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April 7, 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

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, Inc. Ohmeda Drive, Madison, Wisconsin, 53707 regarding the proposed special controls entitled "Guidance Document for Premarket Notification Submissions for Nitric Oxide Delivery Apparatus, Nitric Oxide Analyzer and Nitrogen Dioxide Analyzer". Datex-Ohmeda reserves the right to provide additional comments before the public comment period is closed.

It is our hope that FDA will utilize 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 can be reached at 608-221-1551, extension 3581.

Sincerely,

Daniel Kosednar
Regulatory Affairs Specialist
Datex-Ohmeda, Madison

99D-5297

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Datex-Ohmeda, Madison, Comment Regarding FDA Proposed Special Controls for Nitric Oxide Delivery Devices, Nitric Oxide Monitoring Devices and Nitrogen Dioxide Monitoring Devices

Section	3.3.1 i)
Subject	Gas-specific connectors
Proposed Text/Changes	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 a solution to potential generation of high concentrations of NO₂ and the potential for environmental pollution. These can be addressed in the controls under those risks. The primary intent of this control is to prevent inadvertent connection to an unknown gas source. 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. This is analogous to other drugs or gases (such as heliox) that are provided in differing strengths where the control is through correct labeling of the strength.

Section	3.1.2 a)
Subject	Ventilator Compatibility
Proposed Text/Changes	Remove requirement

Rationale: The requirements for a nitric oxide delivery device should be that it conforms to the products 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.

Why has the burden of showing whether components exposed to nitric oxide are effected within a ventilator been placed on the nitric oxide delivery device and not the ventilator manufacturer? How is endurance testing defined?

This requirement should be removed as it has singled out nitric oxide therapy for requirements that are onerous when compared to other delivery devices or monitors and impossible to show definitively. Humidifiers, nebulizers, gas monitors etc. are not required to show compatibility with ventilators with which they are used.

Furthermore, how is compatibility defined? A separate company does not know how a differing ventilator companies ventilator strategy works or indeed how the delivery mechanism works. Therefore, how can a separate company show compatibility? At what level of ventilator software does the company show they tested to and what happens if the ventilator software is upgraded?

Datex-Ohmeda, Madison, Comment Regarding FDA Proposed Special Controls for Nitric Oxide Delivery Devices, Nitric Oxide Monitoring Devices and Nitrogen Dioxide Monitoring Devices

Section	3.1.3 a)
Subject	Nitrogen dioxide generation
Proposed Text/Changes	Sentence 3 should be removed. Sentence 4 should read: "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 testing requirements called out in Sentence 3 should be removed because the burden of testing should not be placed on the nitric oxide delivery device. Humidifiers and nebulizers etc. are not required to show compatibility with ventilators with which they are used.

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.

Section	3.2.1 a) and 3.3.1 a)
Subject	Nitrogen dioxide analyzer
Proposed Text/Changes	Change 37 degrees Fahrenheit to 37 degrees Celsius

Rationale: Reflects actual testing performed.

Section	4.2
Subject	General Test Methods
Proposed Text/Changes	Change Line Voltage from 110 - 125 Vrms to "108 V rms to 132 V rms"

Rationale: Consistent with FDA recognized consensus standard IEC 601-1

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Section	4.2 b)
Subject	Alarm Volume
Proposed Text/Changes	Change 70 dB(a) to 45 dB(A)

Rationale: Consistent with ISO 9702-2, EN 475 and ASTM 1463

Section	5.1.2 b)
Subject	Battery Charging Mode
Proposed Text/Changes	In devices incorporating means for battery charging, a visual indicator should inform the operator when the batter is charging.

Rationale: Clarification

Section	5.1.6
Subject	Leakage Current
Proposed Text/Changes	Add text: "Note: AAMI ES-1 and UL 2601-1 with exceptions require devices in the US to pass leakage current at 300 microamps."

Rationale: Clarification

Section	6.1.1.2
Subject	Magnetic Fields
Proposed Text/Changes	The device should comply with the relevant requirements of IEC 601-1-2.

Rationale: Consistent with FDA recognized consensus standards.

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General Comment: The practice of referencing Military Standards in a guidance document pertaining to medical equipment should stop for the following reasons:

- Military Standards were written to be applied to military equipment only.
- Standards groups such as IEC, EN, and ASTM provide standards specifically written to apply to medical devices.
- FDA has voting members on these committees.
- FDA has a process by which standards from these groups become recognized consensus standards.

It is our belief that the reference of Military Standards in this instance is a hold over from the requirements called out in the antiquated FDA document "Reviewer Guidance For Premarket Notification Submissions - Anesthesiology and Respiratory Devices Branch, November 1993". Past attempts by Datex-Ohmeda to get this reviewer guidance updated to reference applicable standards have resulted in no action by FDA. If the special controls for Nitric Oxide Administration Apparatus becomes finalized with the existing Military Standards references, it will only further entrench requirements which were never intended to apply to medical devices.

Section	6.1.2.1
Subject	Electrostatic discharge
Proposed Text/Changes	Changes standards reference from IEC 801-2 to IEC 1000-4-2

Rationale: Updated standard reference.

Section	6.1.2.2
Subject	Radiated Electromagnetic fields
Proposed Text/Changes	Device should meet the applicable requirements of IEC 1000-4-3

Rationale: Referenced in IEC 601-1-2, an FDA recognized consensus standard.

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Section	6.1.2.3 a)
Subject	Steady state voltage
Proposed Text/Changes	Device should meet the applicable requirements of IEC 1000-4-11

Rationale: Referenced in IEC 601-1-2, an FDA recognized consensus standard.

Section	6.1.2.3 b)
Subject	Dropout
Proposed Text/Changes	Device should meet the applicable requirements of IEC 1000-4-11

Rationale: Referenced in IEC 601-1-2, an FDA recognized consensus standard.

Section	6.1.2.3 c)
Subject	Slow sags and surges
Proposed Text/Changes	Device should meet the applicable requirements of IEC 1000-4-5

Rationale: Referenced in IEC 601-1-2, an FDA recognized consensus standard.

Section	6.1.2.3 d)
Subject	Fast transient bursts
Proposed Text/Changes	Device should meet the applicable requirements of IEC 1000-4-4

Rationale: Referenced in IEC 601-1-2, an FDA recognized consensus standard.

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Section	6.1.2.3 e)
Subject	Fast surges
Proposed Text/Changes	Device should meet the applicable requirements of IEC 1000-4-4

Rationale: Referenced in IEC 601-1-2, an FDA recognized consensus standard.

Section	6.1.2.4
Subject	Conducted electromagnetic energy
Proposed Text/Changes	Device should meet the applicable requirements of IEC 1000-4-4

Rationale: Referenced in IEC 601-1-2, an FDA recognized consensus standard.

In addition, see the earlier note regarding the use of Military Standards.

Section	6.1.2.5
Subject	Magnetic Fields
Proposed Text/Changes	Delete requirement

Rationale: No FDA recognized consensus standards have requirements in this area. Again, Military Standards were meant to apply to military equipment, not medical equipment and no medical equipment professionals provide input to military standards. The standards to which both FDA and medical equipment professionals do provide input do not have a requirement in this area.

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Section	6.1.2.6
Subject	Quasi-Static Electric Fields
Proposed Text/Changes	Delete requirement

Rationale: No FDA recognized consensus standards have requirements in this area. Again, Military Standards were meant to apply to military equipment, not medical equipment and no medical equipment professionals provide input to military standards. The standards to which both FDA and medical equipment professionals do provide input do not have a requirement in this area.

Section	7.1.5
Subject	Fluid spill resistance
Proposed Text/Changes	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: The 200mL spill test described in Clause 44.3 of IEC 601-1 is more applicable than the drip test called out in Clause 44.6. The drip proof requirement only applies to transport devices.

Section	7.1.6 a)
Subject	Operational temperature
Proposed Text/Changes	The device should operate within its specification when operating in the environmental temperature and humidity ranges specified in IEC 601-1

Rationale: Consistent with FDA recognized consensus standard IEC 601-1

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Section	7.1.6 b)
Subject	Storage temperature
Proposed Text/Changes	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 601-1

Rationale: Consistent with FDA recognized consensus standard IEC 601-1

Section	7.1.7
Subject	Surface temperature
Proposed Text/Changes	Temperature of surfaces of a device an operator can contact during operation should meet the requirements specified in IEC 601-1.

Rationale: Consistent with FDA recognized consensus standard IEC 601-1

Section	7.1.10
Subject	Endurance Testing
Proposed Text/Changes	Delete requirement

Rationale: Device endurance is a reliability issue not a safety issue. Market pressures will dictate device reliability. In addition, these special controls mandate that a back-up nitric oxide administration apparatus is available.

Datex-Ohmeda, Madison, Comment Regarding FDA Proposed Special Controls for Nitric Oxide Delivery Devices, Nitric Oxide Monitoring Devices and Nitrogen Dioxide Monitoring Devices

Section	10
Subject	Labeling
Proposed Text/Changes	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.

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