

formulation at the highest dose strength. For the lower dose strengths, biowaivers can be requested based on the linear pharmacokinetics, the composition proportionality, and the dissolution similarity referencing the strengths used in the BE study. Please refer to the Guidance for BA/BE studies for orally administered drug products - general considerations (<http://www.fda.gov/cder/guidance/5356fnl.pdf>)

- 21) Does the FDA have other suggestions/recommendations regarding chemistry, manufacturing, and controls?

Preliminary Response: We remind you that, as per CDER's current policy on nomenclature, the labeling of your NDA should have "Pitavastatin" as the established name, not (b) (4), because the dosage strength is based on the pitavastatin free base.

Meeting discussion: None

ADMINISTRATIVE

- 22) The largest portion of the clinical development program was conducted outside the IND and forms FDA 1572 may not be available for all trials. When forms 1572 are available does the Division require that they be included in the NDA? Investigators' CVs? Financial disclosure statements?

Preliminary Responses: This will be addressed at the meeting.

Meeting Discussion: Form FDA 1572 should be included in the NDA, if available. Financial disclosure statements and CVs will be included for all investigators. This was found acceptable.

- 23) Kowa plans to submit the NDA in e-CTD format. Does the Division have any other requirements for the NDA or guidance for its content?

Preliminary Response: None at this time

Discussion: The sponsor was encouraged to contact Mr. Ken Edmunds (301-827-3862) regarding the planned electronic NDA submission

DECISIONS (AGREEMENTS) REACHED:

None

UNRESOLVED ISSUES OR ISSUES REQUIRING FURTHER DISCUSSION:

None

ACTION ITEMS:

IND 60,492

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None

ATTACHMENTS/HANDOUTS:

None

Linked Applications

Sponsor Name

Drug Name

IND 60492

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INSTITUTE INC

PITAVASTATIN TABLETS

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

KATI JOHNSON
02/27/2008

February 20, 2009

Mary Parks, M.D., Director
Division of Metabolism and Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266
ATTN: Central Document Room

**RE: NDA 22-363
Pitavastatin (NK-104)
Amendment #0014 to New Drug Application**

Dear Dr. Parks:

Kowa Company Limited (KCL) submitted its initial New Drug Application, NDA 22-363, for pitavastatin tablets (NK-104) dated October 1, 2008.

This amendment is to respond to a February 3, 2009 request received by Kowa via e-mail from the Division (Kati Johnson) as identified below:

According to our data manager, we need some additional data information from the sponsor with regard to this study report. Please ask them to do the following:

1. Provide QTcI adjusting factor, QRS, QT baseline value to the dataset ANALYSIS.XPT.
2. Include SUBJECT, the consistent ID variable that used in ANALYSIS.XPT and CONCQT.XPT for datasets DM.XPT, VS.XPT, EECG.XPT.
3. Either update dataset DM.XPT with SEX, RACE, ETHNIC decoded or update the DEFINE.PDF file to include those decoding.

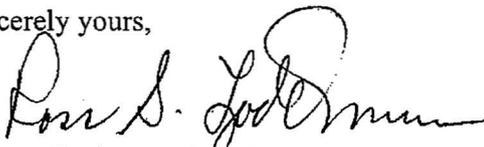
Also, please let the sponsor know that it's better to populate a consistent unique subject ID to all datasets to avoid confusing, also please let them know that a define.pdf should give a short description of each dataset, dataset variables and their derivation rule, variable decoding and etc.

We submitted requested data on this QTc study earlier in amendment #0006. Revised datasets and our response to this current request are contained in Module 5.3.4 in this amendment.

This amendment to NDA 22-363 consists of 1 CD, totaling less than 0.5 gigabytes. The submission is virus free. The following was used to check the files for viruses:

Trend Micro OfficeScan
Version 7.3
Virus Definitions: 5.849.00, created February 16, 2009

Sincerely yours,



Ross S. Laderman, MPH
Senior Director, Regulatory Affairs
Kowa Research Institute, Inc.
(U.S. Agent for Kowa Company Limited)

February 20, 2009

Mary Parks, M.D., Director
Division of Metabolism and Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266
ATTN: Central Document Room

**RE: NDA 22-363
Pitavastatin (NK-104)
Amendment #0013 to New Drug Application**

Dear Dr. Parks:

Kowa Company Limited (KCL) submitted its initial New Drug Application, NDA 22-363, for pitavastatin tablets (NK-104) dated October 1, 2008.

This amendment is to respond to a January 9, 2009 request received by Kowa via e-mail from the Division (Dr. Karen Davis Bruno) stating:

Part of an adequate GLP carc study includes historical control data (background rates) of common tumors found in this strain by the contracting laboratory. We are not asking for ^{(b) (4)} proprietary information. We need to qualify tumor findings observed in your contracted study in order to determine whether they may be drug related or simply background noise for the strain.

We need to know how many Tg RASH2 carc studies ^{(b) (4)} has completed within 5 years of conducting your study and what the range and mean incidence of common tumors are in this mouse strain. This will also assist us in identifying any rare tumors observed in the study. This information needs to be provided before we can complete review of your NDA.

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This request is a continuation of earlier communications which were initially addressed in Amendment #0002 to this NDA. Our contract laboratory, ^{(b) (4)}, was originally hesitant in providing historical data that had been requested. We now have received this data and are providing it in the current Module 4.2.3.4.2.2.

This amendment to NDA 22-363 consists of 1 CD, totaling less than 0.5 gigabytes. The submission is virus free. The following was used to check the files for viruses:

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Virus Definitions: 5.849.00, created February 16, 2009

Sincerely yours,



Ross S. Laderman, MPH
Senior Director, Regulatory Affairs
Kowa Research Institute, Inc.
(U.S. Agent for Kowa Company Limited)

KOWA



RESEARCH INSTITUTE, INC.

February 16, 2009

Mary Parks, M.D., Director
Division of Metabolism and Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266
ATTN: Central Document Room

RE: NDA 22-363
NK-104 (pitavastatin)
Amendment #0012 to New Drug Application

Dear Dr. Parks:

Kowa Company Limited (KCL) submitted its initial New Drug Application, NDA 22-363, for pitavastatin tablets (NK-104) dated October 1, 2008.

Kowa has not conducted any additional clinical trials since the original NDA was submitted so no traditional 120-day safety update will be submitted. However we are submitting an update listing of post marketing reports from Japan. Included is the most recent PSUR (10th) covering the period January 17, 2008 to July 16, 2008 and two tabulations of serious adverse events, the first covering the period 1/1/08 to 12/31/08 and the second covering the period 1/1/09 to 1/15/09. While some information in these reports is contained in the original NDA, the cumulative contents cover through the first 4 months following NDA submission. These documents are contained in Module 5.3.6.

In addition, at the time of the original NDA submission we stated that it was not Kowa's intent to use extension study NK-104-310 as support of safety or efficacy for this NDA since the entire study itself was not planned for completion until after NDA submission. For information purposes we included an interim report in the original NDA. As part of this update we are submitting the final report of this study. It is contained in Module 5.3.5.4.1. It is Kowa's

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conclusion that the outcome of this study has no material effect on the evaluation of the safety or efficacy in this pitavastatin NDA.

This amendment to NDA 22-363 consists of 1 CD, totaling less than 0.5 gigabytes. The submission is virus free. The following was used to check the files for viruses:

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Sincerely yours,

A handwritten signature in black ink, appearing to read "Ross S. Laderman".

Ross S. Laderman, MPH
Senior Director, Regulatory Affairs
Kowa Research Institute, Inc.
(U.S. Agent for Kowa Company Limited)

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February 6, 2009

Mary Parks, M.D., Director
Division of Metabolism and Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266
ATTN: Central Document Room

**RE: NDA 22-363
NK-104 (pitavastatin)
Amendment #0011 to New Drug Application**

Dear Dr. Parks:

Kowa Company Limited (KCL) submitted its initial New Drug Application, NDA 22-363, for pitavastatin tablets (NK-104) dated October 1, 2008.

In the original NDA Kowa proposed to package marketed pitavastatin tablets in all three strengths (1 mg, 2 mg and 4 mg) in HDPE bottles of 90^{(b) (4)}. In addition Kowa proposed to provide physician samples in ^{(b) (4)} strengths in blister cards of 7. ^{(b) (4)}

^{(b) (4)} This amendment updates Modules 3.2.P.2.4, 3.2.P.5.1 and all 2.3.P sections to reflect these changes. Other sections affected by these changes were revised accordingly and submitted in Amendment #0009.

This amendment to NDA 22-363 consists of 1 CD, totaling less than 0.5 gigabytes. The submission is virus free. The following was used to check the files for viruses:

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Trend Micro OfficeScan
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Virus Definitions: 5.809.00, created February 1, 2009

Sincerely yours,

A handwritten signature in cursive script that reads "Ross S. Laderman".

Ross S. Laderman, MPH
Senior Director, Regulatory Affairs
Kowa Research Institute, Inc.
(U.S. Agent for Kowa Company Limited)