



18 April 2000

**Docket No. 99D-5297,  
Dockets Management Branch,  
Division of Management Systems and Policy,  
Office of Human Resources and Management Services,  
Food and Drug Administration,  
5630 Fishers Lane, (HFA-305), Room 1061,  
Rockville, MD 20852  
USA**

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**Subject: Comments on Proposed Special Controls  
Guidance Document for Premarket Notification Submissions for Nitric Oxide  
Delivery Apparatus, Nitric Oxide Analyzer and Nitrogen Dioxide Analyzer**

To Whom It May Concern:

Please find enclosed comments from Datex-Ohmeda Division of Instrumentarium Corp., P.O. Box 900, FIN-00031 Datex-Ohmeda, Finland regarding the proposed document titled "Guidance Document for Premarket Notification Submissions for Nitric Oxide Delivery Apparatus, Nitric Oxide Analyzer and Nitrogen Dioxide Analyzer".

We hope that FDA will consider these comments in order to make this guidance document more accurate and appropriate for the regulation of medical devices involved in the delivery and monitoring of inhaled nitric oxide.

If you have any questions regarding these comments, I will be glad to answer.

Sincerely,

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# **Comments on “Guidance Document for Premarket Notification Submissions for Nitric Oxide Delivery Apparatus, Nitric Oxide Analyzer and Nitrogen Oxide Analyzer”**

3.1.1 i) We propose to change the text to read as follows:

Gas specific connectors for connection only to fittings for pharmaceutical grade nitric oxide in nitrogen (Compressed Gas Association 626) should be used for source gas cylinders or other external detachable connections for compressed nitric oxide in nitrogen. Labeling should identify the source gas concentration intended for use with the administration device.

Rationale:

The use of check valves is just one solution to prevent generation of high concentrations of NO<sub>2</sub> and the potential for environmental pollution. Also other solutions, addressed in the risk management procedure, should be allowed. Commercial distribution of NO in the United States has two approved concentrations of NO in nitrogen, 800 ppm and 100 ppm. Both these concentrations are provided with the same CGA 626 fitting and labeling of the cylinder is the only means of identification.

3.1.2 a) We propose to delete this item

Rationale:

The burden of showing whether components exposed to nitric oxide are effected within a ventilator should be placed on the ventilator manufacturer, not the nitric oxide delivery device.

The requirements for a nitric oxide delivery device should be that it conforms to the product’s specifications such as what effects the device has at the points of contact within the breathing circuit, i.e. its additional resistance to flow, the amount of gas added and subtracted to the breathing system.

Humidifiers, nebulizers, gas monitors etc. are not required to show compatibility with ventilators with which they are used.

It is impossible for a manufacturer of a nitric oxide delivery device to have control over the different versions and possible modifications of a ventilator manufactured by another company.

3.1.3 a): We propose that the third sentence be deleted.

Rationale:

As expressed in the rationale for the previous item, the burden of testing should not be placed on the nitric oxide delivery device, but on the ventilator. Humidifiers and nebulizers etc. are not required to show compatibility with ventilators with which they are used.

Further, we propose that the fourth sentence is amended to read as follows:

Devices should produce gas that contains no more than 3.0 ppm nitrogen dioxide during administration of 40 ppm of nitric oxide in 60% oxygen

Rationale:

The 3.0ppm nitrogen dioxide limit was part of the Nitric Oxide NDA and all of the investigator INDs for inhaled nitric oxide. The 3.0ppm limit was found to be appropriate by CDER.

**3.2.1 a) and 3.3.1 a):** Change 37 degrees Fahrenheit to 37 degrees Celsius

Rationale:

Editorial correction of an obvious error.

**4.2:** Change Line Voltage from 110 –125 Vrms to “108 V rms to 132 V rms”

Rationale:

Consistency with IEC 60601-1, which is also referenced elsewhere in this Guidance document.

**4.2 b):** The minimum sound level for hospital use should be changed from 70 dB(a) to 45 dB(A). Also, consider lowering the minimum level for home use.

Rationale:

International, European and ASTM standards unanimously specify 45 dB(A) as the minimum sound level. 85 dB(A), which in this document is specified as the minimum for home use, is the maximum level according to these standards.

**5.1.2 b):** We propose to modify the wording as follows:

In devices incorporating means for battery charging, a visual indicator should inform the operator when the batter is charging.

Rationale:

Clarity.

**5.1.6:** We suggest that the following clarifying text be added: “Note: AAMI ES-1 and UL 2601-1 with exceptions require devices in the US to pass leakage current at 300 microamps.”

**6.1.1.2:** Amend this paragraph to read as follows:

The device should comply with the relevant requirements of IEC 60601-1-2.

Rationale:

The reference to military standards is an obvious leftover from old guidance documents. The IEC standard has been developed specifically for medical devices, with the participation of FDA, and therefore it should be the only one applied for these devices. As the general standard IEC 60601-1 is used as a reference in other parts of this guidance document, it would be natural to adopt also the collateral standard for EMC.

**6.1.2.1:** Standards reference should be updated from IEC 801-2 to IEC 61000-4-2

**6.1.2.2 to 6.1.2.4:** We propose that these requirements be replaced with references to the relevant parts of IEC 61000-4.

Rationale:

This is referenced in IEC 60601-1-2.

**6.1.2.5 and 6.1.2.6:** We propose that these requirements be deleted.

Rationale:

The requirements in military standards are not intended to be applied to medical equipment. The medical equipment standards have no requirements in this area.

**7.1.5:** We propose the following amendment:

The device should be so constructed that it continues to operate within its specification after fluids have been spilled on the device. Therefore, the device should meet the requirements specified in Clause 44.3 of IEC 601-1.

Rationale:

For other devices used in the same environment the 200ml spill test described in Clause 44.3 of IEC 60601-1 is usually applied. The drip proof requirement of 44.6 only applies to transport devices.

**7.1.6 a):** We propose the following amendment:

The device should operate within its specification when operating in the environmental temperature and humidity ranges specified in IEC 60601-1.

Rationale:

Consistency with FDA recognized consensus standard IEC 60601-1.

**7.1.6 b):** We propose the following amendment:

The device should not be damaged and should remain operational within its specification after storage in the environmental temperature and humidity ranges specified in IEC 60601-1.

Rationale:

See above.

**7.1.7:** We propose the following amendment:

Temperature of surfaces of a device an operator can contact during operation should meet the requirements specified in IEC 60601-1.

Rationale:

See above.

**7.1.10:** We suggest to delete this requirement.

Rationale:

Device endurance is a reliability issue, not a safety issue. In addition, these special controls mandate that a back-up nitric oxide administration apparatus is available.

**10:** We propose to modify the second paragraph to read:

The nitric oxide administration apparatus, nitric oxide gas analyzer, and nitrogen dioxide gas analyzer are restricted to use only upon the written or oral authorization of a practitioner licensed by law to use the device and that the device be restricted to use by persons with experience or training in its use. In accordance with 21 CFR 801.109(b)(1), the labeling for prescription devices is required to bear the required caution prescription statement. This statement should read, "Caution: Federal law restricts this device to sale by or on the order of a physician or other licensed medical practitioner" or "Rx Only".

Rationale:

Recent decisions by FDA allow for the use of either the traditional label currently proposed in the special controls or the use of the "Rx Only" label.

**ex-Ohmeda**

Prioritaire N° D'AUTORISATION 9608  
EN CAS DE NON DISTRIBUTION, PRIERE DE RETOURNER A DCI/TIM 01

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