DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

**TRANSMITTED BY FACSIMILE**

Sunita Sethi
Director, Regulatory Affairs
Scios Inc.
1900 Charleston Road
Mountain View, CA 94043-1218

**RE: NDA # 20-920**
**Natrecor® (nesiritide) for Injection**
**MACMIS ID # 15669**

Dear Dr. Sethi:

The Division of Drug Marketing, Advertising, and Communications (DDMAC) of the U.S. Food and Drug Administration (FDA) has reviewed a mouse pad (P0710400) and pen (P0710500) submitted under cover of Form FDA-2253 by Scios Inc. (Scios). These pieces are violative because, although they have the form of reminder labeling, which is exempted by regulation from the requirements under the Federal Food, Drug, and Cosmetic Act (Act) for the disclosure of risk and other information, for the reasons set forth below, we have determined that your promotional materials are not appropriate reminder labeling. Therefore, the pieces misbrand Natrecor® in violation of the Act, 21 U.S.C. 352(f)(1), 352(a), & 321(n) and FDA's implementing regulations, 21 CFR 201.100(f) & 1.21, as they fail to include, among other things, the drug product's indication as well as information addressing the risks associated with Natrecor.

**Background**

The INDICATIONS AND USAGE section of the approved product labeling (PI) for Natrecor states:

> Natrecor (nesiritide) is indicated for the intravenous treatment of patients with acutely decompensated congestive heart failure who have dyspnea at rest or with minimal activity. In this population, the use of Natrecor reduced pulmonary capillary wedge pressure and improved dyspnea.

Natrecor is associated with numerous risks. For example, the PI contains a warning for patients suspected of having, or known to have, low cardiac filling pressures. The PI also contains precautions regarding administration to patients for whom vasodilating agents are not appropriate, azotemia in susceptible individuals, hypotension, and use in older individuals. Furthermore, the Adverse Reactions section of the PI presents 30-day and 180-day mortality data collected from clinical studies. In seven clinical studies, through 30 days,

5.5% of patients in the Natrecor treatment group died as compared to 4.3% in the active control group.

**Inappropriate Reminder Labeling/Omission of Indication and Risk Information**

According to FDA regulations, reminder labeling is labeling that calls attention to the name of the drug product, but does not include its indication or dosage recommendations or other representations or suggestions relating to the drug product. See 21 CFR 201.100(f). Although the promotional materials cited above do not state the drug product's indication, the image presented on the materials nevertheless makes a representation or suggestion about Natrecor. Specifically, the mouse pad and pen present an image of a distressed older male patient in a hospital bed. The patient is submerged up to his shoulders in water and is connected to a heart monitor and a nasal cannula.

Simply put, the image evokes the concept of a sedentary hospital patient drowning. The combination of this image with the Natrecor logo that is imprinted on the promotional materials suggests that Natrecor is indicated for seriously ill patients who have difficulty breathing while at rest because of fluid accumulation within the lungs, a suggestion that is consistent with Natrecor's indication, in part (see background section). The image, in conjunction with the Natrecor logo, suggests that Natrecor treatment would be appropriate for this patient and others like him. Reminder pieces may not include, among other things, representations or suggestions concerning effectiveness or patient population. Because this image makes these implications, the pieces cited above are not considered reminder labeling and appropriate indication and risk information need to be included. However, these pieces fail to include this information.

**Conclusion and Requested Action**

For the reasons discussed above, the promotional materials misbrand Natrecor under the Act, 21 U.S.C. 352(f)(1), 352(a), & 321(n) and FDA's implementing regulations. 21 CFR 201.100(f) & 1.21.

DDMAC requests that Scios immediately cease the dissemination of violative promotional materials for Natrecor such as those described above. Please submit a written response to this letter on or before November 21, 2007, stating whether you intend to comply with this request, listing all violative promotional materials for Natrecor such as those described above, and explaining your plan for discontinuing use of such materials.

Please direct your response to me at the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising, and Communications, 5901-B Ammendale Road, Beltsville, MD 20705, facsimile at 301-796-9878. In all future correspondence regarding this matter, please refer to MACMIS ID # 15669 in addition to the NDA number. We remind you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Natrecor comply with each applicable requirement of the Act and FDA implementing regulations.

Sincerely,

*{See appended electronic signature page}*

Lisa M. Hubbard, R.Ph.
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

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

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/s/

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Lisa Hubbard
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