DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MAY 27 1998

TRANSMITTED BY FACSIMILE

Patricia J. Richards
Director, Regulatory Affairs
Anesta Corp.
4745 Wiley Post Way, Suite 650
Salt Lake City, Utah 84166

Re:
Actiq (oral transmucosal fentanyl citrate, OTFC)
MACMIS ID#6336

Dear Ms. Richards:

This letter concerns the materials submitted by Anesta Corp. (Anesta) in response to an inquiry by the Division of Drug Marketing, Advertising, and Communications (DDMAC) concerning Anesta's dissemination of materials relating to Actiq (oral transmucosal fentanyl citrate, OTFC).

Based on a review of the materials Anesta has disseminated concerning Actiq, DDMAC has concluded that Anesta is making promotional representations concerning the efficacy and safety of Actiq. The regulations promulgated pursuant to the Federal Food, Drug, and Cosmetic Act (Act), at 21 CFR §312.7 state, among other things, that an investigational new drug may not be promoted as being safe and effective for the uses under investigation. The regulation distinguishes promotional representations from the full exchange of scientific information concerning the drug that are limited to presentations of the scientific findings of the clinical research. As noted below, Anesta's representations are promotional in nature and exceed the presentation of scientific findings.

Press Releases

Specifically, Anesta is disseminating press releases that make misleading promotional representations concerning the efficacy of Actiq. In a press release dated May 20, 1997, Anesta stated that Actiq provided statistically significant better pain relief scores than the patients' previous breakthrough pain medication. However, these statements were based upon open-label, dose-ranging studies for Actiq that were not designed to evaluate the efficacy of Actiq compared to other oral analgesics in the treatment of breakthrough pain, but were designed to determine the tolerability of select doses of Actiq.

Anesta also misrepresented the conclusion of its open-label, extension study in this press release. Anesta states that "Actiq remained effective over time and patients safely used the product in multiple stages of disease progression." However, this extension study was not designed to evaluate the long-term efficacy of the product.

Additionally, Anesta misrepresented the adverse events associated with the use of Actiq. In the May 20, 1997, press release, Anesta stated that the "[s]ide effects observed in all studies were those typical of potent opioid analgesics and did not limit the use of Actiq in this patient population." Anesta failed to disclose the risk of the following adverse events associated with the use of Actiq: asthenia, fever, headache, pain, constipation, diarrhea, nausea, vomiting, peripheral edema, dizziness, somnolence, and dyspnea. This material omission clearly misrepresents the safety of Actiq.

In a press release dated August 18, 1997, Anesta made the claim that "Actiq is the first oral analgesic product ever studied for breakthrough pain that matches the time to produce pain relief with the relatively short time of onset and duration of breakthrough pain." Similarly, in a July 25, 1996, press release, Anesta stated that "Actiq is the first oral product that matches rapid onset of pain relief to the time course associated with episodes of breakthrough pain ...." These statements are beyond the presentation of the findings of clinical research and make promotional representations of the safety or efficacy for a use that Actiq is under investigation.

Investigator Representations

Dr. Paul Coluzzi, an investigator for Anesta, presented statements about the safety and efficacy of Actiq in a promotional context. In the television program, *Orange County Online*, Dr. Coluzzi stated that with Actiq, patients may not get the "dopey effect" associated with other narcotic analgesics. However, this statement contradicts the findings from the clinical trials where a high percentage of patients reported somnolence with the use of Actiq.

Requested Actions

Anesta should discontinue use of all statements that represent that Actiq is safe or effective in the treatment of breakthrough pain, such as those presented on its website. Anesta should submit a written statement of Anesta's intent to comply with the discontinuation of these materials described above by June 10, 1998.

If you have any questions, please contact the undersigned by facsimile (301) 594-6771 or by written communication at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, 5600 Fishers Lane, HFD-40, Rm. 17B-20, Rockville, MD 20857.

In all future correspondence regarding this matter, please refer to MACMIS ID #6336, in addition to the NDA number.

Sincerely,

Thomas W. Abrams, R.Ph., M.B.A.
Branch Chief
Division of Drug Marketing,
Advertising and Communications