IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Brian Ault, *et al*.	Filed: September 3, 2009
Application No: 12/553,107	Attorney Docket No: POZN.P0026US
Examiner: Gina C. Yu Justice	Confirmation No. 5949
Title: Method for Delivering a Pharmaceutical Composition to Patient in Need Thereof	

CERTIFICATE OF ELECTRONIC TRANSMISSION

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December 16, 2014 /Steven L. Highlander/
Date Steven L. Highlander

RESPONSE TO NON-FINAL OFFICE ACTION MAILED JUNE 16, 2014

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Commissioner:

This is in response to the Office Action mailed on June 16, 2014, to which a response is due on December 16, 2014, by virtue of the accompanying Petition for Extension of Time (3 months) and payment of fees. No other fees are believed due in connection with this response; however, should applicants payment be missing, or any other fees due, the Commissioner is authorized to debit Parker Highlander PLLC Deposit Acct. No. 50-5902/POZN.P0026US/SLH.

A **Listing of Claims** begins on page 2 of this response; **Remarks** begin on page 5.

LISTING OF CLAIMS

The following listing of claims replaces all previous listings or versions thereof:

1-18. (Canceled)

19. (Previously presented) A method for treating osteoarthritis, rheumatoid arthritis, or ankylosing spondylitis comprising orally administering to a patient in need thereof an AM unit dose form and, 10 hours (±20%) later, a PM unit dose form, wherein:

the AM and PM unit dose forms each comprises:

naproxen, or a pharmaceutically acceptable salt thereof, in an amount to provide 500 mg of naproxen, and

esomeprazole, or a pharmaceutically acceptable salt thereof, in an amount to provide 20 mg of esomeprazole;

said esomeprazole, or pharmaceutically acceptable salt thereof, is released from said AM and PM unit dose forms at a pH of 0 or greater,

the AM and PM unit dose forms target:

i) a pharmacokinetic (pk) profile for naproxen where:

a) for the AM dose of naproxen, the mean C_{max} is 86.2 µg/mL (±20%) and the median T_{max} is 3.0 hours (±20%); and

b) for the PM dose of naproxen, the mean C_{max} is 76.8 µg/mL (±20%) and the median T_{max} is 10 hours (±20%); and

ii) a pharmacokinetic (pk) profile for esomeprazole where:

a) for the AM dose of esomeprazole, the mean area under the plasma concentration-time curve from when the AM dose is administered to 10 hours (±20%) after the AM dose is administered ($AUC_{0\text{-}10,am}$) is 1216 hr*µg/mL (±20%),

b) for the PM dose of esomeprazole, the mean area under the plasma concentration-time curve from when the PM dose is administered to 14 hours (±20%) after the PM dose is administered ($AUC_{0\text{-}14,pm}$) is 919 hr*µg/mL (±20%), and

c) the total mean area under the plasma concentration-time curve for esomeprazole from when the AM dose is administered to 24 hours

(±20%) after the AM dose is administered (AUC_{0-24}) is 2000 hr*µg/mL (±20%); and

the AM and PM unit dose forms further target a mean % time at which intragastric pH remains at about 4.0 or greater for about a 24 hour period after reaching steady state that is at least about 60%.

20-28. (Canceled)

29. (Previously presented) The method according to claim 19, wherein the mean % time at which intragastric pH remains at about 4.0 or greater for about a 24 hour period after reaching steady state is at least about 71%.

30-32. (Canceled).

33. (Previously presented) The method according to claim 19, wherein said AM and PM unit dose forms are administered for a period of at least about 6 days.

34. (Previously presented) The method according to claim 19, wherein said AM and PM unit dose forms are administered for a period of at least about 9 days.

35-39. (Canceled)

40. (Previously presented) The method according to claim 19, wherein said AM and PM unit dose forms are each a multilayer tablet comprising at least one core and at least a first layer and a second layer, wherein:

i) said core comprises naproxen, or pharmaceutically acceptable salt thereof;

ii) said first layer is a coating that at least begins to release the naproxen, or pharmaceutically acceptable salt thereof, when the pH of the surrounding medium is about 3.5 or greater; and

iii) said second layer comprises esomeprazole or a pharmaceutically acceptable salt thereof, wherein said esomeprazole or pharmaceutically acceptable salt thereof is released at a pH of from 0 or greater.

41. (Canceled)

42. (Previously presented) The method according to claim 40, wherein said esomeprazole or pharmaceutically acceptable salt thereof is released at a pH of from 0 to about 2.

43-44. (Canceled)

45. (Previously presented) The method according to claim 40, wherein said multi-layer tablet is substantially free of sodium bicarbonate.

46-47. (Canceled)

REMARKS

I. Status of the claims

Claims 19, 29, 33, 34, 40, 42 and 45 are pending in the application and stand rejected under 35 U.S.C. §103 and for obviousness-type double-patenting. The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

II. Previous Arguments Regarding the Combination of Naproxen and Esomeprazole

In the Response to Final Office Action dated January 30, 2013 for the captioned application, Applicants' representative stated:

> Although Plachetka does mention both naproxen and esomeprazole, Plachetka places no particular emphasis on the specific combination of the two. Nor does Plachetka describe any formulation or *in vitro* or *in vivo* experiments using such a combination. Thus, a skilled artisan, when reading Plachetka, would have had no guidance or motivation to specifically select the combination of naproxen and esomeprazole, when confronted with hundreds of possible combinations Plachetka presents. Nor would the skilled artisan have had any expectation that the combination of naproxen and esomeprazole, as currently recited in claim 19, would produce Applicants' unexpected pharmacodynamics profile (*see below*).

The above statement that "a skilled artisan, when reading Plachetka, would have had no guidance or motivation to specifically select the combination of naproxen and esomeprazole," is incorrect. Applicants agree generally with the position in the July 30, 2012 Action that Plachetka discloses to a person of ordinary skill in the art the coordinated delivery of esomeprazole and naproxen. But Plachetka, while examining the performance of naproxen and gastric inhibitors, does not disclose any *in vitro* or *in vivo* experiments using a combination of naproxen and esomeprazole. Thus, it is important to consider that, in the context of obviousness, Plachetka does not provide any direct information to one of skill in the art regarding the pharmacodynamics profile of the combination of naproxen and esomeprazole.

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