DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-747/S-008

Anesta Corporation
C/O Cephalon, Inc.
145 Brandywine Parkway
West Chester, PA 19380

Attention: Carol S. Marchione
Senior Director, Regulatory Affairs

Dear Ms. Marchione:

Please refer to your supplemental new drug application (NDA) dated August 8, 2001, received August 9, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Actiq (oral transmucosal fentanyl citrate).

We acknowledge receipt of your submissions dated September 21, November 9, and December 18, 2001, January 23, March 6, April 9, June 5, July 10, August 2, and December 18 and 19, 2002, January 10, 17 and 23, and February 13, 2003.

Your submission of January 17, 2003 constituted a complete response to our December 12, 2002 action letter.

This Supplemental new drug application provides for changes of the supplier, manufacturing process, and regulatory specifications of the drug substance; changes in the formulation, manufacturing process, facilities, regulatory specifications and test methods, container and labeling of the drug product.

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

The final printed labeling (FPL) must be identical to the submitted labeling (package insert, patient package insert, and immediate container and carton labels submitted July 10, 2002).

Please submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20-747/S-008. Approval of this submission by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitments in your submission dated February 13, 2003. These commitments are listed below.

1. Perform a study in which the holders will be leached using Purified Water as the extracting medium maintained at a temperature of(b)(4)---------- as per USP <661>. Materials leached from the holder will be identified to the extent possible and to the Agency's satisfaction.

Protocol Submission:	Within 1 month of the date of this letter
Study Start:	Within 1 month of the date of this letter
Final Report Submission:	Within 2 months of the date of this letter

2. Fully qualify the toxicological properties of the materials identified in the leachability study. This may be achieved by documenting data and rationale available in the literature or by performing a standard 3-month safety (toxicology) study in one species for each identified material, including a standard organ/tissue histopathologic evaluation.

   Timeline for the Literature review:

Protocol Submission:	N/A
Study Start:	Within 2 month of the date of this letter
Final Report Submission:	Within 3 months of the date of this letter

   Timeline for the 3-month safety study in one species:

Protocol Submission:	Within 4 month of the date of this letter
Study Start:	Within 4 month of the date of this letter
Final Report Submission:	Within 11 months of the date of this letter

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final 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 Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."

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

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 Kimberly Compton, Regulatory Project Manager, at (301) 827-7432.

Sincerely,

{See appended electronic signature page}

Bob Rappaport, M.D.
Acting Director
Division of Anesthetic, Critical Care, and
Addiction Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

Bob Rappaport

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