MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 8/4/09

TO: NDA File, NDA 22-363, Livalo (pitavastatin) Tablets

FROM: Kati Johnson, PM

SUBJECT: Administrative forms signed by Japanese sponsor of NDA

NDA 22-363 is sponsored by Kowa Company Ltd. (KCL), based in Japan. The authorized US agent is Kowa Research Institute, Inc., a US based KCL subsidiary. Since it wasn't clear if KCL needed to sign the administrative forms contained in the application, they were asked to do so. The following forms have been signed by KCL:
-356h-Application to Market a New Drug, Biologic, or an Antibiotic Drug for Human Use
-3674-Certification of Compliance, under 42 U.S.C...With Requirements for clinical Trials.gov Data Bank.
-3454-Certification: Financial Interests and Arrangements of clinical Investigators
-Debarment Certification Statement

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, Parts 314 & 601)

Form Approved: OMB No. 0910-0430
Expiration Date: April 30, 2009
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT: Kowa Company Limited

DATE OF SUBMISSION: 10/01/2008

TELEPHONE NO. *(Include Area Code)* 81(0)3 3279 7410

FACSIMILE (FAX) Number *(Include Area Code)* 81(0)3 3242 2270

APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued)*:
4-14 Nihonbashi-honcho 3-chome, Chuo-ku, Tokyo 103-8433,Japan

AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE
Kowa Research Institute, Inc.
430 Davis Drive,
Suite 200,
Morrisville, NC 27560 telephone 919-433-1600 fax 919-433-1620

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(If previously issued)* 22-363

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*: pitavastatin

PROPRIETARY NAME *(trade name)* IF ANY: Livalo (proposed)

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(if any)*: monocalcium bis[(3R,5S,6E)-7-[2-cyclopropyl-4-(4- fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-6-heptenoate]

CODE NAME *(if any)*: NK-104

DOSAGE FORM: tablet

STRENGTHS: 1, 2 and 4 mg

ROUTE OF ADMINISTRATION: oral

(PROPOSED) INDICATION(S) FOR USE: pitavastatin is indicated as an adjunct to diet to reduce total cholesterol, LDL-cholesterol, apolipoprotein B, and triglycerides and to increase HDL-cholesterol in adult patients with primary hypercholesterolemia and mixed dyslipidemia

APPLICATION INFORMATION

APPLICATION TYPE *(check one)*
☑ NEW DRUG APPLICATION (NDA, 21 CFR 314.50) ☐ ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☑ 505 (b)(1) ☐ 505 (b)(2)

IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug — Holder of Approved Application

TYPE OF SUBMISSION *(check one)* ☑ ORIGINAL APPLICATION ☐ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ EFFICACY SUPPLEMENT
☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ OTHER

IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION:

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY ☐ CBE ☐ CBE-30 ☐ Prior Approval (PA)

REASON FOR SUBMISSION

PROPOSED MARKETING STATUS *(check one)* ☑ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 2 DVD

THIS APPLICATION IS ☐ PAPER ☐ PAPER AND ELECTRONIC ☑ ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Drug Product: Patheon Inc., 2100 E. Galbraith Road Cincinnati, OH 45237-1625 phone (513-948-9111) Contact David Leuck, Director, QA, Registration number 1510437

(b) (4)

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

IND 60,492
See attachment for DMF listing

This application contains the following items: *(Check all that apply)*	
☑	1. Index
☑	2. Labeling *(check one)* ☑ Draft Labeling ☐ Final Printed Labeling
☑	3. Summary (21 CFR 314.50 (c))
☑	4. Chemistry section
	☑ A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
	☐ B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
	☑ C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
☑	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
☑	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
☐	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
☑	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
☐	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
☑	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
☑	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
☑	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
☑	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
☑	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
☐	15. Establishment description (21 CFR Part 600, if applicable)
☑	16. Debarment certification (FD&C Act 306 (k)(1))
☐	17. Field copy certification (21 CFR 314.50 (l)(3))
☑	18. User Fee Cover Sheet (Form FDA 3397)
☑	19. Financial Information (21 CFR Part 54)
☐	20. OTHER *(Specify)*

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
	Torao Yamamoto, Representative Director Executive Vice President	07/29/2009

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
4-14 Nihonbashi-honcho 3-chome, Chuo-ku, Tokyo 103-8433, Japan	81(0)3 3279 7410

Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (HFD-143)
Central Document Room
5901-B Ammendale Road
Beltsville, MD 207052-1266

Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (HFM-99)
1401 Rockville Pike
Rockville, MD 20852-1448

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

See OMB Statement on Reverse. Form Approved: OMB No. 0910-0616, Expiration Date: 06-30-2008

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank (42 U.S.C. § 282(j))

(For submission with an application/submission, including amendments, supplements, and resubmissions, under §§ 505, 515, 520(m), or 510(k) of the Federal Food, Drug, and Cosmetic Act or § 351 of the Public Health Service Act.)

SPONSOR / APPLICANT / SUBMITTER INFORMATION

1. NAME OF SPONSOR/APPLICANT/SUBMITTER
Kowa Company Limited

2. DATE OF THE APPLICATION/SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES
10/01/2008

3. ADDRESS *(Number, Street, State, and ZIP Code)*
4-14 Nihonbashi-honcho 3-chome, Chuo-ku, Tokyo 103-8433, Japan

4. TELEPHONE AND FAX NUMBER *(Include Area Code)*
(Tel.) 81(0)3 3279 7410
(Fax) 81(0)3 3242 2270

PRODUCT INFORMATION

5. **FOR DRUGS/BIOLOGICS:** Include Any/All Available Established, Proprietary and/or Chemical/Biochemical/Blood/Cellular/Gene Therapy Product Name(s)
FOR DEVICES: Include Any/All Common or Usual Name(s), Classification, Trade or Proprietary or Model Name(s) and/or Model Number(s)
(Attach extra pages as necessary)

pitavastatin tablets

APPLICATION / SUBMISSION INFORMATION

6. TYPE OF APPLICATION/SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES
☐ IND ☒ NDA ☐ ANDA ☐ BLA ☐ PMA ☐ HDE ☐ 510(k) ☐ PDP ☐ Other

7. INCLUDE IND/NDA/ANDA/BLA/PMA/HDE/510(k)/PDP/OTHER NUMBER *(If number previously assigned)*
NDA 22-363

8. SERIAL NUMBER ASSIGNED TO APPLICATION/SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES
0000

CERTIFICATION STATEMENT / INFORMATION

9. CHECK ONLY ONE OF THE FOLLOWING BOXES *(See Instructions for additional information and explanation)*

☐ A. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act, enacted by 121 Stat. 823, Public Law 110-85, do not apply because the application/submission which this certification accompanies does not reference any clinical trial.

☐ B. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act, enacted by 121 Stat. 823, Public Law 110-85, do not apply to any clinical trial referenced in the application/submission which this certification accompanies.

☒ C. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act, enacted by 121 Stat. 823, Public Law 110-85, apply to one or more of the clinical trials referenced in the application/submission which this certification accompanies and that those requirements have been met.

10. IF YOU CHECKED BOX C, IN NUMBER 9, PROVIDE THE NATIONAL CLINICAL TRIAL (NCT) NUMBER(S) FOR ANY "APPLICABLE CLINICAL TRIAL(S)," UNDER 42 U.S.C. § 282(j)(1)(A)(i), SECTION 402(j)(1)(A)(i) OF THE PUBLIC HEALTH SERVICE ACT, REFERENCED IN THE APPLICATION/SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES *(Attach extra pages as necessary)*

NCT Number(s): NCT00249249 NCT00309777 NCT00309738 NCT00309751 NCT00257686

The undersigned declares to the best of her/his knowledge, that this is an accurate, true, and complete submission of information. I understand that the failure to submit the certification required by 42 U.S.C. § 282(j)(5)(B), section 402(j)(5)(B) of the Public Health Service Act, and the knowing submission of a false certification under such section are prohibited acts under 21 U.S.C. § 331, section 301 of the Federal Food, Drug, and Cosmetic Act.
Warning: A willfully and knowingly false statement is a criminal offense, U.S. Code, title 18, section 1001.

11. SIGNATURE OF SPONSOR/APPLICANT/SUBMITTER OR AN AUTHORIZED REPRESENTATIVE (Sign)

12. NAME AND TITLE OF THE PERON WHO SIGNED IN NO. 11
(Name) Torao Yamamoto
(Title) Representative Director, Executive Vice President

13. ADDRESS *(Number, Street, State, and ZIP Code) (of person identified in No. 11 and 12)*
Kowa Company Limited
4-14 Nihonbashi-honcho 3-chome, Chuo-ku,
Tokyo 103-8433, Japan

14. TELEPHONE AND FAX NUMBER *(Include Area Code)*
(Tel.) 81(0)3 3279 7410
(Fax) 81(0)3 3242 2270

15. DATE OF CERTIFICATION
07/29/2009

PSC Graphics: (301) 443-1090 EF

Instructions for Completion of Form FDA 3674

Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank (42 U.S.C. § 282(j))
Form 3674 must accompany an application/submission, including amendments, supplements, and resubmissions, submitted under §§ 505, 515, 520(m), or 510(k) of the Federal Food, Drug, and Cosmetic Act or § 351 of the Public Health Service Act.

1. **Name of Sponsor/Applicant/Submitter** - This is the name of the sponsor/applicant/submitter of the drug/biologic/device application/submission which the certification accompanies. The name must be identical to that listed on the application/submission.

2. **Date** - This is the date of the application/submission which the certification accompanies.

3. & 4. - Provide complete address, telephone number and fax number of the sponsor/applicant/submitter.

5. **Product Information - For Drugs/Biologics:** Provide the established, proprietary name, and/or chemical/biochemical/blood product/cellular/gene therapy name(s) for the product covered by the application/submission. Include all available names by which the product is known. **For Devices:** Provide the common or usual name, classification, trade or proprietary or model name(s), and/or model number(s). Include all available names/model numbers by which the product is known.

6. **Type of Application/Submission** - Identify the type of application/submission which the certification accompanies by checking the appropriate box. If the name of the type of application/submission is not identified, check the box labeled "Other."

7. **IND/NDA/ANDA/BLA/PMA/HDE/510(k)/PDP/Other Number** - If FDA has previously assigned a number associated with the application/submission which this certification accompanies, list that number in this field. For example, if the application/submission accompanied by this certification is an IND protocol amendment and the IND number has already been issued by FDA, that number should be provided in this field.

8. **Serial Number** - In some instances a sequential serial number is assigned to the application. If there is such a serial number, provide it in this field.

9. **Certification** - This section contains three different check-off boxes.
   Box A should be checked if the sponsor/applicant/submitter has concluded that the requirements of 42 U.S.C. § 282(j), section 402(j) of the Public Health Service Act, do not apply because no clinical trials are included, relied upon, or otherwise referred to, in the application/submission which the certification accompanies.

   Box B should be checked if the sponsor/applicant/submitter has concluded that the requirements of 42 U.S.C. § 282(j), section 402(j) of the Public Health Service Act, do not apply at the time of submission to any clinical trials that are included, relied upon, or otherwise referred to, in the application/submission which the certification accompanies. This means that, at the time the application/submission is being made, the requirements of 42 U.S.C. § 282(j), section 402(j) of the Public Health Service Act, do not apply to any of the clinical trials included, relied upon, or otherwise referred to, in the application/submission which this certification accompanies.

   Box C should be checked if the sponsor/applicant/submitter has concluded that the requirements of 42 U.S.C. § 282(j), section 402(j) of the Public Health Service Act, do apply at the time of submission to some or all of the clinical trials that are included, relied upon, or otherwise referred to, in the application/submission which the certification accompanies. This means that, at the time the application/submission is being made, the requirements of 42 U.S.C. § 282(j), section 402(j) of the Public Health Service Act, apply to one or more of the clinical trials included, relied upon, or otherwise referred to, in the application/submission which this certification accompanies.

10. **National Clinical Trial (NCT) Numbers** - If you have checked Box C in number 9 (Certification), provide the NCT Number obtained from www.ClinicalTrials.gov for each clinical trial that is an "applicable clinical trial" under 42 U.S.C. § 282(j)(1)(A)(i), section 402(j)(1)(A)(i) of the Public Health Service Act, and that is included, relied upon, or otherwise referred to, in the application/submission which the certification accompanies. Type only the number, as NCT will be added automatically before number. Include any and all NCT numbers assigned to the clinical trials included, relied upon, or otherwise referred to, in the application/submission which this certification accompanies. Multiple NCT numbers may be required for a particular certification, depending on the number of "applicable clinical trials" included, relied upon, or otherwise referred to, in the application/submission which the certification accompanies.

11. **Signature of Sponsor/Applicant/Submitter or an Authorized Representative** - The person signing the certification must sign in this field.

12. **Name and Title of Person Who Signed in number 11.** - Include the name and title of the person who is signing the certification. If the person signing the certification is not the sponsor/applicant/submitter of the application/submission, he or she must be an authorized representative of the sponsor/applicant/submitter.

13. & 14. - Provide the full address, telephone and fax number of the person who is identified in number 11 and signs the certification in number 11.

15. Provide the date the certification is signed. This date may be different from the date provided in number 2.

Paperwork Reduction Act Statement

Public reporting burden for this collection of information is estimated to average 15 minutes and 45 minutes (depending on the type of application/submission) per response, including time for reviewing instructions. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to the applicable address below.

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
Form No. FDA 3674
5901-B Ammendale Road
Beltsville, MD 20705-1266

Food and Drug Administration
Center for Biologics Evaluation and Research
1401 Rockville Pike
Rockville, MD 20852-1448

Food and Drug Administration
Center for Devices and Radiological Health
Program Operations Staff (HFZ-403)
9200 Corporate Blvd.
Rockville, MD 20850

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information, unless it displays a currently valid OMB control number.

FDA Form 3674 (continued)

NCT numbers for the NK-104 EU trials on Clinicaltrials.gov

NCT00249249
NCT00309777
NCT00309738
NCT00309751
NCT00257686
NCT00325780
NCT00330876
NCT00344175
NCT00344370