or considered (37 CFR 1.550(g)).

**Notice of Intent to Issue  
Ex Parte Reexamination Certificate**

<b>Control No.</b> 90/009,474	<b>Patent Under Reexamination</b> 4847265	
<b>Examiner</b> EVELYN HUANG	<b>Art Unit</b> 3991	

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

1.  Prosecution on the merits is (or remains) closed in this *ex parte* reexamination proceeding. This proceeding is subject to reopening at the initiative of the Office or upon petition. Cf. 37 CFR 1.313(a). A Certificate will be issued in view of
  - (a)  Patent owner's communication(s) filed: 18 February 2010.
  - (b)  Patent owner's late response filed: \_\_\_\_\_.
  - (c)  Patent owner's failure to file an appropriate response to the Office action mailed: \_\_\_\_\_.
  - (d)  Patent owner's failure to timely file an Appeal Brief (37 CFR 41.31).
  - (e)  Other: \_\_\_\_\_.

Status of *Ex Parte* Reexamination:

  - (f) Change in the Specification:  Yes  No
  - (g) Change in the Drawing(s):  Yes  No
  - (h) Status of the Claim(s):
    - (1) Patent claim(s) confirmed: 1-7.
    - (2) Patent claim(s) amended (including dependent on amended claim(s)): \_\_\_\_\_
    - (3) Patent claim(s) cancelled: \_\_\_\_\_.
    - (4) Newly presented claim(s) patentable: \_\_\_\_\_.
    - (5) Newly presented cancelled claims: \_\_\_\_\_.
2.  Note the attached statement of reasons for patentability and/or confirmation. Any comments considered necessary by patent owner regarding reasons for patentability and/or confirmation must be submitted promptly to avoid processing delays. Such submission(s) should be labeled: "Comments On Statement of Reasons for Patentability and/or Confirmation."
3.  Note attached NOTICE OF REFERENCES CITED (PTO-892).
4.  Note attached LIST OF REFERENCES CITED (PTO/SB/08).
5.  The drawing correction request filed on \_\_\_\_\_ is:  approved  disapproved.
6.  Acknowledgment is made of the priority claim under 35 U.S.C. § 119(a)-(d) or (f).
  - a)  All b)  Some\* c)  None of the certified copies have
    - been received.
    - not been received.
    - been filed in Application No. 07/155,550.
    - been filed in reexamination Control No. \_\_\_\_\_.
    - been received by the International Bureau in PCT Application No. \_\_\_\_\_.

\* Certified copies not received: \_\_\_\_\_.
7.  Note attached Examiner's Amendment.
8.  Note attached Interview Summary (PTO-474).
9.  Other: \_\_\_\_\_.

*E.H.*  
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cc: Requester (if third party requester)  
U.S. Patent and Trademark Office  
PTOL-469 (Rev.08-06)

Art Unit: 3991

1. The Information Disclosure Statements filed on 2/18/2010 is acknowledged and have been considered by the examiner. Once the minimum requirements of 37 CFR 1.97 and 37 CFR 1.98 are met, the examiner has an obligation to consider the information. However, consideration by the examiner of the information submitted in an IDS will be considered in the same manner as other documents in Office search files that are considered by the examiner while conducting a search of the prior art in a proper field of search. See MPEP 609. The initials of the examiner placed adjacent to the citations on the PTO-1449 or PTO/SB/08A and 08B or its equivalent mean that the information has been considered by the examiner to the extent noted above.

The citations in the IDS that are *not* patents or prior art printed publications have been lined through so that they would not be printed in the issued reexamination certificate.

***STATEMENT OF REASONS FOR PATENTABILITY AND/OR CONFIRMATION***

2. The following is an examiner's statement of reasons for patentability and/or confirmation of claims 1-7, which are found patentable in this reexamination proceeding:

a. The rejection for claims 1-4, 6-7 under 35 U.S.C. 103(a) as being unpatentable over any one of Aubert I, Aubert II, 1985 San Diego Posters and Abstracts (Maffrand I, II; Delebasse I, II; Thebault I, II) and 1986 Jerusalem Posters and Abstracts (Delebasse III, IV; Thebault III, IV) in view of the state of the prior art is withdrawn upon reconsideration for the following reasons.

Art Unit: 3991

The claimed dextro isomer substantially separated from its levo isomer would have been obvious to one of ordinary skill in the art in view of the known racemate of MATTPCA or the pharmaceutically acceptable salt thereof, particularly PCR 4099 (as disclosed in Aubert I, Aubert II, the 1985 San Diego Posters/Abstracts or the 1986 Jerusalem Posters/Abstracts), the recommendation of the regulatory authorities to separate and test the individual enantiomers, the general knowledge on the resolution methods and the known fact that the individual isomers may have different properties (as described in the state of the prior art). However, the evidence of record supports the unpredictability of success in the resolution of racemic thienopyridine compounds, as well as the finding of unpredictable and unusual therapeutic properties of the claimed dextro-rotatory isomer of MATTPCA or the salts thereof, as detailed below.

Particularly, at the time of the invention, although resolution of racemic mixture with diastereomeric salt formation process has been shown for other compounds (Fieser, pages 85-88), resolving the racemate with the optically active camphorsulfonic acid had not been described for a thienopyridine compound (McClelland Tr. P17 at A11751, A11754-11756). The art in fact acknowledged the difficulties and unpredictability of the resolution of enantiomers (Ariens, R14, pages 665, 667; William and Lee, R15, page 333; Soudijn, R19, page 89). This is also evidenced by Patent Owner's different results in the attempt to resolve analogous racemic thienopyridine compounds using diastereomeric salt formation method. Particularly, the method was successful with PCR 1033, but not with PCR 3549, the ethyl analog of PCR 1033 (Maffrand Tr. P2, at A12230; Badorc Tr. P7, at A12437). As such, there is no expectation of success in the resolution of racemic MATTPCA or salt thereof, which has an ester substituent instead of a methyl (PCR 1033) or an ethyl (PCR 3549). Further, the ester substituent may have the

Art Unit: 3991

additional risk of racemization during the resolution process or inside the body. Indeed, racemization has been shown to occur in multiple precursors to MATTPCA during the asymmetric synthesis (Badorc Tr. P7, at A12460-12462; Frehel and Badorc II, P20, at 25938-25940).

Notably, the claimed dextro isomer of MATTPCA or salt thereof has been found to possess all the therapeutic anti-platelet aggregation activity without the toxicity of the racemate or the levo isomer (Maffrand Tr. P4, at A10213-14; Maffrand Tr. P2, at A12283 and 12289; Snyder Tr. P5, at A13150-53; Badorc Dep. P24, at A13254; Maffrand Dep. P25, at A13888-90; '265 Patent at col. 9, line 23 to col. 11, line 10; Delebasse V P26, at A18412; Lacheretz Tr. P29, at A13001). These unusual advantageous properties were unpredictable and unexpected, especially in view of the very different results obtained with the analogous PCR 1033 and PCR 3549, which have a methyl and ethyl instead of MATTPCA's methyloxycarbonyl on the bridge carbon. More specifically, in PCR 1033, the enantiomer having the anti-platelet activity also has the undesired toxicity, whereas in PCR 3549, the two enantiomers were equally active as in the racemate (Snyder Tr. P5, at A11211-12; Maffrand Tr. P2, at A12222-24, 12239-40 and 12320-24; Badorc Tr. P7, at A12433 and A12451-52; Davies Tr. P9, at A12597; Hendrickson Tr. P11, at A12121, A12124; PCR 3549 Studies P13, at A26046, A26097). See *In re May*, 574 F2d 1082, 1090-94 (C.C.P.A. 1978); *Forest Labs., Inc. v. Ivax Pharms., Inc.*, 501 F.3d 1263 (Fed. Cir. 2007), 84 USPQ2d 1099.

Further, Plavix® (clopidogrel bisulfate, the bisulfate salt of MATTPCA) has met the long-felt need for an effective and safe antiplatelet drug, as evidenced by the large, double-blinded clinical trials, such as CAPRIE (P59), CURE (P60) and CLASSICS (P62), which have

Art Unit: 3991

demonstrated the effectiveness of clopidogrel bisulfate as an antiplatelet medication having a safety profile more favorable than that of pre-existing antiplatelet drugs, such as aspirin and ticlopidine. Indeed, Plavix® has enjoyed the blockbuster drug status as one of the most widely prescribed drug for preventing second heart attacks and protecting stented patients from thromboses. Many generic pharmaceutical companies have sought to copy the invention.

As such, the objective evidence of nonobviousness has outweighed the evidence of obviousness.

b. The rejection for claims 1-4, 6-7 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 8-10 of U.S. Patent No. 4,529,596 (Aubert I, the '596 patent) in view of the state of the prior art is withdrawn for reasons set forth in above paragraph a.

c. Claim 5, directed to a taurocholate of the dextro-rotatory isomer of MATTPCA substantially separated from the levo- rotatory isomer, has been determined to be patentable for the reasons set forth in the office action mailed on 12/18/2009, and are reiterated as follows.

The closest prior art is Aubert I or Aubert II, wherein the addition salts of MATTPCA with pharmaceutically acceptable mineral or organic acids are generically described, and hydrochloride, bisulphate and hydrobromide salts are exemplified (Examples 1-10). Since taurocholate is not taught or suggested by Aubert I, Aubert II or any of the cited references, claim 5 is neither anticipated nor rendered obvious by the prior art of record.