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Guidance for Industry and for FDA Reviewers

Guidance Document for Premarket Notification Submissions for Nitric Oxide Delivery Apparatus, Nitric Oxide Analyzer and Nitrogen Dioxide Analyzer

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**U.S. Department of Health and Human Services
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**Anesthesiology, Respiratory, and Defibrillator Devices Group
Division of Cardiovascular, Respiratory, and Neurological Devices
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Preface

Public Comment

Until [date 90 days from release date], comments and suggestions regarding this document should be submitted to 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.. Such comments will be considered when determining whether to amend the current guidance.

After [date 90 days from release date], comments and suggestions may be submitted at any time for Agency consideration to: Michael Bazaral, M.D., Ph.D., Center for Devices and Radiological Health (HFZ-450), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850. Comments may not be acted upon by the Agency until the document is next revised or updated. For questions regarding the use or interpretation of this guidance contact Michael Bazaral, M.D., Ph.D. at 301-443-8609.

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Guidance Document for Premarket Notification Submissions for Nitric Oxide Delivery Apparatus, Nitric Oxide Analyzer and Nitrogen Dioxide Analyzer¹

¹ This guidance document represents the agency's current thinking on this subject. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the applicable statute, regulations, or both.

Table of Contents

1			
2			
3	1. INTRODUCTION.....		1
4	1.1 PURPOSE.....		1
5	1.2 BACKGROUND.....		1
6	1.3 SCOPE.....		1
7	2. DEVICE DESCRIPTION		2
8	2.1 NITRIC OXIDE ADMINISTRATION APPARATUS.....		2
9	2.2 NITRIC OXIDE GAS ANALYZER.....		2
10	2.3 NITROGEN DIOXIDE GAS ANALYZER.....		3
11	3. SPECIFIC CRITERIA AND TESTING		4
12	3.1 NITRIC OXIDE DELIVERY APPARATUS.....		4
13	3.1.1 <i>Loss of nitric oxide therapy and incorrect nitric oxide concentration.....</i>		<i>4</i>
14	3.1.2 <i>Insufficient or excess ventilation or oxygenation.....</i>		<i>7</i>
15	3.1.3 <i>Excessive nitrogen dioxide administration.....</i>		<i>8</i>
16	3.1.4 <i>Potential for catastrophic release of nitric oxide</i>		<i>10</i>
17	3.1.5 <i>Adulteration of the nitric oxide</i>		<i>10</i>
18	3.1.6 <i>Electrical hazards.....</i>		<i>10</i>
19	3.1.7 <i>Adverse effects on other electronic devices.....</i>		<i>11</i>
20	3.1.8 <i>Release of nitric oxide and release and generation of nitrogen dioxide</i>		<i>11</i>
21	3.2 NITRIC OXIDE ANALYZER.....		11
22	3.2.1 <i>Nitric Oxide measurement error.....</i>		<i>12</i>
23	3.2.2 <i>Electrical hazards.....</i>		<i>13</i>
24	3.2.3 <i>Adverse effects on other electronic devices.....</i>		<i>14</i>
25	3.3 NITROGEN DIOXIDE ANALYZER.....		14
26	3.3.1 <i>Nitrogen Dioxide measurement error.....</i>		<i>14</i>
27	3.3.2 <i>Electrical hazards.....</i>		<i>16</i>
28	3.3.3 <i>Adverse effects on other electronic devices.....</i>		<i>16</i>
29	4. GENERAL CRITERIA AND TESTING		17
30	4.1 GENERAL CRITERIA.....		17
31	4.2 GENERAL TEST METHODS		17
32	5. ELECTRICAL SAFETY		19
33	5.1 PERFORMANCE CRITERIA.....		19
34	5.1.1 <i>Battery power.....</i>		<i>19</i>
35	5.1.2 <i>Electrical power indicators</i>		<i>19</i>
36	5.1.3 <i>Overcurrent protection.....</i>		<i>20</i>
37	5.1.4 <i>Dielectric withstand.....</i>		<i>20</i>
38	5.1.5 <i>AC power grounding and polarity.....</i>		<i>20</i>
39	5.1.6 <i>Leakage current.....</i>		<i>20</i>
40	5.1.7 <i>Auxiliary output</i>		<i>21</i>
41	5.2 TEST METHODS		21

42	5.2.1	Battery power.....	21
43	5.2.2	Electrical power indicators.....	22
44	5.2.3	Overcurrent protection.....	22
45	5.2.4	Dielectric withstand.....	23
46	5.2.5	AC power grounding and polarity.....	23
47	5.2.6	Leakage current.....	23
48	5.2.7	Auxiliary output.....	23
49	6.	ELECTROMAGNETIC COMPATIBILITY	24
50	6.1	PERFORMANCE CRITERIA.....	24
51	6.1.1	Emissions.....	24
52	6.1.1.1	Radiated and conducted electromagnetic energy.....	24
53	6.1.1.2	Magnetic fields.....	24
54	6.1.2	Immunity.....	24
55	6.1.2.1	Electrostatic discharge.....	25
56	6.1.2.2	Radiated electromagnetic fields.....	25
57	6.1.2.3	AC voltage fluctuations, transients, and surges.....	25
58	6.1.2.4	Conducted electromagnetic energy.....	26
59	6.1.2.5	Magnetic fields.....	27
60	6.1.2.6	Quasi-static electric fields.....	27
61	6.2	TEST METHODS.....	27
62	6.2.1	Emissions.....	27
63	6.2.1.1	Radiated and conducted electromagnetic energy.....	27
64	6.2.1.2	Magnetic fields.....	27
65	6.2.2	Immunity.....	28
66	6.2.2.1	Electrostatic discharge.....	28
67	6.2.2.2	Radiated electromagnetic fields.....	29
68	6.2.2.3	AC voltage fluctuations, transients, and surges.....	32
69	6.2.2.4	Conducted electromagnetic energy.....	34
70	6.2.2.5	Magnetic fields.....	35
71	6.2.2.6	Quasi-static electric fields.....	35
72	7.	PERFORMANCE SPECIFICATIONS, ENVIRONMENTAL AND MECHANICAL SAFETY	37
73	7.1	PERFORMANCE CRITERIA.....	37
74	7.1.1	Controls protection.....	37
75	7.1.2	Connector protective incompatibility.....	37
76	7.1.3	Mechanical safety.....	37
77	7.1.4	Mechanical vibration and shock resistance.....	38
78	7.1.5	Fluid spill resistance.....	38
79	7.1.6	High and low temperature and humidity.....	38
80	7.1.7	Surface temperature.....	38
81	7.1.8	Toxic materials.....	39
82	7.1.9	Strangulation.....	39
83	7.1.10	Determination of Endurance.....	39
84	7.1.11	Material Compatibility.....	39
85	7.1.12	Medical Gas Cylinder Connections.....	39
86	7.2	TEST METHODS.....	39
87	7.2.1	Controls protection.....	39

88	7.2.2	Connector protective incompatibility.....	39
89	7.2.3	Mechanical safety.....	40
90	7.2.4	Mechanical vibration and shock resistance.....	40
91	7.2.5	Fluid spill resistance.....	40
92	7.2.6	High and low temperature and humidity.....	40
93	7.2.7	Surface temperature.....	41
94	7.2.8	Toxic materials.....	41
95	7.2.9	Strangulation.....	41
96	7.2.10	Determination of Endurance.....	41
97	7.2.11	Material Compatibility.....	41
98	8.	HARDWARE DOCUMENTATION	42
99	9.	SOFTWARE DOCUMENTATION	43
100	10.	LABELING.....	44
101	10.1	IDENTIFICATION OF MEDICAL GAS CYLINDERS AND CONNECTIONS.....	44
102	10.2	INSTRUCTIONS FOR USE	44
103	10.2.1	Intended Use.....	44
104	10.2.2	Validated Ventilators.....	44
105	10.2.3	Installation Instructions.....	45
106		DOCUMENT UPDATE AND REVISION LOG.....	46

SECTION 1. Introduction**1.1 Purpose.**

The purpose of this document is to facilitate the preparation and the review of premarket submissions for nitric oxide delivery apparatus, nitric oxide analyzers, and nitrogen dioxide analyzers.

1.2 Background

On September 23, 1996, Ohmeda Inc. submitted a petition under section 513(f)(2) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360c(f)(2)), requesting that the devices included in the Ohmeda I-NOvent Delivery System intended for administration of inhaled nitric oxide, be reclassified from class III into class II. The system includes three devices which may be separately manufactured; a nitric oxide administration apparatus, a nitric oxide gas analyzer, and a nitrogen dioxide gas analyzer. This guidance document is proposed as a special control for these devices.

This guidance document describes a means by which nitric oxide delivery and analyzing devices and nitrogen dioxide analyzing devices for use during the administration of nitric oxide may comply with the requirement of special controls for Class II devices. Designation of this guidance document as a special control means that manufacturers attempting to establish that their device is substantially equivalent to a predicate device should demonstrate that the proposed device complies with either the specific recommendations of this guidance or some alternate control that provides equivalent assurances of safety and effectiveness.

1.3 Scope

This guidance document identifies information that should be included in premarket notifications for the Nitric Oxide Delivery Apparatus, the Nitric Oxide Analyzers, and the Nitrogen Dioxide Analyzers.

A description of certain information typically provided in a premarket notification such as comparative performance evaluations, table of comparison, device description, discussion of similarities and difference, biocompatibility is not included in this guidance. Such information is common for all premarket notifications and is discussed in current guidances and manuals, including the Draft Guidance for Premarket Notification Submissions, and the Premarket Notification [510(k)] Manual. Both of these are available from the Division of Small Manufacturers Assistance (DSMA).

SECTION 2. Device Description

A complete Nitric Oxide Delivery System includes three component medical devices; a nitric oxide administration apparatus, a nitric oxide gas analyzer, and a nitrogen dioxide gas analyzer. Each of the three components of a generic nitric oxide administration system may be manufactured and distributed separately; for that reason this guidance document addresses the three component devices individually.

2.1 Nitric Oxide Administration Apparatus

The nitric oxide administration apparatus (product code MRN) is a device used to add nitric oxide to gases that are to be breathed by a patient. The nitric oxide administration apparatus is to be used in conjunction with a ventilator or other breathing gas administration system. The concentration of nitric oxide is maintained approximately constant during the inspiratory flow regardless of the variation in flow rate within the inspiratory portion of the respiratory cycle. The concentration of inspired nitric oxide can be set, typically in the range of 0 to 80 parts per million (ppm). The administration apparatus includes a pressure regulator and connectors with fittings which are specific for nitric oxide gas cylinders, typically containing 400 or 800 ppm nitric oxide in nitrogen. The nitric oxide administration apparatus design should minimize the time that nitric oxide is mixed with oxygen (dwell time), and thus minimize the concentration of nitrogen dioxide in the gas breathed by the patient (nitrogen dioxide is a toxic reaction product which forms in a chemical reaction of nitric oxide with oxygen).

The administration device should include provisions for a nitric oxide gas concentration gas analyzer with alarms, a nitrogen dioxide gas analyzer with an alarm, and an oxygen analyzer with alarms. Suitable gas analysis devices should be identified in the labeling for the nitric oxide gas administration device.

The delivery system should include or indicate a nitric oxide administration apparatus for use as a "backup" system (product code MRO) for administration of nitric oxide when the main administration apparatus cannot be used.

2.2 Nitric Oxide Gas Analyzer

A nitric oxide gas analyzer (product code MRP) is a device intended to measure the concentration of nitric oxide in respiratory gas mixtures during administration of nitric oxide. The gas should be sampled from the inspiratory limb of the patient circuit. The nitric oxide gas analyzer usually includes provisions for setting upper and lower measured nitric oxide concentrations at which an alarm will be activated.

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188 2.3 Nitrogen Dioxide Gas Analyzer

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190 A nitrogen dioxide gas analyzer (product code MRQ) is a device intended to measure
191 the concentration of nitrogen dioxide in respiratory gas mixtures during administration of
192 nitric oxide. The gas is sampled from the inspiratory limb of the patient circuit. The
193 nitrogen dioxide gas analyzer usually includes provisions for setting an upper measured
194 nitrogen dioxide concentration, with an alarm to be activated when the measured
195 concentration exceeds the set value.

196

SECTION 3. Specific Criteria and Testing

A nitric oxide administration system has each of these three components; a nitric oxide delivery apparatus, a nitric oxide analyzer, and a nitrogen dioxide analyzer. The components may be manufactured and distributed separately; for that reason this section of the guidance document addresses the three component devices individually.

3.1 Nitric Oxide Delivery Apparatus

The design and testing of the nitric oxide delivery apparatus should take into consideration the risks associated with the device. Risks for the nitric oxide delivery apparatus and the applicable controls are discussed in the follow subsections.

3.1.1 Loss of nitric oxide therapy and incorrect nitric oxide concentration. Loss of nitric oxide therapy may result in acute respiratory failure or acute pulmonary hypertension. Incorrect low nitric oxide concentration may result in ineffective treatment, while incorrect high nitric oxide concentration may result in excess side effects, and generation and administration of excess nitrogen dioxide.

The controls for this risk consist of the following elements:

- a. If the device is the primary nitric oxide delivery system, the device should include a reserve (backup) nitric oxide delivery system. Alternatively, labeling may specify a marketed reserve (backup) nitric oxide delivery system. The back-up system will minimize the risk of loss of NO therapy resulting from failure of the primary NO administration apparatus.
- b. The administration device should include provision for nitric oxide gas analysis with alarms. The breathing circuit location for sampling should sample gas which is representative of the inspired gas. Labeling should specify a suitable nitric oxide gas analyzer. The specified nitric oxide analyzer should include an alarm with settable upper and lower nitric oxide concentration limits. The inclusion of nitric oxide gas analysis with alarms will minimize the risk result from loss of nitric oxide therapy or incorrect therapy, by alerting the practitioner of the need to correct a malfunction.
- c. The device should include a cylinder pressure gauge. Information

- 237 provide by the cylinder pressure will permit verification of an adequate
238 reserve of compressed nitric oxide in nitrogen and permit planning for
239 replacement of near-empty cylinders without loss of therapy.
240
- 241 d. The device should include provision for attachment of two nitric oxide
242 cylinders which can be used alternately via a manifold, or other means
243 to assure a continuous supply of nitric oxide for normal operation of a
244 primary administration system during replacement of cylinders. This
245 provision will minimize the risk of loss of nitric oxide therapy.
246
- 247 e. A primary nitric oxide administration device and the gas analysis
248 devices should have battery backup power if the administration device
249 or the gas analysis devices require main electrical power, and if the
250 device is labeled for use with a ventilator having a battery backup
251 power supply, or a ventilator capable of operation without main
252 electrical power. Backup power should be demonstrated to have the
253 duration of the ventilators listed for use with the device, or for at least
254 20 minutes. Backup power will minimize the risk of loss of nitric oxide
255 therapy during transient power failure. If the devices are intended for
256 use only with a ventilator having no backup power supply, then the
257 manual backup nitric oxide administration device may be used, and no
258 battery backup power for the nitric oxide administration system is
259 needed.
260
- 261 f. If a nitric oxide administration device is intended for use only as a
262 backup or reserve system, then the device should be labeled for use
263 only as a backup to a primary system, and only for use with a specified
264 manual ventilator or a non-powered breathing circuit. The manual
265 ventilator or non-powered breathing circuit should be specified. The
266 device should be tested under simulated conditions of use to verify
267 accuracy and the delivery of near-constant concentrations of NO within
268 the respiratory cycle. Nitric oxide administration devices labeled for
269 use as backup devices should not require main electrical power during
270 use. The labeling for the backup device need not specify compatible
271 gas analysis devices. If the backup system provides only a fixed
272 concentration of NO then the manual should note that the system
273 should be used only during periods when the primary system has
274 failed or cannot be used for other unanticipated reasons, unless the
275 patient is known to have no adverse effects at the concentration
276 provided by the backup system. The labeling should also note that if a

277 patient is thought to require a concentration different than provided by
278 the backup system, then a separate system capable of providing the
279 required concentration should be available. A backup system which
280 provides a set single concentration will reduce the risks resulting from
281 failure of the primary system, since for most patients inhaled nitric
282 oxide will be effective over a wide range of concentrations, and the
283 primary system should fail only infrequently. Although the risks may in
284 principle be further minimized by the use of an adjustable
285 concentration system, the use of an adjustable system may introduce
286 additional hazards of complexity. Thus the use either of a fixed
287 concentration system or an adjustable backup system, within the
288 device labeling recommendations, can sufficiently limit the risk
289 resulting from possible failure of the primary administration system.

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g. For either backup or primary nitric oxide administration devices the mean nitric oxide concentration in the inspired gas should be reasonably constant in the circumstances of intended use. Testing should be performed in simulated use to determine the accuracy with which the device can maintain the mean nitric oxide concentration when the mean inspired concentration is sampled while the device is delivering representative respiratory flow patterns. Testing should evaluate the stability of the concentration produced, and the repeatability of the settings. Inspired concentrations within 20% of the set concentration of nitric oxide will be considered sufficiently accurate, since currently available data typically demonstrates that within a study, the effect of nitric oxide is similar over a range of concentrations. The testing will establish that the device is capable of providing sufficient accuracy, and thus will control the risk of incorrect delivered concentration of nitric oxide. Results of testing should be included in the labeling as specifications to allow selection of suitable devices.

h. The device should provide nitric oxide concentrations at the patient connection which are well-defined at all times within the duration of each breath, and which correspond to available data regarding safety. Testing should be done under conditions of intended use to determine the delivered concentration at the patient connection, using a test system having an adequate response time. Sufficient accuracy within a breath cannot be defined on the basis of current data. However the currently available data (NINOS and Ohmeda) were developed using

317 devices which provide reasonably constant concentrations within
318 breaths. Transient concentrations as high as 150% of the mean
319 concentration and as low as 0.0 ppm would be considered reasonably
320 safe if the total duration of these transient concentrations did not
321 exceed 10% of the volumetric duration of the breath. Testing may be
322 done using a tracer gas in place of nitric oxide if adequate response
323 times cannot be achieved for analysis of nitric oxide concentrations.
324 Representative test result tracings should be included in the device
325 labeling. Conformance to the accuracy range stated above will control
326 the risk of incorrect NO concentration, within the stated limit. Also,
327 inclusion of the test results in the labeling will permit the practitioner to
328 select devices on the basis of delivered concentration profile within the
329 respiratory cycle.

330
331 i. Gas-specific connectors with integral check valve which allow
332 connection only to fittings (Compressed Gas Association 626 fitting)
333 for pharmaceutical grade nitric oxide in nitrogen should be used for
334 connections to the source gas cylinder or for other external detachable
335 connections for compressed nitric oxide in nitrogen. Plans for
336 commercial distribution of nitric oxide in the United States include the
337 use of only a single concentration of nitric oxide; the availability of only
338 a single concentration renders the use of a compressed gas cylinder
339 containing an incorrect concentration of compressed nitric oxide in
340 nitrogen unlikely. Thus use of a standard gas-specific fitting (as well
341 as the use of nitric oxide gas analyzer) will control the risk of incorrect
342 drug administration resulting from use of the incorrect compressed
343 gas.

344
345 j. Particular published standards or portions of published consensus
346 standards, and other material in this guidance document address
347 issues such as software and hardware documentation,
348 electromagnetic compatibility documentation, and environmental
349 documentation. Refer to the table of contents for the specific topic.

350
351 3.1.2 Insufficient or excess ventilation or oxygenation may result from the effects
352 of the nitric oxide administration system on the function of the ventilator or
353 other respiratory gas administration system with which the nitric oxide
354 administration system is used.

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356 To control the risk of insufficient or excess ventilation or oxygenation:

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- a. Compatible ventilators or other respiratory gas administration systems should be identified in the labeling. The nitric oxide administration device (including specified gas analysis devices) should not adversely affect the triggering, cycling, alarm function, or other aspects of the safety and effectiveness of the listed ventilators or other respiratory gas administration system. Testing should be performed to demonstrate compatibility of the ventilator and nitric oxide administration device. Testing should include testing of the ventilator and nitric oxide administration device, and also endurance testing of the ventilator to evaluate the effect of nitric oxide on ventilator components. The proposed testing will control risks related to adverse interactions of the nitric oxide administration apparatus and ventilator or the respiratory gas administration system.
- b. The nitric oxide administration apparatus or specified ventilator should include an oxygen gas analyzer (or provisions for a specified oxygen analyzer) which samples gas representative of the inspired gas and which includes alarms appropriate to the intended use. Oxygen gas analyzers for such use should be demonstrated to maintain specified accuracy and useful life in the highest concentration of nitric oxide and nitrogen dioxide with which they will be used. The inclusion and testing of an oxygen analyzer will control the risk that unanticipated malfunctions of any part of the system will result in inhalation of hypoxic gas mixtures.

3.1.3 Excessive nitrogen dioxide administration is a risk associated with nitric oxide administration. Nitrogen dioxide is a toxic gas formed by reaction of nitric oxide with oxygen. Conditions for this reaction are well-described. The toxicity of nitrogen dioxide may in part be mediated by the formation of acid products by reaction of nitrogen dioxide with water. While levels of nitrogen dioxide less than 5 ppm meet OSHA standards for industrial exposure, and the recommended NIOSH limit is 1 ppm, patient exposure should be at a practical minimum. The currently available data (NINOS and Ohmeda) was developed using devices which provide minimal dwell time. Other devices under development are also capable of similar low values of nitrogen dioxide production.

To control the risk of excessive nitrogen dioxide administration:

397 a. The nitric oxide administration device should not produce excessive
398 nitrogen dioxide. The labeling should specify the inhaled
399 concentration of nitrogen dioxide during delivery at 40 ppm (or the
400 highest concentration if less than 40 ppm) of nitric oxide in 60%;
401 testing should support the accuracy of the specifications. Testing
402 should be done for each ventilator listed for use with the nitric oxide
403 administration device, under the simulated circumstances of use which
404 produce the highest concentrations of nitrogen dioxide. Devices
405 should produce gas that contains no more than 1.0 ppm nitrogen
406 dioxide during administration of 40 ppm of nitric oxide in 60% oxygen.
407 If the dwell time for mixtures of nitric oxide oxygen differs significantly
408 for other combinations of flows and concentrations, then additional
409 labeling and testing may be necessary. Engineering analysis, and
410 testing when practical, should be used to estimate the peak
411 concentration of nitrogen dioxide within the respiratory cycle. If the
412 physical configuration and other parameters contributing to dwell time
413 remain unchanged, then the nitrogen dioxide concentration at other
414 oxygen or nitric oxide concentrations may be estimated from known
415 chemical kinetics. This information will permit control of the risks of
416 excessive nitrogen dioxide production.

417
418 During delivery of low concentrations of nitric oxide (5 ppm or less)
419 longer dwell times may be acceptable. The equivalence with respect
420 to nitrogen dioxide production of devices providing low concentrations
421 of nitric oxide would be evaluated on the basis of clinical data, and
422 other data which may become available.

423
424 Nitrogen dioxide in the inspired gas provided by a backup system
425 should also be evaluated. The inspired concentration in simulated use
426 should be measured at 10 ppm NO and approximately 98% oxygen,
427 and should meet specifications provided in the device labeling. If the
428 specified manual ventilator includes a reservoir which is not
429 continuously flushed, then the maximum concentration of inspired
430 nitrogen dioxide during the respiratory cycle should be evaluated, and
431 the result provided for review.

432
433 b. The administration device should include provision for nitrogen dioxide
434 gas analysis with alarms. The breathing circuit location for sampling
435 should sample gas which is representative of the inspired gas.
436 Labeling should specify a suitable nitrogen dioxide gas analyzer. The

437 analyzer should include an alarm with upper nitrogen dioxide
438 concentration limits. Use of nitrogen dioxide analysis with alarms will
439 permit detection and correction of malfunctions resulting in excess
440 nitrogen dioxide production, and thus provides a supplementary
441 method to control the risk of excessive nitrogen dioxide concentration.
442

443 c. Instructions for flushing the device and for operation of the device
444 should be sufficient to prevent administration of nitrogen dioxide in
445 excess of labeled limits. Testing should be performed to demonstrate
446 the adequacy of these procedures. This testing will permit control of
447 the risks of excessive nitrogen dioxide production.
448

449 3.1.4 Potential for catastrophic release of nitric oxide results from the use of
450 compressed gas cylinders containing substantial quantities of nitric oxide.
451 This risk is limited by limiting the total quantity of nitric oxide subject to
452 release in case of device failure or damage to the device or cylinder. This
453 requirement will be met if the devices uses #82 cylinders pressurized to no
454 more than 2200 psi, and containing 400 ppm or 800 ppm nitric oxide. A data
455 summary provided by Ohmeda lists the expected peak concentrations
456 resulting from the release of the content of one cylinder (400 ppm) over 17
457 seconds into a 3.1 x 6.2 x 4.65 meter room; without air exchange, the
458 expected peak nitric oxide concentration is be 9 ppm and the expected peak
459 nitrogen dioxide concentration is be 1.8 ppm, within OSHA standards of 25
460 and 5 ppm respectively.
461

462 3.1.5 Adulteration of the nitric oxide may occur by reaction with the nitric oxide
463 administration apparatus, or by reaction with the ventilator, humidifier, or
464 other devices specified for use with the nitric oxide administration apparatus.
465 The inspired gas at the patient connection should be tested by sensitive
466 methods for the detection of adulterants. Methods may include Fourier
467 transform infrared. This testing will control the risk of adulteration of the
468 inhaled nitric oxide.
469

470 3.1.6 Electrical hazards to patients and others may result from the use of electrical
471 devices. Published standards or portions of standards are identified and
472 discussed in Section 5. Compliance with these standards, or equivalent
473 demonstrations of safety, are commonly used in review of medical devices,
474 such as ventilators, to provide adequate control of risks related to various
475 types of malfunctions, and will adequately control the electrical hazards of
476 the nitric oxide administration device.

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3.1.7 Adverse effects on other electronic devices used for patient care may result from the use of electrical devices. Published standards or portions of standards for electromagnetic compatibility and testing are identified and discussed in Section 6 of this document as a special control. Compliance with these standards, or equivalent demonstrations of safety, are commonly used in review of medical devices to provide adequate control of risks related to electromagnetic interference, and will adequately control the electromagnetic interference hazards of the nitric oxide administration device.

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3.1.8 Release of nitric oxide and release and generation of nitrogen dioxide will result in the use of a nitric oxide administration device, and this may constitute a hazard under some circumstances. Because the concentration of nitric oxide concentrations used are low, generally less than 40 ppm, the nitric oxide concentration accumulated in room air concentrations are unlikely to exceed the NIOSH recommended time-weighted concentration limit of 25 ppm or the recommended acute exposure for nitrogen dioxide of 1 ppm. Calculations of dilution as well as experimental simulated use demonstrate that the ambient concentration of nitric oxide or nitrogen dioxide expected to result from use of the device is less than 50 ppb. Thus there is no need to scavenge the exhausted gas under typical circumstances. However individuals who may be particularly sensitive to nitric oxide or nitrogen dioxide, or who will be exposed for long periods should be informed of the exposure by labeling, including labeling on the device itself. In addition the practitioner should be instructed by labeling to evaluate the particular location in which the device is used, if the ventilation is in question. This labeling will adequately control risks which may result from release of nitric oxide and the release and generation of nitrogen dioxide in the nearby area under most circumstances. Optionally, scavenging devices may be fitted to ventilators if required. Scavenging devices are class II devices (21 CFR 868.5430). If there are circumstances in which use of the nitric oxide administration device results in excessive ambient nitric oxide and nitrogen dioxide, use of scavenging devices will adequately control risk.

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3.2 Nitric Oxide Analyzer

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The design and testing of the nitric oxide analyzer should take into consideration the risks associated with the device. Risks for the nitric oxide analyzer and the applicable controls are discussed in the follow subsections.

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518 3.2.1

Nitric Oxide measurement error is a particular risk of the nitric oxide analyzer. False low displayed or alarm values for of nitric oxide concentration can result in administration of excess nitric oxide, and false high displayed values for nitric oxide concentration can result in administration of insufficient nitric oxide. False display or alarm values for nitric oxide concentration will raise concerns that the administration device is malfunctioning, or that the nitric oxide cylinder contents are adulterated; the result may be interruption of essential nitric oxide therapy.

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To control the risk of error in measurement of nitric oxide the following specifications, labeling and testing should be incorporated in the design of the nitric oxide analyzer:

530

531

- a. Accuracy should be specified in the labeling. Testing should be performed to demonstrate the accuracy over the range of displayed values and under the conditions of simulated use. The testing conditions should include testing at 37 degrees Fahrenheit using mixtures as shown in table 1 below. The nitric oxide gas analyzer should measure concentrations of nitric oxide as low as 1 ppm. The accuracy of the displayed value should be within +/- (0.5 ppm + 20% actual concentration) between 1 and 20 ppm ($\mu\text{L/L}$). Above 20 ppm, the displayed value should be within +/- (0.5 ppm + 10% actual concentration). A 0-90% rise time of 30 seconds is sufficient.

540

541

NO (ppm)	0 ppm NO ₂ Ambient pressure 90% Humidification Balance gas O ₂	0 ppm NO ₂ Ambient pressure 90% Humidification Balance gas Air	5 ppm NO ₂ Ambient pressure 90% Humidification Balance gas O ₂	0 ppm NO ₂ 50 CmH ₂ O 90% Humidification Balance gas O ₂	0 ppm NO ₂ Ambient pressure Dry Gas Balance gas O ₂
0	✓	✓	✓	✓	✓
1	✓	✓	✓	✓	✓
5	✓				
20	✓	✓	✓	✓	✓
Full Scale	✓				

542

* Balance is the gas to which the 800 or 400 ppm nitric oxide in nitrogen is added. Balance gas should constitute at least 85% of the tested gas mixture, (volume %).

543

544

Table 1

545

546

547

- 548 b. The equivalence of the nitric oxide gas analysis devices with respect to
549 nitric oxide measurements at levels less than 1 ppm will be evaluated
550 on the basis of the accuracy relative to the clinical indications and
551 other data which may become available.
552
- 553 c. Labeling should include methods for calibration. Nitric oxide
554 calibration gas suitable for use with the device should be specified by
555 the manufacturer of the nitric oxide gas analyzer. The calibration gas
556 should be labeled with an expiration date, and test data should be
557 provided to demonstrate that the calibration gas is adequately stable
558 for use within the expiration limit, and will permit calibration of the nitric
559 oxide gas analyzer to the analyzer's specified accuracy.
560
- 561 d. The expected life of the sensor or other life-limited components should
562 be specified. Testing to validate the endurance sensor or other life-
563 limited components should include simulated use with the patient
564 circuit as specified in the device labeling, with the humidifier set to
565 simulate the conditions of clinical use.
566
- 567 e. Alarms, if provided, should be capable of being set over the range of
568 displayed nitric oxide concentrations, and be demonstrated to alarm at
569 set value. Note that a primary nitric oxide administration device should
570 include provision for nitric oxide gas analysis with upper and lower
571 concentration alarms.
572
- 573 f. If the device is for use within or for attachment to a patient breathing
574 circuit operating at other than ambient pressure, accuracy should be
575 verified by testing during simulated positive pressure ventilation
576 generally in accordance with procedures used for testing of oxygen
577 gas analyzers. This information can be found in ASTM F 1462 - 93
578 Specifications for Oxygen Analyzers.
579
- 580 g. Particular published standards or portions of published consensus
581 standards, and other material in this guidance document address
582 issues such as; software and hardware documentation,
583 electromagnetic compatibility documentation, and environmental
584 documentation. Refer to the table of contents for the applicable
585 section.
586
- 587 3.2.2 Electrical hazards to patients and others may result from the use of electrical

588 devices. Published standards or portions of standards are identified and
589 discussed in Section 5. Compliance with these standards, or equivalent
590 demonstrations of safety, are commonly used in review of medical devices,
591 such as ventilators, to provide adequate control of risks related to various
592 types of malfunctions, and will adequately control the electrical hazards of
593 the nitric oxide analyzer.

594

595 3.2.3 Adverse effects on other electronic devices used for patient care may result
596 from the use of electrical devices. Published standards or portions of
597 standards for electromagnetic compatibility and testing are identified and
598 discussed in Section 6 of this document as a special control. Compliance
599 with these standards, or equivalent demonstrations of safety, are commonly
600 used in review of medical devices, to provide adequate control of risks
601 related to electromagnetic interference, and will adequately control the
602 electromagnetic interference hazards of the nitric oxide analyzer.

603

604 3.3 Nitrogen Dioxide Analyzer

605

606 The design and testing of the nitrogen dioxide analyzer should take into consideration
607 the risks associated with the device. Risks for the nitrogen dioxide analyzer and the
608 applicable controls are discussed in the follow subsections.

609

610 3.3.1 Nitrogen Dioxide measurement error is a particular risk in the use of Nitrogen
611 Dioxide gas analyzer. False low displayed or alarm values of nitrogen
612 dioxide concentration can result in failure to detect administration of toxic
613 concentrations of nitrogen dioxide. False high displayed alarm values for
614 nitrogen dioxide concentration will raise concerns that the administration
615 device is malfunctioning, or that the nitric oxide cylinder contents are
616 adulterated; the result may be interruption of essential nitric oxide therapy.

617

618 To control the risk of error in measurement of nitric oxide the following
619 specifications, labeling and testing should be incorporated in the design of
620 the nitrogen dioxide analyzer:

621

622

623 a. Concentrations as low as 0 ppm and as high as 5 ppm should be
624 measured by the analyzer with sufficient accuracy. Accuracy should
625 be specified in the labeling. Testing should be performed to
626 demonstrate the accuracy under the conditions of use. The testing
627 conditions in Table 2 should be used (at 37 degrees Fahrenheit). On the

628 basis of current data, accuracy can be considered sufficient if the
 629 displayed value is within 20% of the actual concentration, or 0.5 ppm,
 630 whichever is greater. A 0-90% rise time of 30 seconds is sufficient.
 631 Accuracy results should be stated in the device labeling.
 632

NO ₂ (ppm)	0 ppm NO Ambient pressure 90% Humidification Balance* gas O2	0 ppm NO Ambient pressure 90% Humidification Balance gas Air	20 ppm NO Ambient pressure 90% Humidification Balance gas O2	0 ppm NO 50 CmH ₂ O 90% Humidification Balance gas O2	0 ppm NO Ambient pressure Dry Gas Balance gas O2
0	✓	✓	✓	✓	✓
1	✓	✓	✓	✓	✓
5	✓				
Full Scale	✓				

633 * Balance is the gas to which the 800 or 400 ppm nitric oxide in nitrogen is added. Balance gas should
 634 constitute at least 85% of the tested gas mixture, (volume %).

635

636

Table 2

637

638

639

- b. Labeling should include methods for calibration. Nitrogen dioxide calibration gas suitable for use with the device should be specified by the manufacturer of the nitrogen dioxide gas analyzer. The calibration gas must be labeled with an expiration date, and test data must be provided to demonstrate that the calibration gas is adequately stable for use within the expiration limit, and will permit calibration of the nitrogen dioxide gas analyzer to the analyzer's specified accuracy.

646

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659

- c. The expected life of the sensor or other life-limited components should be specified. Testing to validate the endurance sensor or other life-limited components should include simulated use with the patient circuit as specified in the device labeling, with the humidifier set to simulate the conditions of clinical use.
- d. An upper alarm limit, if provided, should be capable of being set to levels as low as 1 ppm, and be demonstrated to alarm at the set value. Note that a primary nitric oxide administration device should include provisions for nitrogen dioxide gas analysis with an upper concentration alarm.
- e. If the device is for use within or for attachment to a patient breathing

660 circuit operating at other than ambient pressure, accuracy should be
661 verified by testing during simulated positive pressure ventilation
662 generally in accordance with procedures used for testing of oxygen
663 gas analyzers. This information can be found in ASTM F 1462 - 93
664 Specifications for Oxygen Analyzers.

665

666 f. Particular published standards or portions of published consensus
667 standards, and other material in this guidance document address
668 issues such as; software and hardware documentation,
669 electromagnetic compatibility documentation, and environmental
670 documentation. These testing and documentation procedures are
671 discussed in this document in separate sections. Refer to the table of
672 contents for the applicable section.

673

674 3.3.2 Electrical hazards to patients and others may result from the use of electrical
675 devices. Published standards or portions of standards are identified and
676 discussed in Section 5. Compliance with these standards, or equivalent
677 demonstrations of safety, are commonly used in review of medical devices,
678 such as ventilators, to provide adequate control of risks related to various
679 types of malfunctions, and will adequately control the electrical hazards of
680 the nitrogen dioxide analyzer.

681

682 3.3.3 Adverse effects on other electronic devices used for patient care may be
683 result from the use of electrical devices. Published standards or portions of
684 standards for electromagnetic compatibility and testing are identified and
685 discussed in Section 6 of this document as a special control. Compliance
686 with these standards, or equivalent demonstrations of safety, are commonly
687 used in review of medical devices, to provide adequate control of risks
688 related to electromagnetic interference, and will adequately control the
689 electromagnetic interference hazards of the nitrogen dioxide analyzer.

690 **SECTION 4. General Criteria and Testing**

691

692 The following subsections apply to the nitric oxide administration devices, nitric oxide
693 analyzers and nitrogen dioxide analyzers.

694

695 **4.1 General Criteria**

696

697 The 510(k) premarket notification application should include testing information
698 demonstrating safety and effectiveness of the performance characteristics of the device
699 in the intended environment of use. The type of the device and its intended
700 environment will determine the type of testing that is necessary. Recommended
701 environmental, electrical, electromagnetic compatibility, and mechanical test
702 procedures and protocols are discussed in the following sections.

703

704 The submitted information should include the test procedures and protocols, an
705 explanation as to how the test procedures simulate the intended environment of use
706 and are comparable to the test procedures outlined below, test results, and an analysis
707 of the results. If device failure occurs during the testing, a justification as to why such a
708 failure does not affect safety or effectiveness, and/or a description of device
709 modifications (i.e., identification of each modification, rationale for each modification)
710 and follow-up testing demonstrating that the modification alleviates the problem should
711 be provided.

712

713 **4.2 General Test Methods**

714

715 General test methods should be established and utilized for verifying that device
716 performance is within specification when subjected to the environmental testing
717 procedures in the subsequent sections. This testing information should be included in
718 the premarket notification submission. Also, information concerning the design of, and
719 rationale for, the tests used to demonstrate the safety and effectiveness of the device in
720 the intended environment, together with the testing procedures and protocols, results,
721 and analyses of the results, should be provided in the 510(k) premarket notification
722 submission.

723

724 Unless otherwise specified, the test conditions should be as follows:

725

726 Temperature: 15 to 35 C

727 Humidity: 30 to 90 percent

728 Barometric pressure: 68 to 106 kPa

729 Line voltage: 110 V rms to 125 V rms

730

731 For modular devices, test in more than one typical module configuration with the other
732 modules operating.

733

734 The following should be used to verify proper device alarming capabilities and self test
735 functions in the subsequent sections of the test methods.

736

737 a. Visual status indicators (alarms)

738

739 Determine by inspection the presence and proper operation of warning
740 indicators and device status indicators.

741

742 b. Audible status indicators (alarms)

743

744 Determine by inspection the presence and proper operation of the audible
745 status indicators. Measure and record the frequency, temporal
746 characteristics, and sound level of the indicators at 1 meter. Devices
747 intended for home use should feature continuously sounding warning
748 indicators with sound levels not less than 85 dB(A) and warning indicators of
749 devices intended for hospital use should feature sound levels not less than
750 70 dB(A).

751

752 c. Remote alarm

753

754 Determine proper operation of the remote alarm by connecting the remote
755 alarm during the testing of the device and verifying proper response. Also,
756 verify that use of remote alarms does not disable the device's alarms.

757

758 d. Self test

759

760 If a self test capability is part of the device design, the self test capability
761 should be verified. Determine by inspection the presence and proper
762 operation of an indicator self-test capability that exercises all indicators upon
763 turn-on. Determine by inspection, the presence or absence of a sensing
764 and/or functional self-test. If a functional self-test is present, verify its
765 operation.

766

767 **SECTION 5. Electrical Safety**

768

769 **5.1 Performance Criteria**

770

771 **5.1.1 Battery power**

772

773 a. When a line-powered medical device is equipped with a battery power
774 back-up, this battery back-up should, unless the overcurrent protection
775 mechanism described in paragraph 5.1.3 of this section has activated,
776 automatically activate when power fails for any other reason. The device
777 should operate within its specification within 5 seconds or less after the
778 battery backup power activates.

779

780 b. On medical devices equipped with a battery back-up system, the battery,
781 when charged fully, should be capable of supplying power for normal
782 operation for the time duration specified in the device specifications, and
783 consistent with its intended use.

784

785 c. When a battery back-up is provided, audible and visual battery depletion
786 warning indicators should be provided that activate when the battery
787 depletes to a level of charge that is approaching the lower limit of power that
788 can operate the device within its specification. The operating time between
789 the onset of the battery depletion alarm and the end of normal device
790 operation should be stated in the device specification. The alarm should
791 remain activated during this period.

792

793 d. Housings containing batteries from which gases can escape during charging
794 or discharging should be ventilated to minimize the risk of accumulation and
795 ignition. Battery compartments shall be designed to prevent the risk of
796 accidentally short-circuiting the battery.

797

798 e. If a safety hazard or device malfunction might develop by the incorrect
799 connection or replacement of a battery, the device should be fitted with a
800 means of preventing incorrect polarity of connection.

801

802 **5.1.2 Electrical power indicators**

803

804 a. Power visual status indicators should be provided to indicate that the device
805 is energized. Such indicators should be located conspicuously on the device
806 and should distinguish between battery power and line power sources when

807 both sources are provided.

808

809 b. In devices incorporating a means for battery charging, the charging mode
810 should be visibly indicated to the operator.

811

812 5.1.3 Overcurrent protection

813

814 a. Overcurrent protection should be provided for all line-powered devices.

815

816

817 b. An audible warning status indicator should be activated if the overcurrent
818 protection mechanism is activated and operation of the device cannot occur.
819 This status indicator (alarm) should be capable of sounding for the time
820 duration identified in device specifications.

821

822 c. Medical devices should not be fitted with protective mechanisms which
823 cause disconnection of the device from the power line (supply mains) by
824 producing a short-circuit which results in operation of an overcurrent
825 protection mechanism.

826

827 5.1.4 Dielectric withstand

828

829 Power source conductors, patient contact circuits, and transducer circuits should be
830 adequately insulated to assure protection of the patient and device from over voltages.
831 Therefore, the device should meet the requirements of IEC 601-1, Clause 20.

832

833 5.1.5 AC power grounding and polarity

834

835 If the device power connector is not polarized, the device should operate within its
836 specification in both polarities of power line connector insertion. Devices that operate
837 or recharge batteries from the ac power line shall operate within specifications when
838 operating from a grounded or an ungrounded power source (i.e., with the third-wire
839 ground connected and with it disconnected at the plug end of the power cord).

840

841 5.1.6 Leakage current

842

843 The leakage current testing procedures and protocols, test results including leakage
844 current measurements, and identification of standards to which the measured leakage
845 current complies should be provided in the 510(k) premarket application. Devices
846 should meet the requirements of IEC 601-1.

847

848 5.1.7 Auxiliary output

849

850 Where an auxiliary output is provided:

851

852 a. The device should operate within its specification during and after
853 application of a short-circuit applied to the auxiliary output for 1 minute.

854

855 b. The leakage current requirements of 5.1.6 should not be exceeded upon
856 proper connection of an auxiliary device to the auxiliary output. This proper
857 connection should be described in the operator's manual.

858

859

860 5.2 Test Methods

861

862 For modular devices, test in more than one typical module configuration with the other
863 modules operating.

864

865 5.2.1 Battery power

866

867 a. For ac powered devices with battery back-up, with the device powered from
868 the ac line, simulate normal operation. Remove ac power and determine if
869 battery back-up power activates within 5 seconds. With the device operating
870 on battery power, test as discussed in Sections 4.1 and 4.2. Failure of the
871 device to perform within its specification should constitute failure of this test.

872

873 b. Operate the device from a fully charged battery. After operation for 90
874 percent of the battery power time duration specified in the device
875 specifications, test in accordance with Sections 4.1 and 4.2. Failure of the
876 device to perform within its specification should constitute failure of this test.

877

878 c. Operate the device from a fully charged battery. Record the start time and
879 the time at which battery depletion is indicated. Test in accordance with
880 Sections 4.1 and 4.2 and verify that battery depletion to the level at which
881 the device fails to operate occurs no less than the minimum time duration
882 defined in the device specifications after indication of battery depletion.
883 Failure of the device to perform within its specification should constitute
884 failure of this test.

885

886 d. Determine by inspection that housings containing batteries from which gases

887 can escape during charging or discharging are adequately vented.
888 Determine by inspection that battery compartments are designed to prevent
889 accidental short-circuiting of the battery.

890

891 e. For user-replaceable batteries, attempt to incorrectly connect, insert, or
892 replace the battery. Determine by inspection that there is clear indication
893 that the device is not functioning. Then insert or connect the battery
894 correctly and test the device in accordance with Sections 4.1 and 4.2.
895 Failure of the device to perform within its specification should constitute
896 failure of this test.

897

898 5.2.2 Electrical power indicators

899

900 a. Determine by inspection that visual status indicators indicate when the
901 device is energized and that they distinguish between battery power and line
902 power sources when both sources are provided.

903

904 b. For devices incorporating a means for battery charging, place the device in
905 the charging mode and determine by inspection that the charging mode is
906 visibly indicated.

907

908 5.2.3 Overcurrent protection

909

910 a. For ac line-powered devices, determine by inspection the presence of
911 overcurrent protection.

912

913 b. For ac line-powered devices, activate the overcurrent protection mechanism.
914 Record the time at which the audible warning status indicator activates and
915 the time at which it ceases to sound. Failure of the alarm to activate or to
916 sound for at least the time duration identified in the device specifications
917 should constitute failure of this test.

918

919 c. For ac line-powered devices, operate from a power distribution strip that
920 incorporates a slow-blow fuse or a circuit breaker appropriately rated for the
921 device under test. Activate the device overcurrent protection mechanism.
922 Activation of the power distribution strip fuse or circuit breaker should
923 constitute failure of this test.

924

925 5.2.4 Dielectric withstand

926

927 Test for dielectric withstand in accordance with Clause 20 and Appendix E of IEC
928 601-1.

929

930 5.2.5 AC power grounding and polarity

931

932 For devices that recharge batteries or operate from the ac power line, disconnect all
933 connections to ground and test the device in accordance with Sections 4.1, 4.2, 5.2.1.a,
934 and 5.2.3. If the ac power connector is not polarized, reverse the polarity of the ac
935 connection and repeat the test. Failure of the device to perform within its specification
936 should constitute failure of this test.

937

938 5.2.6 Leakage current

939

940 Test the device in accordance with IEC 601-1 or in accordance with other applicable
941 standards with leakage current specifications.

942

943 5.2.7 Auxiliary output

944

945 If the device is provided with an auxiliary output:

946

947 a. This output should be short-circuited (all pins connected together) for at least
948 1 minute, with the device in the standard operating modes. During and after
949 application of the short-circuit, the device should operate within its
950 specification.

951

952 b. With the auxiliary output connected as specified by the manufacturer, test
953 device per 5.2.6.

954

955 **SECTION 6. Electromagnetic Compatibility**

956

957 **6.1 Performance Criteria**

958

959 Devices should meet the electromagnetic compatibility requirements contained in
960 sections 6.1 and 6.2 and should also meet these requirements when recharging
961 batteries (if applicable) from or operating from a grounded or an ungrounded ac power
962 source (i.e., with the third-wire ground connected and with it disconnected at the plug
963 end of the power cord).

964

965 **6.1.1 Emissions**

966

967 The device should operate within its specification without emitting electromagnetic
968 energy in excess of the levels specified below. The required emission limit should be
969 that specified by the referenced document, adjusted downward by the rms sum of all
970 errors in the measurement of that quantity.

971

972 **6.1.1.1 Radiated and conducted electromagnetic energy**

973

974 The device should comply with the relevant requirements of CISPR 11 when tested
975 according to the specified test methods of this guidance document.

976

977 **6.1.1.2 Magnetic fields**

978

979 The device should comply with the relevant requirements of RE101 (Army, 7-cm
980 distance) of MIL-STD-461D from 30 Hz to 100 kHz when tested at the 7-cm distance
981 according to RE101 of MIL-STD-462D.

982

983 **6.1.2 Immunity**

984

985 The device should operate within its specification during and after exposure to
986 electromagnetic interference at the levels specified below. The required immunity level
987 should be the level stated, adjusted upward by the rms sum of all errors in the
988 measurement of that quantity, with the exception of the lower steady-state ac voltage
989 limit and the line-voltage sag level, which should be adjusted downward by the rms sum
990 of the measurement errors. The device should not, as a result of the specified test
991 condition: indicate an equipment alarm, exhibit temporary degradation or loss of
992 function or performance which requires operator intervention or system reset, or exhibit
993 loss or corruption of stored data. Details of test conditions are specified in section 6.2
994 of this guidance document.

995

996 6.1.2.1 Electrostatic discharge

997

998 The device should operate within its specification within 5 seconds of air discharges of
999 2, 4, 6, and 8 kV applied to insulating surfaces and contact discharges of 2, 4, and 6 kV
1000 applied to conductive surfaces, both positive and negative, to include any point on the
1001 device accessible to the operator or patient, when tested according to IEC 801-2, as
1002 specified in section 6.2. The device should operate within its specification within 5
1003 seconds of contact discharges applied to horizontal and vertical conducting planes in
1004 the vicinity of the device, as specified in section 6.2.

1005

1006 6.1.2.2 Radiated electromagnetic fields

1007

1008 The device should operate within its specification during and after exposure to
1009 electromagnetic fields at frequencies between 26 MHz and 1 GHz at field strengths up
1010 to 3 V/m (when unmodulated), amplitude modulated 80 percent with a sine wave or 100
1011 percent with a square wave. A modulation frequency that is within each significant
1012 signal-processing passband of the device should be used. For devices not having a
1013 defined passband, a modulation frequency of 0.5 Hz should be used. The modulation
1014 frequency should be specified in 510(k) premarket notification.

1015

1016 6.1.2.3 AC voltage fluctuations, transients, and surges

1017

1018 The following items apply to all devices that recharge batteries from or operate from the
1019 ac power line:

1020

1021 a. Steady-state voltage

1022

1023 The device should operate within its specification, without changing a
1024 voltage selection switch, when powered from line voltages between 95 and
1025 132 volts rms. The battery power back-up, if featured, should automatically
1026 activate when the line voltage falls below the minimum level necessary for
1027 line-powered device operation, which should be no greater than 95 volts
1028 rms, and line-powered operation should automatically resume when the line
1029 voltage returns to the 95-to-132-volt range.

1030

1031 b. Dropout

1032

1033 The device should operate within its specification during and after line
1034 voltage dropouts for durations of 10 milliseconds and less.

1035 c. Slow sags and surges

1036

1037 The device should operate within its specification during and after line
1038 voltage surges to 150 V rms and sags to 90 V rms for durations of 500 ms
1039 and less.

1040

1041 d. Fast transient bursts

1042

1043 The device should operate within its specification during and after bursts of
1044 transients of 0.5, 1, and 2 kV applied to ac power leads and transients of
1045 0.25, 0.5, and 1 kV coupled by way of a capacitive clamp to signal leads,
1046 when tested according to IEC 801-4, with the exception that the burst
1047 repetition frequency should not exceed 30 per minute.

1048

1049 e. Fast surges

1050

1051 The device should operate within its specification during and after exposure
1052 to combination voltage/current transients applied to AC power leads as
1053 specified in section (m) from a test generator as follows:

1054

1055 Open-circuit voltage, differential mode: 1 kV

1056 Open-circuit voltage, common mode: 2 kV

1057 Open-circuit voltage risetime: 1.2 microseconds

1058 Open-circuit voltage falltime: 50 microseconds

1059 Generator source impedance: 2 ohms

1060 Short-circuit current risetime: 8 microseconds

1061 Short-circuit current falltime: 20 microseconds

1062 Surge repetition rate: 1 per minute

1063

1064 6.1.2.4 Conducted electromagnetic energy

1065

1066 The device should operate within its specification during and after exposure of each
1067 interconnecting cable, including power cables, to conducted electromagnetic energy at
1068 frequencies between 10 kHz and 100 MHz at the levels specified in CS114, Curve #3,
1069 of MIL-STD-461D, when tested according to CS114 of MIL-STD-462D. A modulation
1070 frequency that is within each significant signal-processing passband of the device
1071 should be used. For devices not having a defined passband, a modulation frequency of
1072 0.5 Hz should be used. The modulation frequency should be specified in the 510(k)
1073 premarket notification.

1074

1075 6.1.2.5 Magnetic fields

1076

1077 The device should operate within its specification during and after exposure to magnetic
1078 fields at frequencies between 30 Hz and 100 kHz as specified in RS101 (Army) of MIL-
1079 STD-461D, when tested according to RS101 of MIL-STD-462D. A modulation
1080 frequency that is within each significant signal-processing passband of the device
1081 should be used. For devices not having a defined passband, a modulation frequency of
1082 0.5 Hz should be used. The modulation frequency should be specified in the 510(k)
1083 premarket notification.

1084

1085 6.1.2.6 Quasi-static electric fields

1086

1087 The device should operate within its specification during and after exposure to a
1088 sinusoidally varying electric field at 0.5 Hz with peak field strengths up to 2000 volts per
1089 meter. Note: This test simulates the movement of electrostatically charged fabrics and
1090 objects that could come into close proximity to the device.

1091

1092 6.2 Test Methods

1093

1094 Devices should be tested for electromagnetic emissions and immunity to
1095 electromagnetic interference as described herein. Devices should be tested with the
1096 third wire ground connected at the plug end of the power cord. Devices intended for
1097 home use should be tested with the third wire ground connected and with it
1098 disconnected at the plug end of the power cord.

1099

1100 6.2.1 Emissions

1101

1102 Emissions measurements should be made as specified in the referenced document.
1103 The required emission limit should be that specified by the referenced document,
1104 adjusted downward by the rms sum of all errors in the measurement of that quantity.
1105 Emission in excess of the adjusted limit should constitute failure of this test. These
1106 tests should be conducted using passive patient simulators, which in general are not
1107 capable of simulating normal patient signals.

1108

1109 6.2.1.1 Radiated and conducted electromagnetic energy

1110

1111 The device should be tested according to CISPR 11.

1112

1113 6.2.1.2 Magnetic fields

1114

1115 The device should be tested for radiated magnetic field emissions between 30 Hz and
1116 100 kHz as specified in RE101 of MIL-STD-462D, using the Army 7-cm limit.
1117 Measurements should be made at the 7-cm distance only.

1118

1119 6.2.2 Immunity

1120

1121 Immunity of the device to electromagnetic interference should be determined as
1122 specified in the referenced document, with the modifications listed below. The required
1123 immunity level should be the level stated, adjusted upward by the rms sum of all errors
1124 in the measurement of that quantity, with the exception of the lower steady-state ac
1125 voltage limit and the line-voltage sag level, which should be adjusted downward by the
1126 rms sum of the measurement errors. Any of the following should constitute failure of
1127 this test: an equipment alarm, temporary degradation or loss of function or
1128 performance which requires operator intervention or system reset, or loss or corruption
1129 of stored data. Patient simulators should be used to provide simulated normal stimulus
1130 to sensors during electromagnetic immunity testing.

1131

1132 6.2.2.1 Electrostatic discharge

1133

1134 The device should be tested with air discharges at 2, 4, 6, and 8 kV applied to
1135 insulating surfaces and contact discharges at 2, 4, and 6 kV applied to conductive
1136 surfaces. Failure to resume normal operation (with no operator intervention) within 5
1137 seconds of a discharge should constitute failure of this test. All test failure conditions
1138 listed above apply. The device should be tested according to IEC 801-2, with the
1139 following conditions and modifications:

1140

- 1141 a. The device should be tested according to the test method described in IEC
1142 801-2 for table-top equipment.
- 1143 b. The relative humidity should not exceed 50 percent during air discharges.
1144
- 1145 c. Air discharges should be conducted at 2, 4, 6, and 8 kV. Contact discharges
1146 should be conducted at 2, 4, and 6 kV. Discharges of both positive and
1147 negative polarity should be conducted at each voltage.
1148
- 1149 d. In addition to air and contact discharges directly to the device, contact
1150 discharges should be made to the horizontal coupling plane under the
1151 device and to the vertical coupling plane positioned parallel to the faces of
1152 the device. At least 10 single discharges at each test voltage and polarity
1153 should be applied to each test point.
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6.2.2.2 Radiated electromagnetic fields

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a. Test conditions

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i. The device should be tested for immunity to radiated electromagnetic energy over the frequency range 26 MHz to 1 GHz at a field strength of 3 V/m. The RF carrier should be amplitude modulated 80 percent by a sine wave or 100 percent with a square wave. A modulation frequency that is within each significant signal-processing passband of the device should be used. For devices not having a defined passband, a modulation frequency of 0.5 Hz should be used. The modulation frequency should be specified in the 510(k) premarket application.

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ii. If a continuous sweep of the test frequency is used, the sweep rate should not exceed 0.1 MHz/second. If the sweep is incremental, the step size should not exceed 1 MHz and the dwell time at each frequency should be 10 seconds.

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iii. Devices which can operate from both line and battery power should be tested both with the ac power connection (e.g., power cord, battery charger) attached and detached from the device.

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iv. Patient simulators used during the test should be either simple passive devices, isolated from earth ground using fiber optics, or battery operated and shielded.

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v. Connections not normally used during device operation that are made to the device to assess performance during the test should be isolated using fiber optics.

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vi. The radiated electric field should be linearly polarized. The test should be performed with both horizontal and vertical polarization.

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vii. A planar area of uniform field should be established, that contains the front surface of all components of the device under test, including cables. The boundaries of the area of uniform field should include the maximum planar area occupied in any orientation of the parts of the device. The E-field should be measured at multiple points within the

1195 area of uniform field, with all accessories and physical components of
1196 the device removed from the field.

1197

1198 Within the area of uniform field, the uniformity of the component of the
1199 electric field that is aligned with the intended E-field polarization should
1200 be -0, +6 dB, measured with no amplitude modulation present on the
1201 exposure field. At a minimum, point measurements should be
1202 performed at every incremental frequency in the 26 to 1000 MHz
1203 frequency range as specified in 6.2.2.2.ii. E-field measurements
1204 should be made at uniformly spaced points throughout the entire
1205 surface of the area of uniform field for both horizontal and vertical
1206 polarization. The spacing between these points in both the vertical
1207 and horizontal directions should be 0.5 m or less. At each point, the
1208 component of the E-field that is aligned with the intended polarization
1209 should not differ from the total E-field at that point by more than 3 dB.

1210

1211

1212 For a given facility, if placement of absorber, antennas, and area of
1213 uniform field are carefully reproduced, it should be necessary to map
1214 the area of uniform field only occasionally, e.g. once per year. Prior to
1215 a series of tests, the area of uniform field should be checked along a
1216 vertical line near the center, with measurements made at uniformly
1217 spaced points having a spacing of 0.5 m or less. The E-field
1218 measured at these points should meet the uniformity requirements
1219 specified above.

1220

1221 RF electric field instruments and measurement procedures should
1222 meet the requirements of ANSI/IEEE C95.3 - 1991. The instruments
1223 should not perturb the E-fields being measured by more than 2 dB and
1224 should measure local E-field strength with an error of less than ± 3 dB
1225 over the frequency range of use. The field-sensing elements of the
1226 instrument should fit within a spherical volume with a diameter of 15
1227 cm. The instrument should be capable of measuring the magnitude of
1228 each of the three orthogonal components of the electric field. In
1229 addition, the instrument should be capable of determining the total
1230 electric field strength (the square root of the sum of the squares of the
1231 three E-field vector components). The above measurements should
1232 be measured accurately (± 1 dB) regardless of the direction of the
1233 radiated electric field (i.e., the field measuring instrument should be
1234 isotropic).

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viii. When practical, the test should be repeated with each of the six faces of the device facing the antenna. To the extent possible, all cables should be horizontal over the majority of their length throughout the test.

ix. One or more of the following exposure methods should be used: (1) an open-area test site, with the signal and power leads fully extended horizontally; (2) an anechoic chamber; (3) a parallel-plate line; (4) a screen room; (5) a semi-anechoic chamber; or (6) a TEM cell. In order to cover the entire frequency range, combinations of several exposure methods may be used over the portions of the range for which they are most appropriate. Where the methods yield different results, the open-site test should take precedence from 26 to 200 MHz and the anechoic chamber test should take precedence from 200 MHz to 1 GHz.

a. Test setup

i. When practical, all device components and cables should be elevated at least 0.8 m above any conducting ground plane by low dielectric constant (<2.5), nonconducting RF-transparent material. When this is not possible, device components should be mounted on a bulk non-conducting support at least 0.1 m high. All device components should be at least 0.8 m away from any RF-reflecting objects (e.g., walls of the exposure facility). The distance may need to be increased at certain frequencies to achieve the required field uniformity.

ii. For exposure methods in which the device cables cannot be extended fully, if the length of any conducting cable is 1 m or less, it should be arranged horizontally in the planar area of uniform field. If the length of any conducting cable is greater than 1 m in length, up to the first three meters should be bundled in a serpentine configuration in the planar area of uniform. Conductive leads should be configured on a clean, dry, plastic foam (e.g., Styrofoam[®]) sheet with the dimensions and construction. Support pegs should be made of dielectric (e.g., Teflon[®]) rods (one quarter inch in diameter). Cables in excess of 3 m should be bundled low-inductively and placed on the non-conducting support.

iii. RF/EMI filters should be used at the device's ac power plug.

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6.2.2.3 AC voltage fluctuations, transients, and surges

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The tests described below should be performed on all devices intended to recharge batteries or operate from the ac power line.

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a. Steady-state voltage

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- i. Raise the line voltage to 132 volts rms and allow the device to stabilize. Test device operation according to sections (k) and (l). Repeat for a voltage of 95 volts rms.

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- ii. For devices with battery backup, simulate normal patient signals while reducing the line voltage to zero. Record the voltage at which the device switches to battery power. In addition to the failure criteria listed above, failure of the device to automatically switch to battery power, or switching to battery power before the line voltage reaches 95 volts rms should constitute failure of this test. Continue to test device operation while raising the line voltage to 120 volts rms. In addition to the failure criteria listed above, failure of the device to automatically switch to line power when the line voltage exceeds 95 volts rms should constitute failure of this test.

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b. Dropout

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Operate the device at 95 volts rms, lower the line voltage to 0 volts for 10 milliseconds, and then restore it to 95 volts rms, doing so 10 times at a rate not to exceed 30 per minute.

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c. Slow sags and surges

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Operate the device at 120 volts rms. Raise the line voltage to 150 volts rms for 500 ms. Repeat at 10-second intervals for a total of 10 times. Again operate the device at 120 volts rms. Lower the line voltage to 90 volts rms for 500 ms. Repeat at 10-second intervals for a total of 10 times.

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1311

d. Fast transient bursts

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1313

Test ac power leads and signal leads according to IEC 801-4 for type test of table-top equipment, with the exception that the burst repetition frequency

1314

1315 should not exceed 30 per minute. Test supply leads at 0.5, 1, and 2 kV, and
1316 signal leads at 0.25, 0.5, and 1 kV.

1317

1318 e. Fast surges

1319

1320 i. Test generator

1321

1322 (a) The values of elements R_{s1} , R_{s2} , R_m , L_r , and C_c are such that the
1323 generator delivers at a single output a combination voltage/current
1324 wave characterized by a 1.2/50 μ s voltage surge when measured
1325 across a high-resistance load (more than 100 ohms) and a 8/20 μ s
1326 current surge when measured into a short circuit, i.e. the generator
1327 has an effective output impedance of 2 ohms.

1328

1329 (b) The generator should be capable of producing an open circuit
1330 output voltage of up to 2 kV, both positive and negative polarity, with
1331 wave. The generator should be capable of delivering short circuit
1332 output current of at least 1 kA.

1333

1334 The generator should be triggerable so that the phase angle of the
1335 discharge can be set at 0, 90, 180, and 270 degrees with respect to
1336 the ac line voltage.

1337

1338 ii. Test setup

1339

1340 (a) Capacitive coupling should be used to apply the combination wave
1341 to the ac power leads of the device under test.

1342

1343 (b) A decoupling network should be used to isolate the device under
1344 test from the ac power network. Residual test pulse voltage on
1345 unsurged leads should not exceed 15 percent of the maximum applied
1346 test voltage when the device is disconnected. Residual test pulse
1347 voltage on the inputs of the decoupling network when the device and
1348 the power supply network are disconnected should not exceed 10
1349 percent of the applied test voltage or twice the peak value of the power
1350 line voltage, whichever is greater.

1351

1352 (c) Surges should be applied at the point where the device would
1353 normally be connected to ac line power.

1354

- 1355 (d) For the line-to-line test, an 18-uF coupling capacitor should be
1356 used.
- 1357
- 1358 (e) For the line-to-ground tests, a 10-ohm resistor should be used in
1359 series with the test generator and a 9-uF coupling capacitor should be
1360 used.
- 1361
- 1362 iii. Test procedure
- 1363
- 1364 (a) The line-to-line test should be performed using 1-kV surges of both
1365 positive and negative polarity applied using a generator source
1366 impedance of 2 ohms and coupling capacitance of 18 uF with the
1367 generator output floating.
- 1368
- 1369 (b) The line-to-ground test should be performed using 2-kV surges of
1370 both positive and negative polarity applied using a generator source
1371 impedance of 12 ohms and coupling capacitance of 9 uF with the
1372 generator output grounded. The test should be repeated with surges
1373 applied successively between each line and ground.
- 1374
- 1375 (c) Surges at each amplitude and polarity should be applied at phase
1376 angles of 0, 90, 180, and 270 degrees with respect to the ac line.
- 1377
- 1378 (d) Each test should be repeated 10 times at a rate of 1 surge per
1379 minute.
- 1380

1381 6.2.2.4 Conducted electromagnetic energy

1382

1383 The device should be tested for immunity to conducted electromagnetic energy on each
1384 power and signal lead at frequencies between 10 kHz and 100 MHz at the levels
1385 specified in curve #3 of CS114 of MIL-STD-461D, using the test methods specified in
1386 CS114 of MIL-STD-462D, with the modifications and additions listed below.

1387

- 1388 a. If continuous sweep of the test frequency is used, the sweep rate should not
1389 exceed 1×10^{-3} decades/second. If the sweep is incremental, the step size
1390 should not exceed 1 percent of decade, and the minimum dwell time is 10
1391 seconds per step.
- 1392
- 1393 b. A modulation frequency that is within each significant signal-processing
1394 passband of the device should be used. For devices not having a defined

- 1395 passband, a modulation frequency of 0.5 Hz should be used.
1396
1397 c. The leads under test should be elevated 5 cm above the ground plane.
1398
1399 d. For power cables, the interference signal should be injected at a distance of
1400 5 cm from the point at which ac line power enters the device. For battery
1401 chargers which plug directly into ac outlets, a 10 cm length of wire should be
1402 added between the LISN and the charger, and the test signal should be
1403 injected 5 cm from the charger. The low-voltage output cable of the charger
1404 should be elevated 5 cm above the ground plane.
1405

1406 6.2.2.5 Magnetic fields

1407
1408 Test according to RS101 of MIL-STD-462D. The test should be performed from 30 Hz
1409 to 100 kHz.
1410

1411 6.2.2.6 Quasi-static electric fields

- 1412
1413 a. Test setup
1414
1415 i. The device should be tested between parallel horizontal planes. They
1416 should be metallic sheets (copper or aluminum) of 0.25 mm minimum
1417 thickness which extend at least 0.1 m beyond the device. The
1418 horizontal planes should be separated by insulating material, with a
1419 separation at least three times the height of the device in the position
1420 of normal use.
1421
1422 ii. The device should be supported by insulating material so that it is
1423 positioned entirely between 1/3 and 2/3 the distance between the
1424 horizontal planes.
1425
1426 iii. Cables and tubing should be supported by insulating material at a
1427 height above the bottom horizontal plane of 1/3 the distance between
1428 the planes and should exit the test apparatus and continue at this
1429 height for at least 0.1 meter beyond the horizontal planes.
1430
1431 iv. The output of a signal generator capable of producing a sinusoidally
1432 varying voltage at a frequency of 0.5 Hz with amplitude sufficient to
1433 produce peak electric field strengths up to 2000 V/m between the
1434 horizontal planes should be connected to the horizontal planes.

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Note: $E_p = V_p/D$, where E_p is the peak field strength in V/m, V_p is the peak of the signal generator output voltage waveform, and D is the distance between the horizontal planes in meters.

b. Test procedure

Adjust the signal generator peak output voltage such that the device is exposed to a sinusoidally varying electric field at 0.5 Hz with peak field strength of 500 V/m.

Gradually increase the peak field strength to 2000 V/m.

1446 **SECTION 7. Performance Specifications, Environmental and Mechanical**
1447 **Safety**

1448
1449 7.1 Performance Criteria

1450
1451 7.1.1 Controls protection

1452
1453 The controls of medical devices should be protected from inadvertent or unauthorized
1454 changes or adjustment. The means of protection should be such as to preclude their
1455 defeat by patients, or other unauthorized persons.

1456
1457 All controls which increase or decrease a function should be marked with a legible
1458 indication to inform the operator which action(s) is (are) required to increase/decrease
1459 the controlled function. Controls and their associated markings should be visible or
1460 legible, or both, to an operator having a visual acuity of at least 1.0 when the operator is
1461 located at least 1 meter in front of the device and the ambient illuminance level is 215 lx,
1462 when viewing the information, marking, etc. perpendicular to, and including 15 degrees
1463 above, below, left and right. Controls should be identified with their associated
1464 markings.

1465
1466 For controls, movement upwards, to right, or in a clockwise direction should increase
1467 the control function. Movement downwards, to the left, or a counterclockwise direction
1468 should decrease the control function. Rotary gas flow controls are exempt from this
1469 performance criterion.

1470
1471 7.1.2 Connector protective incompatibility

1472
1473 a. Device connectors, including those on wires and tubing, should be designed
1474 such that insertion into a receptacle other than the one into which they are
1475 intended to be inserted or into a receptacle using an improper orientation
1476 should not be possible.

1477
1478 b. Electrical connectors of a device (e.g., electrical lead wires) should include a
1479 mechanism to prevent connection of the patient to a power source that may
1480 cause a current flow in excess of that specified in paragraph (h)(6).

1481
1482 7.1.3 Mechanical safety

1483
1484 Each device should:

1485

- 1486 a. Not have any exposed sharp edges.
1487
1488 b. Be mechanically stable in the intended position(s) of use.
1489
1490 c. Provide protection to the operator and patient from moving parts.
1491

1492 7.1.4 Mechanical vibration and shock resistance 1493

1494 The device (i.e., the complete system suitable for its intended use) should withstand the
1495 mechanical shocks and vibrations expected in the environments of intended use as
1496 defined by the test methods contained herein, and should remain operational within its
1497 specification.
1498

1499 7.1.5 Fluid spill resistance 1500

1501 The device should be so constructed that it continues to operate within its specification
1502 after fluids have been dripped on the device. Therefore, the device should meet the
1503 requirements for drip-proof equipment as specified in Clause 44.6 of IEC 601-1 and IEC
1504 529.
1505

1506 7.1.6 High and low temperature and humidity 1507

- 1508 a. The device should operate within its specification when operating in the
1509 environmental temperature range of 5 C to 40 C, and in the environmental
1510 humidity range of 15 percent to 95 percent, noncondensing.
1511
1512 b. The device should not be damaged and should remain operational within its
1513 specification after storage in the environmental temperature range of -20 C
1514 to 60 C and at relative humidity up to 95 percent, non-condensing.
1515

1516 7.1.7 Surface temperature 1517

1518 Temperature of surfaces of a device an operator can contact during operation should
1519 not exceed 50 degrees C in an ambient of 35 degrees C. The temperature of surfaces
1520 that may come in contact with the patient should not exceed 41 degrees C in an
1521 ambient of 35 degrees C. Any surface temperature that may come in contact with the
1522 patient exceeding 41 degrees C, should be justified with a scientifically valid
1523 explanation and data should be provided which demonstrates that the safety of the
1524 patient is not compromised.
1525

1526 7.1.8 Toxic materials

1527

1528 No toxic material from a device should come in contact with patient or operator during
1529 normal use.

1530

1531 7.1.9 Strangulation

1532

1533 Provision should be made in routing, retention devices, or other means to minimize the
1534 risk of strangulation of the patient by wires or tubing. This may also be accomplished
1535 by providing instructions for routing of patient wires and tubing in the device labeling.

1536

1537 7.1.10 Determination of Endurance

1538

1539 Compliance with device specifications should be determined with one or more samples
1540 of production system or components of the system (Nitric Oxide analyzer or Nitrogen
1541 Oxide analyzer). Each system or component should be tested for endurance as
1542 described in 7.2.11. The system should run for 2000 h.

1543

1544 7.1.11 Material Compatibility

1545

1546 Parts should be made of materials that are compatible with the gases and agents with
1547 which those components are designed to come into contact, and minimize health risks
1548 due to substances leached from the device in use.

1549

1550 7.1.12 Medical Gas Cylinder Connections

1551

1552 Connectors of calibration gas cylinders not already specified in relevant national
1553 standards such as CGA C-9-1982 should be designed differently from the connectors
1554 specified for other medical gases.

1555

1556 7.2 Test Methods

1557

1558 7.2.1 Controls protection

1559

1560 Test by inspection.

1561

1562 7.2.2 Connector protective incompatibility

1563

1564 Test by inspection and by attempting the prohibited connections.

1565

1566 7.2.3 Mechanical safety

1567

1568 Test by inspection.

1569

1570 7.2.4 Mechanical vibration and shock resistance

1571

1572 Test the device (i.e., the complete system suitable for its intended use) to the following
1573 severity levels as specified in the following IEC 68-2 Basic Environmental Testing
1574 Procedures. Following each of these tests, the device should be visually inspected.
1575 Any evidence of damage or inability to perform within specification should constitute
1576 failure of the test.

1577

1578 a. IEC 68-2-27: SHOCK
1579 Peak acceleration: 100 g (980 m/s²)
1580 Duration: 6 msec
1581 Pulse shape: half sine

1582

1583 b. IEC 68-2-6 SINUSOIDAL VIBRATION
1584 Frequency range: 10 to 500 Hz
1585 Acceleration amplitude: 1 g (9.8 m/s²)
1586 Type and duration of endurance: 10 sweep cycles in each axis.

1587

1588 c. IEC 68-2-34 RANDOM VIBRATION, WIDE BAND
1589 Frequency range: 20 Hz - 500 Hz
1590 Acceleration spectral density: 0.02 g²/Hz
1591 Degree of reproducibility: low
1592 Duration of conditioning: 9 minutes

1593

1594 7.2.5 Fluid spill resistance

1595

1596 Test the device as specified in Clause 44.6 of IEC 601-1 for drip-proof and equipment.
1597 Following each of these tests, the device should be visually inspected. Any evidence of
1598 damage or inability to perform within specification should constitute failure of the test.

1599

1600 7.2.6 High and low temperature and humidity

1601

1602 Test the device as specified in Method Numbers 501.3, 502.3, and 507.3 of MIL-STD-
1603 810E according to the requirements of section (i)(6) of this document. Failure of the
1604 device to perform within its specification should constitute failure of these tests.

1605

1606 7.2.7 Surface temperature

1607

1608 Operate the device in an ambient temperature of 35 C. Measure the temperature of the
1609 device surfaces which are not intended to contact the patient. The presence of any
1610 temperature greater than 50 C should constitute failure of this test. Measure the
1611 temperature of device surfaces which are likely to contact the patient in normal use.
1612 Any temperature above 41 C should constitute failure of this test.

1613

1614 7.2.8 Toxic materials

1615

1616 Determine by inspection that listed and any other known toxic materials used in the
1617 device are packaged in a manner that prevents patient and operator contact.

1618

1619 7.2.9 Strangulation

1620

1621 Test by inspection.

1622

1623 7.2.10 Determination of Endurance

1624

1625 Simulated testing should be performed using a ventilator, test lung, humidifier, delivery
1626 apparatus and analyzers. The inspiratory/expiratory phase time ratio should be as
1627 close to 1:2 as possible, and run the test system for 2000 hours with appropriate patient
1628 population settings. The delivery apparatus should titrate at least 20 ppm of Nitric
1629 Oxide throughout the duration of the testing.

1630

1631

1632 7.2.11 Material Compatibility

1633

1634 Parts which come in contact with the gases and agents should be revalidated to ensure
1635 that the specifications are met after the endurance testing. Simulated testing should
1636 address issues such as corrosion and chemical interaction which could affect
1637 mechanical or electrical properties.

1638

1639 **SECTION 8. Hardware Documentation**

1640

1641 This information should include a description of the hardware requirements, device
1642 performance requirements, the potential system hazards, and the hardware and/or
1643 software functions implemented as a result of such potential hazards. Documentation
1644 of the hardware development process including quality assurance activities,
1645 configuration management plan, and verification activities and summaries, in
1646 accordance with the appropriate level of concern, should also be provided. The
1647 hardware information should include the most recent verification and validation test
1648 plans/protocols, identification of which activities were performed prior to and after
1649 hardware/software integration, verification and validation results, and analyses showing
1650 that specifications were met at each appropriate level of hardware. Written affirmation
1651 stating that the described hardware was developed and tested according to the stated
1652 procedures/methods and test showed requirements were met should be provided. The
1653 hardware information should also identify of the version level featured in the final design
1654 of the device.

1655

1656 **SECTION 9. Software Documentation**

1657

1658 If the device is software-driven, the premarket notification should include software
1659 information in accordance with the Guidance for the content of Premarket Submissions
1660 for Software Contained in Medical Devices. This information should include a
1661 description of the software requirements, device performance requirements, the
1662 potential system hazards, and the software and/or hardware functions implemented as
1663 a result of such potential hazards. Documentation of the software development
1664 process including quality assurance activities, configuration management plan, and
1665 verification activities and summaries, in accordance with the appropriate level of
1666 concern, as discussed in the current guidance for software, should also be provided.
1667 The level of concern should be identified with the hazard analysis. The software
1668 information should include the most recent verification and validation test
1669 plans/protocols, identification of which activities were performed prior to and after
1670 software/hardware integration, verification and validation results, and analyses showing
1671 that specifications were met at each appropriate level of software. Written affirmation
1672 stating that the described software was developed and tested according to the stated
1673 procedures/methods and test showed requirements were met should be provided. The
1674 software information should also identify of the software version level featured in the
1675 final design of the device.

1676

1677 **SECTION 10. Labeling**

1678

1679 The premarket notification should include all labeling (i.e., device labels, instructions for
1680 use, promotional material) for the device under review. Recommendations for labeling
1681 content are included in the Device Labeling Guidance (ODE Blue Book #G91-1) and
1682 specific labeling discussed in this guidance.

1683

1684 The nitric oxide administration apparatus, nitric oxide gas analyzer, and nitrogen dioxide
1685 gas analyzer are restricted to use only upon the written or oral authorization of a
1686 practitioner licensed by law to use the device and that the device be restricted to use by
1687 persons with experience or training in its use. In accordance with 21 CFR
1688 801.109(b)(1), the labeling for prescription devices is required to bear the required
1689 caution prescription statement. This statement should read, "Caution: Federal law
1690 restricts this device to sale by or on the order of a physician or other licensed medical
1691 practitioner.

1692

1693 The nitric oxide administration apparatus, nitric oxide gas analyzer, and nitrogen dioxide
1694 gas analyzer labeling should include a warning that "Persons using this device should
1695 be trained and experienced in the use of this device, to assure effective administration
1696 of nitric oxide, and to avoid injury to the patient or to others resulting from inhalation of
1697 excess nitric oxide, nitrogen dioxide or other reaction products."

1698

1699 **10.1 Identification of Medical Gas Cylinders and Connections**

1700

1701 Colors of calibration gas cylinders not already specified in relevant national standards
1702 such as CGA C-9-1982 shall be color-coded differently from the colors specified for
1703 medical gases.

1704

1705 **10.2 Instructions for Use**

1706

1707 **10.2.1 Intended Use**

1708

1709 The instructions for use should include a description of the intended use and a
1710 description of the principles of operation of the components of the Nitric Oxide System

1711

1712 **10.2.2 Validated Ventilators**

1713

1714 The instructions for use should include a list of ventilators that have been validated for
1715 use with the nitric oxide administration device, nitric oxide analyzer and nitrogen dioxide
1716 analyzer.

1717

1718 10.2.3 Installation Instructions

1719

1720 The instructions for use should include a description of the correct installation of the
1721 Nitric Oxide System or any of its components.

1722

1723

1724

Document Update and Revision Log

1725

1726 The log below identifies the most current configuration of the document. For easy
 1727 identification, the version number and version date are printed on the top right and top
 1728 left corners of each page. Copies of the document and the most current revision log
 1729 are available from FDA/CDRH/OHIP Division of Small Manufacturers Assistance, 1-
 1730 800-638-2041.

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1733	<u>Version</u>	<u>Dated</u>	<u>Section(s)</u>	<u>Pages</u>	<u>Comments</u>
1734	draft 1.0	1/13/97			
1735	draft 1.1	7/22/97	all		internal
1736	draft 1.2	6/10/99	all		internal
1737	draft 1.3	9/16/99	Intro, 8		internal
1738	draft 1.4	11/22/99	Background		internal
1739			Special control wording included		
1740	Final 1.0	1/7/00			