May 9, 2001

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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20857

RE: Docket No. 01D-0056

Dear Sir/Madam:

Provided below are comments on behalf of Novo Nordisk Pharmaceuticals, Inc. on the draft guidance for industry entitled, *Postmarketing Safety Reporting for Human Drug and Biological Products Including Vaccines*. The proposed regulation was published by the FDA in the Federal Register on March 12, 2001 (Vol. 66, No. 48: pp. 14391 – 14392).

Comment 1:

Lines 316 – 324 (IV. WHAT TO REPORT?, B. Data Elements to Include in a Postmarketing Individual Case Safety Report): The draft guidance states that "An applicant that is actively seeking information on an adverse experience should use verbal contact with the initial reporter of the adverse experience (e.g., in person, by telephone or other interactive means such as a videoconference). The applicant should not merely send the initial reporter a letter requesting information concerning the adverse experience".

In addition to what is described above, the agency should also include in this guidance an option for applicants to acquire written information from the initial reporter. It is not always feasible to contact the initial reporter for verbal information and some reporters find written communication more convenient. Having the option to obtain follow up information by letter should be retained.

Comment 2:

Lines 435 – 441 (V. TYPES OF REPORTS, B. 1. Timing of Postmarketing Periodic Reports): The draft guidance states that "Postmarketing periodic reports are required to be submitted to the FDA for each approved NDA, ANDA, and BLA and are due quarterly for the first 3 years after U.S. approval of the application and annually thereafter".

We agree with the requirements described in the ICH E2C guidance that periodic safety update reports should be prepared at 6-month intervals or based on multiples of 6 months. Therefore, we suggest a reporting requirement at 6-month intervals for the first 2 years of marketing then annually for the next 5 years. After five years the frequency of reporting may be reviewed. This suggestion would be similar to the EU and Japanese reporting requirements and would avoid duplication of effort to regulatory authorities.

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Comment 3:

Lines 898 – 902 (VI. SPECIAL REPORTING SITUATIONS, K. Multiple Suspect Products): The draft guidance states that "If a reportable adverse experience involves two or more suspect products from the same applicant, only one FDA Form 3500A should be completed. A report should be submitted to the NDA, ANDA, or BLA considered *most suspect* by the initial reported. If each product is equally suspect, the report should be submitted to the product first in alphabetical order".

Lines 922 – 928 (VI. SPECIAL REPORTING SITUATIONS, L. Suspect Drugs with Multiple NDAs or ANDAs by the same Applicant): The draft guidance states that "If an applicant receives a report for a drug and the specific application is identifiable, the report should be submitted to that application. However, if a drug substance has more than one application and it cannot be determined which of the approved applications is involved, the report should be submitted to the application for the drug product that was approved first and has the same general route of administration as the suspect drug substance. This would usually be the application with the lowest number."

The ICH guideline for industry published in the Federal Register on March 1, 1995 (60 FR 11284) entitled, *Clinical Safety Data Management: Definitions And Standards For Expedited Reporting* states that "To avoid ambiguities and uncertainties, an ADR that qualifies for expedited reporting with one presentation of a product (e.g., a dosage form, formulation, delivery system) or product use (e.g., for an indication or population), should be reported or referenced to regulatory filings across other product presentations and uses". The guidance also states "It is recommended that any adverse drug reactions that qualify for expedited reporting observed with one product dosage form or use be cross referenced to regulatory records for all other dosage forms and uses for that product. This may result in a certain amount of overreporting or unnecessary reporting in obvious situations (for example, a report of phlebitis on IV injection sent to authorities in a country where only an oral dosage form is studied or marketed). However, underreporting is completely avoided".

The proposed FDA Guidance for Industry requires one report for adverse events that involves two or more suspect drugs or drugs with multiple applications, however, the ICH guidance document recommends that in these situations adverse event reports should be reported or referenced across all presentations. We ask the agency to recommend which guidance should be followed.

Comment 4:

Lines 1332 – 1364 (XI. B. Submission of PSUR format for the Periodic Report): The draft guidance states that "Applicants can request a waiver of the requirement to submit postmarketing

periodic safety reports in the format described in the draft guidance. Instead, applicants can prepare these reports using the PSUR (Periodic Safety Update Report) format described in ICH E2C guidance". The Agency also recommends additional information described at Lines 1337 – 1364.

We agree with the agency to accept the PSUR format described in the ICH E2C guidance but without additional information described at Lines 1337 – 1364. We also suggest that the agency accept company core labeling as a reference document when preparing the PSUR.

Novo Nordisk Pharmaceuticals appreciates the opportunity to comment on these important regulations. If there are any questions please contact Dan Cugini, Senior Director, Product Safety Surveillance, Regulatory Affairs at (609) 987-5803.

Sincerely,

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