



Department of Health and Human Services

Public Health Service
Food and Drug
Administration
Seattle District
Pacific Region
22201 23rd Drive SE
Bothell, WA 98021-4421
Telephone: 425-486-8788
FAX: 425-483-4996

July 26, 2010

**CERTIFIED MAIL
RETURN RECEIPT REQUESTED**

In reply refer to Warning Letter: SEA 10-27

Mr. Bill Evan McAllister, President
Nitrox, Inc.
2706 164th Street Southwest
Lynnwood, Washington 98037-7808

WARNING LETTER

Dear Mr. McAllister:

During our March 22, 2010 through April 19, 2010 inspection of your manufacturing facility located at 2706 164th Street Southwest, Lynnwood, Washington 98037, investigators from the Food and Drug Administration (FDA) identified significant violations of Current Good Manufacturing Practice (CGMP) regulations for Finished Pharmaceuticals, Title 21, Code of Federal Regulations, Parts 210 and 211. These violations cause your drug products to be adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. § 351(a)(2)(B)] in that the methods used in, or the facilities or controls used for, their manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with CGMP.

Specific violations observed during the inspection include, but are not limited to, the following:

1. Your firm does not have, for each batch of drug product, appropriate laboratory determination of satisfactory conformance to final specifications for the drug product, including the identity and strength of each active ingredient, prior to

release [21 C.F.R. § 211.165(a)]. For example, your firm does not perform finished product testing on filled cylinders of Dolonox, a 50% USP Nitrous Oxide and 50% USP Oxygen compressed medical gas mixture, prior to release. From September 2003 to May 2009, your firm released **(b)(4)** high-pressure cylinders of Dolonox without testing the product for identity and strength.

2. Your firm has not established scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that drug products conform to appropriate standards of identity, strength, quality, and purity [21 C.F.R. § 211.160(b)].

For example, your firm has not established appropriate written procedures to test liquid Nitrogen NF for assay and limit of Oxygen. Your firm's only written Standard Operating Procedure (SOP) for testing liquid Nitrogen NF specifies that the Splitter Test is to be used for identity testing. The Splitter Test is not considered a scientifically sound test method. Further, during the inspection, you told our investigators that the standard practice for assay testing of liquid Nitrogen NF was to use **(b)(4)** handheld analyzers. However, you could not provide documentation of **(b)(4)** handheld analyzer testing. Please note that the FDA does not consider the **(b)(4)** handheld analyzer to be an acceptable test method for the assay of liquid Nitrogen NF because your firm has not demonstrated that it is equivalent to the monograph test method for assay.

3. Your firm did not prepare batch production and control records for each batch of drug product produced, including documentation that each significant step in the manufacture, processing, packing, or holding of the batch was accomplished [21 C.F.R. § 211.188(b)]. For example, your firm manufactures Dolonox without producing batch production and control records to document performance of the necessary cylinder prefill checks such as visual examination, dead ring test for corrosion, prefill odor check, and vacuum evacuation.

4. Your firm does not have adequate written procedures for production and process controls designed to assure that the drug products you manufacture have the identity, strength, quality, and/or purity they purport or are represented to possess [21 C.F.R. § 211.100(a)]. For example, your firm has not established written procedures for the manufacturing, testing, and distribution of Dolonox.

5. Your firm did not have drug product production and control records reviewed and approved by a Quality Control Unit (QCD) to determine compliance with all established, approved written procedures before a batch is released or distributed [21 C.F.R. § 211.192]. For example, your firm's QCU did not review or approve batch production records for liquid Nitrogen NF distributed between November 24, 2009, and February 19, 2010.

6. Your firm did not follow written production and process control procedures in the execution of the various production and process control functions [21 C.F.R. §

211.100(b)]. For example, SOP "Medical Gas Supplier Audit Report" requires your Firm to audit your medical gas supplier every However, your firm has not conducted audits of your supplier of liquid Nitrogen NF.

Additionally, under section 510 of the Act [21 U.S.C. § 360], manufacturers of drug products are required to annually register with the FDA. Our records indicate that you have not registered your establishment since April 22, 2008. Therefore, liquid Nitrogen NF and Dolonox are misbranded according to section 502(o) [21 U.S.C. § 352] in that they were manufactured in an establishment not registered as required under section 510 of the Act [21 U.S.C. § 360].

You should take prompt action to correct the violations cited in this letter. Failure to promptly correct these violations may result in legal action without further notice, including, without limitation, seizure and injunction. Other federal agencies may take this Warning Letter into account when considering the award of contracts. Additionally, FDA may withhold approval of requests for export certificates, or approval of pending new drug applications listing your facility, until the above violations are corrected. FDA may reinspect to verify corrective actions have been completed.

Please note that several of the violations described above were cited in FDA-483s issued at the conclusion of the October 2003 and March 2000 inspections. The most recent inspection found that your firm has failed to implement sufficient corrective actions and many of the same violations persist.

In addition, you admitted to our investigators that your firm does manufacture and distribute Dolonox. In your response, please list which specific medical gas products your firm intends to manufacture and how you plan to meet FDA's regulations for these medical gas drug products. Your response should also state if your firm no longer manufactures or distributes the drug product(s) manufactured at this facility, and if your firm destroyed or removed any of your drug product(s) from the market following the most recent inspection. Please also provide the date(s) and reason(s) your firm performed such action(s).

The violations cited in this letter are not intended to be an all-inclusive list of deficiencies that exist at your facility. You are responsible for investigating and determining the causes of the violations identified above and for preventing their recurrence and the occurrence of other violations. It is your responsibility to assure compliance with all requirements of federal law and FDA regulations.

Within fifteen working days of receipt of this letter, please notify this office in writing of the specific steps you have taken to correct violations. Include an explanation of each step being taken to prevent the recurrence of violations and copies of supporting documentation. If you cannot complete corrective action within fifteen working days, state the reason for the delay and the date by which you will have completed the correction.

Your reply should be sent to the following address: Food and Drug Administration, Seattle District Office, 22201 23rd Drive SE, Bothell, Washington 98021-4421, to the attention of Brenda L. Reihing, Compliance Officer. Should you have any questions concerning this letter, you can contact Ms. Reihing at (425) 483-4899.

Sincerely,

/S/

Charles M. Breen
District Director