Department of Health and Human Services

Public Health Service
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Warning Letter 320-16-35

Via UPS
Return Receipt Requested

September 26, 2016

Mr. Hiromichi Kaneko
General Manager
Nippon Fine Chemical Co., Ltd
1-1, 5-Chome, Umei
Takasago City, Hyogo 676-0074
Japan

Dear Mr. Kaneko:

On December 14, 2015, the U.S. Food and Drug Administration (FDA) arrived at your drug manufacturing facility, Nippon Fine Chemical Co., Ltd, located at 1-1, 5-Chome, Umei, Takasago City, Hyogo, to conduct an inspection. The FDA investigator documented that your firm limited and/or refused an FDA inspection. Under the Federal Food, Drug, and Cosmetic Act (the FD&C Act), as amended by the Food and Drug Administration Safety and Innovation Act (FDASIA), section 707, 21 U.S.C. 351(j), your drugs are adulterated in that they have been manufactured, processed, packed, or held in an establishment where the owner or operator has limited inspection and refused inspection. We reviewed your responses dated January 5, 2016, April 25, 2016, the two letters from August 18, 2016, and correspondence from counsel dated September 14, 2016, in detail.

Your firm limited an inspection and/or refused to permit the FDA inspection as follows:

1. Barring access to areas
During the inspection, your firm limited the investigator's access to the quality control laboratory. The quality control manager directed employees to stand shoulder-to-shoulder, barring our investigator from accessing portions of the laboratory and the equipment used to analyze drugs for U.S. distribution.

2. Refusal to provide copies of documents
Your firm manufactures certain drugs for the Japanese and U.S. markets using the same equipment and processes, and divides lots for distribution between the two markets. During the inspection, our investigator reviewed complaints you received about your drugs from your

customers, including complaints that your drugs contained glass, hair, cardboard, metal, product discoloration, and a black spider. Your firm limited the inspection by refusing to provide FDA copies of these records.

3. Limiting photography

During the inspection, our investigator attempted to take pictures of the **(b)(4)** apparatus used to manufacture drugs for U.S. distribution. Your quality assurance manager impeded the inspection by preventing our investigator from photographing this piece of equipment.

Your firm was placed on Import Alert 99-32 on August 8, 2016.

The violations cited in this letter are not intended to be an all-inclusive list. You are responsible for investigating and determining the causes, for preventing their recurrence, and for preventing the occurrence of other violations.

Until FDA is permitted to inspect your facility and confirms compliance with CGMP, this office may recommend withholding approval of any new applications or supplements listing your firm as a drug manufacturer. In addition, shipments of articles manufactured at Nippon Fine Chemical Co, Ltd, Takasago City, into the United States are subject to refusal of admission pursuant to section 801(a)(3) of the FD&C Act, 21 U.S.C. 381(a)(3).

After you receive this letter, respond to this office in writing within 15 working days.

Send your electronic reply to CDER-OC-OMQ-Communications@fda.hhs.gov or mail your reply to:

LaKeesha M. Foster, Compliance Officer
U.S. Food and Drug Administration
White Oak Building 51, Room 4359