



DEPARTMENT OF HEALTH & HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
FOOD AND DRUG ADMINISTRATION

M426N

PHILADELPHIA DISTRICT

900 U.S. Customhouse  
2nd and Chestnut Streets  
Philadelphia, PA 19106

Telephone: 215-597-4390

**WARNING LETTER**

June 25, 1998

98-PHI-26

CERTIFIED MAIL  
RETURN RECEIPT REQUESTED

Douglas R. Spencer, Vice President/General Manager  
Maternal/Infant Care  
Hill-Rom Air-Shields  
330 Jacksonville Road  
Hatboro, PA 19040

Dear Mr. Spencer:

From January 26 through March 26, 1998, Philadelphia District Investigators John S. Shea and Michael J. Nerz conducted an inspection of your medical device manufacturing facility. The Isolette® C2000 Infant Incubators (C2000) you manufacture are medical devices within the meaning of Section 201(h) of the Federal Food, Drug, and Cosmetic (FD&C) Act and, as such, are subject to the requirements of *Title 21 Code of Federal Regulations (21 CFR)*.

On April 24, 1998, we received your letter dated April 17, 1998 which was sent in response to the form FDA 483 issued to you at the conclusion of the above-referenced inspection. We have carefully reviewed this response and apologize for the length of time spent performing this review and for the delay in issuing this letter. However, our review finds that the response does not satisfactorily address all of the FDA 483 observations as described below. As a result, we find that the C2000 devices are adulterated within the meaning of Section 501(h) of the FD&C Act in that the methods used in, or the facilities or controls used for, their manufacturing, packing, storage, or installation are not in conformance with current good manufacturing practice (CGMP) regulations codified at 21 CFR Part 820, as follows:

1. Failure to validate all automated systems used in conjunction with manufacturing or quality systems in that the [REDACTED] automated simulator, which is used during incoming inspection of the controller, sensor module, and scale components of the C2000 device, is not validated. (FDA 483 Observation 1)

Page 2  
June 25, 1998  
Douglas R. Spencer

2. Failure to assure that all inspection and testing equipment is suitable for its intended purposes and is capable of producing valid results. The inspection revealed that the [REDACTED] automated simulator test has not been updated to keep current with hardware and software changes made to the C2000 device. (FDA 483 Observation 2)

We acknowledge the fact that, on May 8, 1998, your firm voluntarily ceased distributing the C2000 in response to our ultimate determination that these devices represent a moderate risk of serious adverse health consequences and that your firm initiated a Class II recall (consisting of user notification) of devices currently on the market. As representatives from this office have previously conveyed to you and other members of your staff, we consider this recall an interim fix until outstanding CGMP deficiencies can be resolved.

We also acknowledge your efforts to validate the software associated with the [REDACTED] automated simulator. However, the inspection revealed that the [REDACTED] has both software and hardware components. These hardware components also require validation. In addition, we are unable to fully review the proposed additional production/quality control (QC) tests discussed in the response because the information provided does not include a diagram of the equipment and instrument set-up. In addition, it appears that these additional tests may also depend upon a validated [REDACTED] simulator. If you intend to use these tests when you resume shipping this device, then we request that you provide us with the test set-up and also clarify whether or not the additional tests use the [REDACTED] simulator.

3. Failure to assure that all production processes provide for the device to conform to its specifications in that there is no justification or rationale for not including the check for "safe system shutdown" in the C2000 manufacturing process. (FDA 483 Observation 9)

We find that your response does not satisfactorily address this observation for several reasons. First, your response states that you believe that your controller vendor conducts an appropriate verification of the watchdog circuitry, yet our inspection revealed, and your firm has acknowledged, that these controllers are associated with a [REDACTED] failure rate at incoming inspection. Second, the information from the vendor that you included in your response indicates that the watchdog circuit is not tested on a system level, and we could not identify where in the controller testing procedures provided that this circuit is verified. Third, information provided in your response regarding the low feasibility of testing the watchdog circuit at Air-Shields because the test is potentially destructive conflicts with information provided to the investigator during the inspection, which was that this test would be easy to do.

Please identify how the watchdog circuit is tested within the production cycle.

4. Failure to investigate a complaint regarding the possible failure of a device to meet any of its specifications in that there was no failure investigation into a complaint reported 12/2/96

Page 3  
June 25, 1998  
Douglas R. Spencer

regarding the humidity in a C2000 dropping by 10% every one hour and then recovering.  
(FDA 483 Observation 15)

The inspection revealed that no investigation into the potential cause of this problem, which involves the controller, was done other than to review the complaints received to date and to determine that this complaint was the only one of its type. Your response does not adequately address this observation in that you do not indicate whether or not an investigation was done and, if an investigation was not conducted, the reason why.

5. Failure to include the primary identification label and labeling used for each production unit in the Device History Record (DHR). (FDA 483 Observation 21)

We acknowledge your response to this observation which indicates that information appearing on the device labeling also appears in the DHR. However, the requirement that the DHR include the primary identification label and labeling stems from the agency's belief that increased control over product labeling is necessary as a result of recalls associated with mislabeled product. The agency recognizes that some devices can have many different labels attached to it and, in order to reduce the potential burden associated with this regulation, only requires that the primary identification label and labeling be included in the DHR. The agency also believes that this requirement, along with the regulations regarding labeling controls, will reduce the number of recalls associated with mislabeled devices.

6. Failure to include, or reference the location of, information regarding component specifications in the Device Master Record (DMR) relative to the C2000 controller. (FDA 483 Observation 23)

We acknowledge your response to this observation but note that the specific *Federal Register* comments you cite pertain to the purchasing controls regulation. Further, those comments appear to pertain to components purchased off-the-shelf, usually through a distributor. We do not consider the C2000 controller to be an off-the-shelf component as it was designed per Air-Shields' specifications and is manufactured for Air-Shields' use in the C2000. We are aware of the circumstances surrounding Air-Shields' relationship with [REDACTED] nevertheless, we expect that the C2000 DMR contain the information required under 21 CFR § 820.181 for components.

Also, we have the following comments with respect to your responses to the specific FDA 483 observations noted below:

Page 4  
June 25, 1998  
Douglas R. Spencer

FDA 483 Observation 5

We have reviewed the revised standard operating procedure (SOP) included with your response and note that Section 5.4.3. requires the Manager of Quality Engineering to review and document his/her acceptance or rejection of the vendor's response to Air-Shields' Inspection Report. Please be advised that 21 CFR § 820.100(a)(3) requires, among other things, that you identify the actions needed to correct and prevent recurrence of non-conforming product. If this is not already addressed in another SOP, then we recommend that this section include information to that effect.

FDA 483 Observation 7

Please confirm who will be responsible for signing off on the "QC Approved By" line of the QC Product Discrepancy Report. Also, we note that the revised SOP included in your response does not reference the planned weekly meetings between quality assurance (QA) and production. Regarding the weekly QA/Production meetings referenced here and in your response to FDA 483 Observation 6, is there a contingency plan in place in the event that these meetings are not held as scheduled?

FDA 483 Observation 8

We agree with your response to this observation and recommend that this corrective action extend to all of your firm's devices. However, has an assessment been done to determine what impact, if any, the out-of-specification results noted in the observation have on the devices that were released?

FDA 483 Observation 18

Your response indicates that your firm plans to [REDACTED] Please describe what, if any, interim steps you have taken to notify users of this potential problem.

FDA 483 Observation 22

We agree with your response to this observation. However, we request that you identify any limits you may have in place as to how many times a component can be reworked and still used in a finished device and what controls, if any, you have in place to verify that components exceeding any rework limits are not used.

Page 5  
June 25, 1998  
Douglas R. Spencer

FDA 483 Observation 24

As mentioned previously, we are aware of the circumstances that surround your relationship with [REDACTED] and of the steps you have taken and are taking to improve the quality of controllers used in the C2000. However, we would like to also point out that the *Federal Register* comment you refer to in your response also suggests that a supplier's refusal to provide notification of component changes may render that component supplier unacceptable. This observation specifically pertains to the fact that [REDACTED] fails to meet your firm's internal requirements for a component vendor, and your response essentially does not refute this observation.

Further, while we note your contention that the C2000 "meets its intended use for our customers" because you have "no reportable serious injuries" and "only [REDACTED] MDR reportable malfunction" with more than [REDACTED] units in the field, we remind you that complaints and MDR-reportable events are not the sole measures of the quality of a device. Our inspection revealed significant deviations from the quality system and CGMP regulations (as outlined above), in particular, a [REDACTED] failure rate of the C2000 device and a [REDACTED] failure rate of the C2000 controller. Our agency found that, as a result of these deviations, the C2000 poses a moderate risk of serious health adverse health consequences. As you have noted in your response, the agency does not regulate component suppliers but places the burden of assuring the quality of the components on the finished device manufacturers. While the agency recognizes the hurdles that device manufacturers may face in attempting to exert control over their vendors, the agency also recognizes that, when a vendor cannot or will not meet a manufacturer's requirements, it may be time to deem a particular vendor unacceptable.

The remaining responses to the FDA 483 observations appear to satisfactorily address those FDA 483 observations to which they refer; however, we will fully evaluate the appropriateness of those corrective actions during the next inspection at your firm.

The above is not intended to be an all-inclusive list of deficiencies at your firm. It is your responsibility to ensure adherence to each requirement of the FD&C Act and its associated regulations. The specific violations noted in this letter and in the FDA 483 issued at the conclusion of the inspection may be symptomatic of serious underlying problems in your establishment's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

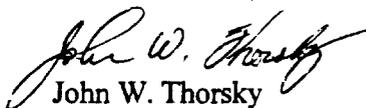
Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Also, no requests for Certificates to Foreign Governments will be approved until the violations related to the subject devices have been corrected.

Page 6  
June 25, 1998  
Douglas R. Spencer

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the FDA without further notice. These actions include, but are not limited to, seizure, injunction and/or civil penalties.

Please notify this office within fifteen (15) days of receipt of this letter of the specific steps you have taken or intend to take to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed. Your response should be sent to Karyn M. Campbell, Compliance Officer, at the address noted on the letterhead.

Sincerely,



John W. Thorsky  
Acting District Director  
Philadelphia District

cc: Robert E. Bastian, Director  
Division of Primary Care and Home Health Services  
PA Department of Health  
132 Kline Plaza, Suite A  
Harrisburg, PA 17104