12/15/08

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 22-363

Kowa Research Institute, Inc.
US Agent for Kowa Company Ltd.
Attention: Ross Laderman
Senior Director, Regulatory Affairs
430 Davis Drive, Suite 200
Morrisville, NC 27560

Dear Mr. Laderman:

Please refer to your new drug application (NDA) dated October 1, 2008, received October 3, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for Livalo (pitavastatin) Tablets, 1 mg, 2 mg, and 4 mg.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is August 3, 2009.

We also request that you submit the following information:

1. Because the dosage strengths are based on the free base pitavastatin, the established name of your product is "pitavastatin". Revise all labeling, where applicable, to replace (b) (4) with the correct established name "pitavastatin".
2. Confirm that the manufacturing and testing facilities listed in the NDA Form 356h are all the facilities involved in the manufacture and testing of the commercial drug substance and drug product and indicate whether each facility is ready for inspection or, if not, when it will be ready.
3. Provide the physical dimension of the finished tablet.
4. Provide a justification for the omission of (b) (4) (b) (4)
5. Provide references to the 21 CFR food additive regulations for the drug-contact components of the container closure systems used to package the drug substance and drug product.

If you have not already done so, you must submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at

http://www.fda.gov/oc/datacouncil/spl.html. The content of labeling must be in the Prescribing Information (physician labeling rule) format.

Please respond only to the above requests for additional information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We reference the deferral granted on September 20, 2005 (End-of-phase 2 meeting) for the pediatric study requirement for this application for all pediatric patients.

If you have any questions, call Kati Johnson, Regulatory Project Manager, at (301) 796-1234.

Sincerely,

{See appended electronic signature page}

Mary H. Parks, M.D.
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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
12/15/2008 04:34:08 PM
signing for Mary Parks, M.D.

KOWA

RESEARCH INSTITUTE, INC.

December 12, 2008

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 #0004 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 two requests for information received by Kowa via e-mail from the Division (Kati Johnson) as identified below:

- An e-mail dated 12/1/2008 stating:

  "I would request the sponsor to send us a file (like the "define" file for variables) to describe which of their SAS code is for which analysis because of the difficulty to get the information from their magical names. The requested file should be for both efficacy and safety analyses."

- A second and related e-mail dated 12/1/2008 stating:

  "Following up on Wei's request, the sponsor has submitted a large number of SAS programs which are not well identified. He would like the sponsor to provide a listing of these programs along with a description of the type of analysis performed by the program. The sponsor should also clearly identify the primary SAS programs used to generate the main results for primary and secondary lipid endpoints and for subgroup results for LDL-C.

430 Davis Drive, Suite 200, Morrisville, North Carolina 27560 Telephone: 919.433.1600 Fax: 919.433.1620

We are providing the requested information in a number of files. In addition to the programs used to generate the derived data sets, tables, listings and figures, we are also submitting the SAS macros that are called by these programs.

This amendment to NDA 22-363 consists of 1 CD, totaling less than 0.1 gigabyte. The submission is virus free. The following was used to check the files for viruses:

Trend Micro OfficeScan
Version 7.0
Virus Definitions: 5.701.00, created December 10, 2008

Sincerely yours,

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

12/2/08

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

IND 60,492

Kowa Research Institute
Attention: Ross Laderman
Senior Director, Regulatory Affairs
430 Davis Drive, Suite 200
Morrisville, NC 27560

Dear Mr. Laderman:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for NK-104 (pitavastatin) Tablets.

We also refer to your amendment dated June 12, 2007, containing a proposed tradename for a future NDA submission. The NDA was subsequently submitted October 1, 2008.

We have completed our review and find your proposed tradename LIVALO® acceptable. The proposed tradename will be re-evaluated 3 months prior to the anticipated approval date.

If you have any questions, contact Kati Johnson, Regulatory Project Manager, at (301) 796-1234.

Sincerely,

{See appended electronic signature page}

Mary H. Parks, M.D.
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Linked Applications	Sponsor Name	Drug Name
IND 60492	KOWA RESEARCH 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/

ERIC C COLMAN
12/02/2008
Eric Colman for Mary Parks

KOWA

RESEARCH INSTITUTE, INC.

RECEIVED

DEC 02 2008

CDR

ORIGINAL

ORIGINAL AMENDMENT

November 26, 2008

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 #0002 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 two requests for information received by Kowa via e-mail from the Division (Kati Johnson) as identified below:

- An e-mail dated 10/29/2008 requesting datasets for the two transgenic mouse studies that were submitted in the original NDA.

- An e-mail dated 10/31/2008 requesting historical baseline data for the histopathological (neoplastic) findings in control Tg rasH2 mice at the (b) (4) Lab (0.5% carboxymethylcellulose sodium in aqueous solution).

430 Davis Drive, Suite 200, Morrisville, North Carolina 27560 Telephone: 919.433.1600 Fax: 919.433.1620

This amendment to NDA 22-363 consists of 1 CD, totaling less than 0.1 gigabyte. The submission is virus free. The following was used to check the files for viruses:

Trend Micro OfficeScan
Version 7.0
Virus Definitions: 5.671.00, created November 23, 2008

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.

November 26, 2008

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 #0003 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 request for information received by Kowa via e-mail from the Division (Kati Johnson) as identified below:

- An e-mail dated 11/20/2008 stating:

  Please submit, or show us the location of the "coding dictionary". The "coding dictionary" consists of a list of all investigator verbatim terms and the preferred terms to which they were mapped. It is most helpful if this comes in as a SAS transport file so that it can be sorted as needed; however, if it is submitted as a PDF document, it should be submitted in both directions (verbatim -> preferred and preferred -> verbatim).

We have included in this submission the SAS transport file of all the unique AE raw terms for the ISS along with the Body System and Preferred Terms. We used the MedDRA dictionary Version 8.1 for all studies.

430 Davis Drive, Suite 200, Morrisville, North Carolina 27560 Telephone: 919.433.1600 Fax: 919.433.1620

KOWA

RESEARCH INSTITUTE, INC.

This amendment to NDA 22-363 consists of 1 CD, totaling less than 0.1 gigabyte. The submission is virus free. The following was used to check the files for viruses:

Trend Micro OfficeScan
Version 7.0
Virus Definitions: 5.671.00, created November 23, 2008

Sincerely yours,

Ross S. Laderman

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

KOWA

RESEARCH INSTITUTE, INC.

November 21, 2008

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 #0001 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 two requests for information received by Kowa via e-mail from the Division (Kati Johnson and Dr. Iffat Choudhury) as identified below:

- An e-mail dated 11/12/2008 from Ms. Johnson stating:

  "The clinical reviewer, in looking at the NDA, can't find the following info. If it is in the NDA, can you tell me where it is. and if not, send it in.

  1. Datasets for the pivotal active controlled and placebo-controlled studies
  2. List of the number of subjects screened and number of subjects enrolled by each study site for the pivotal studies
  3. List of the number of subjects with protocol violations by specific sites for the pivotal studies
  4. List of the number of subjects discontinued by specific sites for the pivotal studies
  5. Rationale for assuming the applicability of foreign data to the US population in the submission"

430 Davis Drive, Suite 200, Morrisville, North Carolina 27560 Telephone: 919.433.1600 Fax: 919.433.1620

- An e-mail dated 11/12/2008 from Dr. Choudhury stating:

  "Thanks for your prompt reply. I agree that since the placebo-controlled trials were in Phase 2 development, no need for you to submit the detailed information as I am asking for the Phase 3 trials.

  Would it be possible to have the information I requested in a chart with the following columns: Site ID #, Investigator, Location/Address, # of Subjects Screened, # of Subjects Randomized, # of Subjects Discontinued, # of Subjects with Protocol Violations?"

The Division has already been informed (via e-mail on 11/12/2008) that the datasets requested in item # 1 above appear in disc #1 of the original NDA submission. The tabular presentations for studies NK-104-301 and NK-104-302 (items 2, 3 and 4 above) requested by Dr. Choudhury appear as new data in Module 5.3.5.1.6 and 5.3.5.1.7. The statement in response to item #5 above appears as new information in Module 1.12.11.

This amendment to NDA 22-363 consists of 1 CD, totaling less than 0.1 gigabytes. The submission is virus free. The following was used to check the files for viruses:

Trend Micro OfficeScan
Version 7.0
Virus Definitions: 5.661.00, created November 18, 2008

Sincerely yours,

Ross S. Laderman

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

1.2 Cover Letters

A detailed cover letter is being submitted with this New Drug Application. The letter will provide the reviewer(s) with a snapshot of the history of the IND, the relationship of this CTD to that submitted in Europe by Kowa's European subsidiary, and other important information not captured elsewhere in the CTD.

Referenced in the cover letter is a proposed trade name, Livalo, for the pitavastatin product that is the subject of this NDA. Kowa requests the FDA's concurrence with this proposed name. Supporting documents for this name are attached to the cover letter.

Also attached to the cover letter is a tabular listing and copies of the FDA correspondence and meeting minutes during the period that Kowa has had ownership of IND 60,492 for pitavastatin.