DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-176/S-017

Daiichi Sankyo, Inc.
Attention: Sandra Smith, RPh, MBA
Senior Director, Regulatory Affairs
399 Thornall Street, 10th Floor
Edison, NJ 08837

Dear Ms. Smith:

Please refer to your supplemental new drug application dated December 22, 2006 (letter dated December 26, 2006), received December 22, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for WelChol (colesevelam hydrochloride) Tablets.

We acknowledge receipt of your submissions dated April 19 and 27, May 24, June 15, July 16, September 12, 24, and 28, October 12, 17, and 26, November 5 and 27, December 18, 2007, and January 17, 2008.

This supplemental new drug application provides for the use of WelChol as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

We have completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

We waive the requirements of 21 CRF 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical in content to the enclosed labeling (text for package insert and text for patient package insert submitted on January 17, 2008). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "SPL for approved NDA 21-176/S-017."

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 are waiving the pediatric study requirement for this application.

We remind you of your postmarketing study commitments in your submission dated January 17, 2008. These commitments are listed below.

1. To study WelChol as monotherapy treatment for type 2 diabetes mellitus:
   Protocol Submission: by July 31, 2008
   Study Start: by January 31, 2009
   Final Report Submission: by July 31, 2011

2. To study WelChol in combination with thiazolidinediones as treatment for type 2 diabetes mellitus:
   Protocol Submission: by October 31, 2008
   Study Start: by April 30, 2009
   Final Report Submission: by October 31, 2011

3. To conduct drug-drug interaction testing between WelChol and the following drugs:
   - a commonly used angiotensin converting enzyme (ACE) inhibitor
   - a commonly used angiotensin receptor blocker (ARB)
   - a long-acting beta-blocker
   - aspirin
   - rosiglitazone
   - glimepiride
   - glipizide ER
   - sitagliptin
   - metformin ER
   - phenytoin

   You have committed to the following time lines for *in Vivo* Studies for an ARB, glimepiride, glipizide ER, and phenytoin:
   Protocol Submission: by June 30, 2008
   Study Start: by September 30, 2008
   Final Report Submission: by September 30, 2009

   We note that you have committed to meet with the Agency in the first quarter of 2008 to determine a development plan for screening the remaining drugs listed above for potential interaction. Based on the results of this screen, you will conduct clinical drug interaction studies for those drugs with the highest probability of an *in vivo* interaction with WelChol.

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final study reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

The present submission references the April 25, 2000, Environmental Assessment (EA) submitted in the initial NDA submission. An updated and revised EA will be required for future applications and

supplements of WelChol. The updated EA should include information on the current drug sponsor and estimates of environmental concentrations (EECs) of colesevelam HCl based on all indications for the drug product. In addition, since colesevelam HCl is an insoluble polymer that would be expected to partition to wastewater treatment plant biosolids, EECs for land-applied biosolids and toxicity studies in terrestrial organisms should be considered. Consultation with the Environmental Staff is recommended prior to submission of a revised EA.

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Julie Marchick, Regulatory Project Manager, at (301) 796-1280.

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

Enclosure: Package Insert

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

/s/

Mary Parks

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