

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-273**

**APPROVABLE LETTER 1**



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-273

Organon, Inc.  
Attention: Albert P. Mayo  
Vice President, Regulatory Affairs  
375 Mount Pleasant Avenue  
West Orange, NJ 07052

Dear Mr. Mayo:

Please refer to your new drug application (NDA) dated July 21, 2000, received July 24, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Follistim<sup>®</sup> AQ (follitropin beta injection).

We acknowledge receipt of your submissions dated: November 19, December 6, 2004; February 8, March 10, 21(2), and 25, 2005.

The November 19, 2004 submission constituted a complete response to our July 17, 2003 action letter.

We completed our review of this application, as amended, and it is approvable. Before the application may be approved, however, it will be necessary for you to address the following deficiency:

Following the inspection (April 25, 2005 through May 3, 2005) of the Swords, County Dublin, Ireland manufacturing facility for this application, our field investigator conveyed deficiencies to the facility's representative. Satisfactory resolution of these deficiencies is required before this application may be approved.

Labeling discussions for this product will be deferred until all manufacturing facility deficiencies have been satisfactorily resolved. If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(b). The safety update should include data from all non-clinical and clinical studies of the drug under consideration regardless of indication, dosage form, or dose level.

1. Describe in detail any significant changes or findings in the safety profile.
2. When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:
  - Present new safety data from the studies for the proposed indication using the same format as the original NDA submission.

- Present tabulations of the new safety data combined with the original NDA data.
  - Include tables that compare frequencies of adverse events in the original NDA with the retabulated frequencies described in the bullet above.
  - For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.
3. Present a retabulation of the reasons for premature study discontinuation by incorporating the drop-outs from the newly completed studies. Describe any new trends or patterns identified.
  4. Provide case report forms and narrative summaries for each patient who died during a clinical study or who did not complete a study because of an adverse event. In addition, provide narrative summaries for serious adverse events.
  5. Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original NDA data.
  6. Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.
  7. Provide English translations of current approved foreign labeling not previously submitted.

Within 10 days after the date of this letter, you are required to amend this application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. If you do not follow one of these options, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

Under 21 CFR 314.102(d), you may request an informal meeting or telephone conference with this division to discuss what steps need to be taken before the application may be approved.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, call John Kim, R.Ph., J.D., Regulatory Health Project Manager, at (301) 827-3003.

Sincerely,

*{See appended electronic signature page}*

Daniel Shames, M.D.  
Director  
Division of Reproductive and Urologic Drug  
Products, HFD-580  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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/s/

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Margaret Kober  
5/17/05 03:07:08 PM  
signed for Dr. Shames