SAMPLE WARNING LETTER CITATIONS

9. Failure to verify the device design confirms that the design output meets the design input requirements, as required by 21 CFR 820.30(f). For example, your shelf-life for the CycleSure™ Biological Indicator Stability of the Bst SCBI is report RPT 1608-A dated 11/12/98. This document did not have charts/strips documenting temperature control parameters in the Device History Files for spore crops lot # [redacted] and # [redacted]. Furthermore, spore crop lot# [redacted] was replaced with lot [redacted]. You state the replacement was due to a new formulation but we found no investigation of why lot # [redacted] at [redacted] month stability reported low D-values.

Failure to establish and maintain procedures to control the design of the device to ensure that specified design requirements are met [21 CFR 820.30(a)(1)].

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

October 15, 2003 W/L 04-04

Barry M. Tydings
President/CEO
Drug Free Enterprises
5302 Derry Ave., Ste A
Agoura Hills, CA 91301

Dear Mr. Tydings:

We are writing to you because an investigator from the United States Food and Drug Administration (FDA) conducted an inspection of your facility located in Agoura Hills, California between January 21 and February 11, 2003, which determined that your firm is a specification developer, and by regulation [Title 21, Code of Federal Regulations (CFR), Section 807.3(d)(3)] a manufacturer of drugs-of-abuse test kits. Information collected during the inspection revealed serious regulatory problems involving your DRUGCHECK NO STEP-ONSITE drugs-of-abuse test kits. Also, during our inspection between June 17 and 30, 2003 additional serious regulatory problems involving your consumer study for your drugs-of-abuse kits were revealed.

Under a United States Federal law, the Federal Food, Drug and Cosmetic Act (the Act), these kits are considered to be medical devices because they are intended to be used to diagnose or treat a medical condition (Section 201(h) of the Act).

Our inspections revealed that your devices are adulterated under section 501(h) of the Act, in that the methods used in, or facilities or controls used for, the manufacture, packing, storage, or installation are not in conformance with the Current Good Manufacturing Practice (CGMP) requirements for medical devices which are set forth in the Quality System (QS) regulation, as specified in Title 21, CFR, Part 820. Significant deficiencies observed include, but are not limited to the following:

- Your firm lacks adequate design controls. Specifically, you do not have documentation that your marketed product was developed following the approved design or that all subsequent changes made in your drugs-of-abuse test kits have been adequately defined and evaluated. Nor do you have documentation of complete manufacturing specifications for your contract manufacturer. [Title 21 CFR 820.30 and 820.3(k)]
- A quality system has not been fully implemented and maintained at all levels of the organization. Specifically, your quality policy and objectives and your quality plan have not been fully established. [Title 21 CFR 820.20]
- Document control procedures have not been fully implemented and maintained. Specifically, the device master records for product codes 60300, 60500, 65500-4 and 60505 are incomplete, change control records are not maintained on-site and complaint documents received by field representatives are not maintained at the firm. [Title 21 CFR 820.181 and 820.198]
- Your device history records are inadequate. Specifically, you are not maintaining acceptance records that demonstrate your drugs-of-abuse test kits are manufactured in accordance with the

approved device master record. [Title 21 CFR 820.184]

- Failure to establish and maintain procedures to ensure all purchased or otherwise received product and services conform to specified requirements. Specifically, your firm has not evaluated and documented the abilities of your supplier and consultant to meet specified requirements, including quality requirements and your firm does not have a complete written contract with the contract manufacturer who produces your drugs-of-abuse kits or the consultant who oversees your firm's quality system. [Title 21 CFR 820.50]

Additional CGMP deficiencies were observed and reported during our January 21 - February 11, 2003 inspections. Your written response of March 5, 2003 provided documentation of correction of your lack of written procedures for CAPA, complaints and required audits. Review of the supporting documentation submitted for these corrections revealed several are incomplete, do not have implementation dates, contain minor errors and conflicting time periods for your Management Review. We strongly suggest you re-evaluate your written procedures and correct these deficiencies.

The Act requires that manufacturers of medical devices obtain marketing clearance for their devices from FDA before they may be offered for sale. This helps protect the public health by ensuring that newly introduced medical devices are safe and effective or substantially equivalent to other devices already legally marketed in this country. Furthermore, once marketing clearance is obtained, products must conform to the approved application.

Two of your kits (Product Codes 60900 and 60903) are adulterated under section 501(f)(1)(B) and misbranded under section 502(o) in that they include testing for tricyclic antidepressants. Your cleared pre-market notification (K012390) does not include testing for this drug category. Products including testing for tricyclic antidepressants are unapproved, may not be legally marketed, and should be withdrawn from the market. You must submit a new 510(k) and obtain FDA clearance before you can make such a claim.

At least one of your kits (Product Code 60903) is also adulterated under section 5o1(f)(1)(B) and misbranded under section 502(o) in that it includes testing for opiates at a cut-off level of 300 ng/ml. Your cleared pre-market notification (K012390) identifies an opiate cut-off level of 2000 ng/ml. Again, products including testing for opiates at a cut-off level of 300 ng/ml are unapproved, may not be legally marketed, and should be withdrawn from the market. You must submit a new 510(k) and obtain FDA clearance before you can make such a claim.

Your DRUGCHECK NO STEP-ONSITE drugs-of-abuse test kits are misbranded within meaning of Section 502(b) of the Act in that the devices are in package form and their labels fails to contain the name and address of the manufacturer or distributor.

This letter is not intended to be an all-inclusive list of violations. As a manufacturer of medical devices it is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the two FDA-483s, Inspectional Observations, issued at the close of our inspections may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating

and determining the causes of the violations identified by the FDA. You also must promptly initiate permanent corrective and preventative action on your Quality System.

You should know that these serious violations of the law may result in the FDA taking regulatory action without further notice to you. These actions include, but are not limited to, seizing your product inventory, obtaining a court injunction against further manufacturing of the product, or assessing civil money penalties. Also Federal agencies are informed about the Warning Letters we issue, such as this one, so that they may consider this information when awarding government contracts.

Additionally, we note that you have changed the name of the drug-of-abuse test kits cleared in the original 510(k) from Drug Free Enterprises NexStp Drug Check to DRUGCHECK NO STEP-ONSITE. While FDA was reviewing the 510(k) for this device we advised you that we found your proposed "NO STEP" name to be misleading. Your device received FDA clearance after you advised that the name of this device would be changed to NexStp Drug Check. Now you have gone back to using a name which the Agency found to be misleading.

It is necessary for you to take action on this matter now. Please let this office know, in writing, what steps you have taken to correct the problems within fifteen (15) working days of receipt of this letter. We also ask that you provide an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within fifteen (15) working days, state the reason for the delay and the time within which the corrections will be completed. Also include copies of any available documentation demonstrating

that corrections have been made. If you have any questions or need clarification regarding this letter, you may contact Barbara Rincon, Compliance Officer at telephone number (949) 608-4439.

Products that are adulterated and/or misbranded should be removed from the market via a voluntary recall. For information and assistance with the recall of your products in distribution you may contact our Recall Coordinator, Craig Hoover at (949) 798-7730.

You should know and understand that there re many FDA requirements pertaining to the manufacture and marketing of medical devices. You may obtain general information about all of FDA's requirements for manufacturers of medical devices by contacting the

Center for Devices and Radiological Health's Division of Small Manufacturers, International, and Consumer Assistance at I-800-638-2041 or through the Internet at www.fda.gov.

Your reply should be directed to:

Acting Director, Compliance Branch
U.S. Food & Drug Administration
19701 Fairchild
Irvine, CA 92612

Sincerely,
/s/
Alonza Cruse
District Director

Failure to implement procedures to control the design process of a device as required by 21 CFR 820.30(a). Specifically,

- design validation conducted to support the stability claim for Enzymatic Homocysteine Assay was not performed on reagents in kit configuration under the 510(k) for that device.
- no design history file was established for the Homocysteine ELISA Assay.
- management failed to approve each design milestone prior to proceeding to the next milestone for the Enzymatic Homocysteine Assay as specified in the written procedure.
- design input requirements for acceptance criteria for sensitivity of the Enzymatic Homocysteine Assay was not documented.

We are in receipt of your May 10, 2005 response to the Form FDA-483, Inspectional Observations, issued to you at the close of the most recent inspection. While your response commits to correction of your documentation, your response is silent as to any corrective action planned to address the lack of a thorough investigation of complaints and RMAs to determine if additional product may be adulterated and / or if a root cause of quality shortcomings can be identified. Additionally, your response does not clearly detail nor provide supporting documentation of corrections. While written procedures are required, it is of far greater importance

that appropriate action be taken with respect to any and all potential quality issues. You should provide written commitment of your planned actions with respect to investigation of RMAs, complaints and other potential quality concern data sources.

Our inspection disclosed that your Esprit ventilator device is adulterated within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation do not conform with the Good Manufacturing Practice (GMP) requirements set forth in the Quality System Regulation, Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

1. The design validation activities conducted for the Esprit ventilator software version 3.2 failed to ensure that the device conforms to the defined user / patient needs and intended uses [21 CFR 820.30]. Specifically:

- There was no documented evidence that any integration and throughput testing of the device was performed to eliminate software communication problems prior to the final acceptance of the design of the device.
- Your design review procedures were not properly defined to ensure that the participants at each design review included proper representatives of all functions concerned with design stage. Our investigator was advised that the decision to conduct integration and throughput testing rested with management only.
- There was no risk assessments performed to ensure that any changes made in the device to eliminate or minimize any hazards associated with

tom and separated check valves did not introduce any new hazards or adversely affect the device.

- Design verification did not confirm that the design output meets the design input requirements. Specifically, design verification and validation activities associated with the changes in the check valves to eliminate and minimize torn and separated check valves was only conducted on an exhalation check valve and no such activities were conducted on the inspiration check valves.

2. The Esprit Throughput Testing Package, a written software test procedure for the throughput testing that is used in conducting software integration testing, was found in use even though it had not been released, controlled, or approved in accordance with written document control procedures [21 CFR 820.40(a)].

We have also reviewed your firm's July 29, 2003 letter. We believe that item 6.2.3 on page 9 of the Adverse Event Reporting document included with that letter could be confusing, does not accurately reflect the definition of a MDR Serious Injury, and could result in unreported serious injuries. Also, all references in your letter and attached documents to distributor MDR reporting requirements should be deleted and replaced with the distributor complaint file requirements of 21 CFR 803.18(d) (1), (2), & (3), because the former requirement was revoked by Section 213(a) of the Food and Drug Administration Modernization Act [65 Federal Register 4112, 4113 (Jan. 26, 2000)].

Given the facts provided in this letter, we believe a regulatory meeting between your firm and FDA is warranted to discuss the corrective and preventative actions taken since the completion of our inspection.

We have identified the following concerns that we wish to discuss with you at the meeting:

- Design procedures and design history for the Esprit ventilator, especially software changes made to the device;

Our inspection disclosed that the devices are adulterated within the meaning of Section 501(h) of the Act [21 U.S.C. 351(h)], in that the methods used in, or the facilities or controls used in, repackaging and relabeling your devices are not in conformance with the Good Manufacturing Practice (GMP) requirements under the Quality System Regulations, as specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

1. Failure to establish, maintain, and control a quality system that is appropriate for specific devices manufactured [21 CFR 820.20]. For example,

- Management with executive responsibility has not established a policy and objectives for, and commitment to, quality, as required by 21 CFR 820.20(a).
- No quality plan defining the quality practices, resources, and activities relevant to devices that are designed and manufactured has been established or implemented, as required by 21 CFR 820.20(d).
- No quality system procedures and instructions have been established and implemented, as require by 21 CFR 820.20(d).
- No procedures for conducting management reviews, as required by 21 CFR 820.20(c).
- No management representative has been appointed or documented to ensure that quality system requirements are effectively established and maintained and reporting on the performance

of the quality system activities to management with executive responsibility, as required by 21 CFR 820.20(b)(3).

7. Your firm failed to establish procedures to control the design process of the device and your design history file does not demonstrate the device design was developed following an approved design plan and design control requirements as required by 21 CFR 820.30(a) & (j). Your firm failed to document all appropriate areas of design control including design plan, design review, design validation, and risk analysis (FDA 483, Item #s 6 & 7).

10. Your firm failed to establish and maintain procedures to control the design of the device in order to ensure that specified design requirements are met as required by 21 CFR 820.30(a). Your firm failed to establish any design control procedure (FDA 483, item #11A).

11. Your firm failed to identify, document, validate/verify, review and approve design changes prior to implementation as required by 21 CFR 820.30(i). Revised labeling included claims that the Instrument Pre-Soak was a high level disinfectant without completion of any design validation or risk analysis and no pre-market notification was submitted to FDA (FDA 483, item # 11B).

9. Failure to establish and maintain a Design History File (DHF) for each type of device, as required by 21 CFR 820.30(j). No risk analysis was documented for latex and blood control products (FDA 483; Item #6).

3. Your firm designed the device, but failed to establish any design control procedures or to maintain a Design History File (DHF) for the identification, documentation,

validation or where appropriate verification, review and approval of design changes prior to the implementation as required, 21 CFR 820.30(i). Your firm changed vendors of the pump and has no documentation that the current pump meets the specifications of the original pump manufacturer. In addition, an O-ring on the electric pump was changed without following any procedures for such a change. As a result, there was no evaluation conducted, documented or approved to ensure the change in the pump or O-rings did not have any effect on the safety or effectiveness of the device.

Additionally, no external penile rigidity devices to date have received marketing clearance from FDA for claims found in your advertising brochure, your web sites at http://www.impoaid.com and http://www.revivesystem.com, and labeling, including the information panels on the device cartons and user manual, that include being effective for improving blood flow to the penis, allowing many men to achieve normal erections on their own, removing plaques and cholesterol building up, and to open penile arteries and possibly restore them to their natural elasticity. The Condom Lot ring claims state "holds condom secure" and "keeps the condom securely in place." The trade name "Condom Lot" also implies this function.

These claims significantly modify the intended use(s) of the devices, as defined under 21 CFR 801.4, and would require the submission and prior clearance of a new 510(k) as required by 21 CFR 897.81(a)(3)(ii). In addition, with these claims, the vacuum erection systems are adulterated within the meaning of section 501(f)(1)(B) of the Act in that they are Class III devices under section 513(f), and do not have an approved application for premarket (PMA) in effect pursuant to section 515(a), or

an approved application for investigational device exemption (IDE) under section 520(g).

The vacuum erection systems are also misbranded within the meaning of section 502(o) of the Act, in that a notice or other information respecting the modification in the intended use of the devices was not provided to FDA as required by 21 CFR 807.81 (a)(3(ii)), and the devices were not found to be substantially equivalent to a predicate device.

Your web site material also states “F.D.A. registered equipment” and “It is a medical grade F.D.A. registered product.” Title 21 CFR, Part 807.39 specifically provides that [any] representation that creates an impression of official approval because of registration [of a device establishment] or possession of a registration number is misleading and constitutes misbranding.” The registration of your establishment is just one requirement that must be met for you to conduct the type of activities in which are are engaged. Registration is also not a determination of FDA approval as to the status of the device, as clearly stated in 21 CFR 807.35(c).

Any reference of regulatory compliance, whether for registration or any other statutory requirement, provided for under the authority of the Federal Food, Drug, and Cosmetic Act (the Act) or promulgated pursuant to the Act, may not be used to denote FDA approval or compliance.

Your vacuum erection systems are also misbranded within the meaning of section 502(t)(2) in that your firm failed or refused to furnish material or information required by or under section 519 respecting the device and 21 CFR Part 803 (Medical Device Reporting regulation). Specifically, your firm failed to develop, maintain, and implement written MDR procedures and

failed to establish and maintain MDR event files, which are material and information required under section 519 and 21 CFR 803.17 and 803.18. Under 21 CFR 803.17, written MDR procedures must include the following requirements: