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# Certification Process for Designated Medical Gases

## Guidance for Industry

### ***DRAFT GUIDANCE***

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For questions regarding this draft document contact Michael Folkendt at 301-796-1900.

**U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Drug Evaluation and Research (CDER)  
Center for Veterinary Medicine (CVM)**

**November 2015  
Procedural**

**Revision 1**

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**U.S. Department of Health and Human Services  
Food and Drug Administration  
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*Contains Nonbinding Recommendations*

*Draft – Not for Implementation*

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**ATTACHMENT: Request for Certification of Medical Gas**

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**Certification Process for Designated Medical Gases  
Guidance for Industry<sup>1</sup>**

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

**I. INTRODUCTION**

Title XI, Subtitle B of the Food and Drug Administration Safety and Innovation Act (FDASIA)<sup>2</sup> added sections 575 and 576 to the Federal Food, Drug, and Cosmetic Act (FD&C Act), creating a new certification process for approval of designated medical gases. Section 575 defines “designated medical gas” to include oxygen, nitrogen, nitrous oxide, carbon dioxide, helium, carbon monoxide, and medical air that meet the standards set forth in an official compendium. Section 576 permits any person to file a request for certification of a medical gas as a designated medical gas for certain indications specified in the statute. A designated medical gas for which a certification is granted is deemed to have in effect an approved marketing application under Section 505 of the FD&C Act (human drugs), Section 512 of the FD&C Act (animal drugs), or both, depending on the type of certification requested and granted. This guidance explains how the Food and Drug Administration (FDA) administers the certification process. Specifically, the guidance discusses what products qualify as designated medical gases, who should submit a certification request, what information should be submitted, how FDA will evaluate and act on the request, and how FDA plans to enforce these new medical gas provisions.

Until a certification has been granted, anyone marketing a medical gas for human or animal drug use without an approved application under section 505 or 512 of the FD&C Act is marketing an unapproved new drug.<sup>3</sup> See sections 505(a) and 512(a)(1)(A) of the FD&C Act. FDA expects that persons or entities wishing to market designated medical gases for the indication or indications specified in section 576(a)(3)(A)(i) will request certification from FDA, or ensure

<sup>1</sup> This guidance has been prepared by the Office of Regulatory Policy, the Office of Pharmaceutical Quality, and the Office of Compliance in the Center for Drug Evaluation and Research (CDER) and the Office of New Animal Drug Evaluation in the Center for Veterinary Medicine (CVM) at the Food and Drug Administration.

<sup>2</sup> Public Law 112-144, 126 Stat. 993 (July 9, 2012).

<sup>3</sup> See section IV below regarding who should request a certification and section VI below regarding the marketing of carbon monoxide for use in lung diffusion testing.

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36 that the gases they receive and distribute are certified (i.e., are covered by a granted  
37 certification).<sup>4</sup> Gases not intended for human or animal drug use, e.g., gases intended for  
38 industrial applications or non-drug medical applications (such as calibration gases), do not fall  
39 within the definition of “medical gas” provided in section 575(2) of the FD&C Act, and are not  
40 subject to the certification process described in this guidance.

41  
42 To facilitate the process of requesting certifications, FDA has developed a form that requestors  
43 should complete when making their requests (see attachment).

44  
45 This guidance does not discuss how FDA plans to implement its new authority to designate gases  
46 in addition to those listed above<sup>5</sup> or to expand the indications for use for designated medical  
47 gases beyond those specified at section 576(a)(3)(A)(i) of the FD&C Act. This document also  
48 does not discuss any of the other new authorities and obligations related to medical gases added  
49 to the FD&C Act by FDASIA (e.g., section 577 of the FD&C Act and sections 1112 and 1113 of  
50 FDASIA).

51  
52 In general, FDA’s guidance documents do not establish legally enforceable responsibilities.  
53 Instead, guidances describe the Agency’s current thinking on a topic and should be viewed only  
54 as recommendations, unless specific regulatory or statutory requirements are cited. The use of  
55 the word *should* in FDA guidances means that something is suggested or recommended, but not  
56 required.

## **II. THE CERTIFICATION PROCESS**

57  
58  
59  
60 Any person may file a request for certification of a medical gas as a designated medical gas. A  
61 certification request must contain a description of the medical gas for which the certification is  
62 sought, the name and address of the sponsor, the name and address of the facility or facilities  
63 where the medical gas is or will be manufactured, and any other information deemed appropriate  
64 by FDA to determine whether the medical gas is a designated medical gas (see section 576(a)(1)  
65 of the FD&C Act). A certification request is deemed to be granted unless, within 60 days of  
66 filing, FDA finds that (1) the medical gas for which the certification is requested is not a  
67 designated medical gas, (2) the request lacks the information required by section 576(a)(1) noted  
68 at the outset of this paragraph or otherwise lacks sufficient information to permit FDA to  
69 determine that the medical gas is a designated medical gas, or (3) denying the request is  
70 necessary to protect the public health (see section 576(a)(2) of the FD&C Act).

71  
72 A designated medical gas for which a certification is granted is deemed to have in effect an  
73 approved application under section 505 (for gases intended for human use) or 512 (for gases

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<sup>4</sup> Those seeking to market any other medical gas, or seeking to market a designated medical gas (alone or in combination with one or more other medical gases, designated or otherwise) for an indication that is neither specified in 576(a)(3)(A)(i) of the FD&C Act for that designated medical gas or later added by FDA under its authority at section 576(a)(3)(A)(i)(VIII), cannot obtain approval to do so through the certification process and must obtain approval by a different pathway (e.g., a new drug application (NDA) or a new animal drug application (NADA)). See Part IV.A of this draft guidance.

<sup>5</sup> See section 575(1)(H) of the FD&C Act.

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74 intended for animal use) of the FD&C Act (or both) for the indications listed below and is  
75 subject to all applicable post-approval requirements (see section 576(a)(3)(A)(i)). The approval  
76 applies to the designated medical gas alone or in combination, as medically appropriate, with  
77 one or more other designated medical gases for which certifications have been granted (see  
78 section 576(a)(3)(A)(i)).  
79

80 Under section 576, at this time the designated medical gases may be certified only for the  
81 following indications:  
82

- 83 • Oxygen: for treatment or prevention of hypoxemia or hypoxia.
- 84 • Nitrogen: for use in hypoxic challenge testing.
- 85 • Nitrous oxide: for analgesia.
- 86 • Carbon dioxide: for use in extracorporeal membrane oxygenation therapy or respiratory  
87 stimulation.
- 88 • Helium: for treatment of upper airway obstruction or increased airway resistance.
- 89 • Medical air: to reduce the risk of hyperoxia.
- 90 • Carbon monoxide: for use in lung diffusion testing.

91  
92 Section 576(a)(3)(A)(ii) of the FD&C Act provides that the labeling requirements at sections  
93 503(b)(4) and 502(f) are deemed to have been met for a designated medical gas if the labeling on  
94 final use containers for the medical gas bears--“(I) the information required by section 503(b)(4);  
95 (II) a warning statement concerning the use of the medical gas as determined by the Secretary by  
96 regulation; and (III) appropriate directions and warnings concerning storage and handling.”  
97 With regard to the warning statement referred to at section 576(a)(3)(A)(ii)(II), a warning  
98 statement applicable to carbon dioxide, helium, and nitrous oxide can be found at 21 CFR  
99 201.161(a). However, no regulation sets forth warning statements for the other designated  
100 medical gases or for combinations of designated medical gases. Until such time as FDA  
101 promulgates relevant final regulations, FDA recommends that the labeling for final use  
102 containers containing nitrogen, medical air, carbon monoxide, or any medically appropriate  
103 combination of designated medical gases bear the warning statement set forth at 21 CFR  
104 201.161(a). FDA further recommends that labeling for final use containers containing oxygen  
105 should convey that uninterrupted use of high concentrations of oxygen over a long duration,  
106 without monitoring its effect on oxygen content of arterial blood, may be harmful, and that  
107 oxygen should not be used on patients who have stopped breathing unless used in conjunction  
108 with resuscitative equipment.  
109

110 Section 576 further provides that, in the case of oxygen provided for certain uses specified at  
111 576(b)(2)(B), the requirements of section 503(b)(4) shall be deemed to have been met if the  
112 labeling bears a warning that oxygen can be used for emergency use only, and that for all other  
113 medical applications a prescription is required. Accordingly, FDA recommends that labeling for  
114 final use containers containing oxygen that may be provided without a prescription for the uses  
115 listed at section 576(b)(2)(A) of the Act bear a warning statement in accord with section  
116 576(b)(2)(B).  
117  
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### 119 **III. THE CURRENT LIST OF DESIGNATED MEDICAL GASES**

120  
121 Section 575(1) of the FD&C Act provides that oxygen, nitrogen, nitrous oxide, carbon dioxide,  
122 helium, medical air, and carbon monoxide are “designated medical gases” if they “meet the  
123 standards set forth in an official compendium.” Section 201(j) of the FD&C Act defines “official  
124 compendium” to include the official United States Pharmacopoeia (USP), the official  
125 Homeopathic Pharmacopoeia of the United States (HPUS), the official National Formulary (NF),  
126 or any supplement to any of them.

127  
128 Based on the statutory language and the current language in these official compendia,<sup>6</sup> FDA  
129 considers the following to be the current list of the gases that constitute designated medical gases  
130 for which a certification can be sought:<sup>7</sup>

131  
132 Oxygen. The product must conform to the requirements and standards set forth in the USP  
133 monograph entitled “Oxygen” and all applicable requirements and standards contained in the  
134 USP General Notices (see section 575(1)(A) of the Act).

135  
136 *Note:* The USP monograph entitled “Oxygen” states that “Oxygen contains not less than  
137 99.0 percent, by volume, of O<sub>2</sub>.” There is another USP monograph entitled “Oxygen 93  
138 Percent” that describes a product that is “Oxygen ... [that] contains not less than 90.0  
139 percent and not more than 96.0 percent, by volume of O<sub>2</sub>, the remainder consisting mostly  
140 of argon and nitrogen.” “Oxygen 93 Percent” is different from “Oxygen” and does not fall  
141 within the meaning of 575(1)(A). Thus, FDA considers only products that conform to the  
142 “Oxygen” monograph (and not the “Oxygen 93 Percent monograph”) to be “oxygen, that  
143 meets the standards set forth in an official compendium” (section 575(1)(A)).

144  
145 Nitrogen. The product must conform to the requirements and standards set forth in the NF  
146 monograph entitled “Nitrogen” and all applicable requirements and standards contained in the  
147 USP General Notices (see section 575(1)(B) of the Act).

148  
149 *Note:* The NF monograph entitled “Nitrogen” states that “Nitrogen contains not less than  
150 99.0 percent, by volume, of N<sub>2</sub>.” The NF also contains a monograph entitled “Nitrogen 97  
151 Percent.” FDA considers only products that conform to the “Nitrogen” monograph to be  
152 “nitrogen, that meets the standards set forth in an official compendium” (section 575(1)(B));  
153 conformance with the “Nitrogen 97” monograph is not sufficient.

154  
155 Nitrous Oxide. The product must conform to the requirements and standards set forth in the USP  
156 monograph entitled “Nitrous Oxide” and all applicable requirements and standards contained in  
157 the USP General Notices (see section 575(1)(C) of the Act).<sup>8</sup>

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<sup>6</sup> Should a monograph in an official compendium for one of the designated gases change, persons or entities marketing that gas must comply with those changes.

<sup>7</sup> Section 575(1)(H) authorizes the Secretary to add other gases to the list of designated medical gases. The Secretary has not taken any such action at this time. As noted in the Introduction, this guidance does not discuss how FDA plans to implement this authority.

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158  
159 Carbon dioxide. The product must conform to the requirements and standards set forth in the  
160 USP monograph entitled “Carbon Dioxide” and all applicable requirements and standards  
161 contained in the USP General Notices (see section 575(1)(D) of the Act).  
162  
163 Helium. The product must conform to the requirements and standards set forth in the USP  
164 monograph entitled “Helium” and all applicable requirements and standards contained in the  
165 USP General Notices (see section 575(1)(E) of the Act).  
166  
167 Medical air. The product must conform to the requirements and standards set forth in the USP  
168 monograph entitled “Medical Air” and all applicable requirements and standards contained in the  
169 USP General Notices (see section 575(1)(G) of the Act).  
170  
171 Carbon monoxide. There is currently no monograph in the USP or the NF for “Carbon  
172 Monoxide.” Therefore, FDA does not plan to grant certification requests for this medical gas.<sup>9</sup>  
173 FDA does not intend to object to the marketing of this medical gas for use in lung diffusion  
174 testing pending its inclusion in the USP or NF, as discussed in Part VI of this guidance. If a  
175 monograph for “Carbon Monoxide” is added to the USP or NF at a later date, FDA would expect  
176 persons or entities marketing carbon monoxide for use in lung diffusion testing to request a  
177 certification. In addition, future requestors must conform to the requirements and standards set  
178 forth in such a monograph as well as all applicable requirements and standards contained in the  
179 USP General Notices, for the product to be considered a designated medical gas (see section  
180 575(1)(F) of the Act).

### **IV. REQUESTING A CERTIFICATION**

181  
182  
183  
184 FDA expects all persons or entities that initially introduce or deliver for introduction a  
185 designated medical gas into interstate commerce to obtain a granted certification.<sup>10</sup> To facilitate  
186 the certification process, FDA has developed the attached Request for Certification of  
187 Designated Medical Gas form. FDA strongly encourages requestors to use this form, and to  
188 closely follow the instructions attached to that form.

#### **A. Who should submit a request for certification?**

189  
190  
191  
192 Only the first person or entity that initially introduces or delivers for introduction a designated  
193 medical gas into interstate commerce should request a certification. In most cases, this will be

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<sup>8</sup> The HPUS also includes a monograph for nitrous oxide. However section 501(b) of the FD&C Act states that “[w]hen a drug is mentioned in both the USP and the HPUS it shall be subject to the requirements of the USP unless it is labeled and offered for sale as a homeopathic drug.” See also FDA’s Compliance Policy Guide 400.400, Conditions Under Which Homeopathic Drugs May be Marketed, available at <http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074360.htm>.

<sup>9</sup> While there is a HPUS monograph for carbon monoxide, it is inapplicable when the designated medical gas is not labeled as a homeopathic. See FDA’s Compliance Policy Guide 400.400.

<sup>10</sup> See generally section 505(a) of the FD&C Act for human drugs and sections 501(a)(5) and 512(a)(1)(A) and of the FD&C Act for animal drugs.



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194 the original manufacturer of the gas, that is, the person or entity that initially produces the gas by  
195 chemical reaction, physical separation, compression of atmospheric air, or other means. In some  
196 instances, original manufacturers may produce gases solely for industrial or other non-medical  
197 uses. Such manufacturers are not subject to the certification requirements in the FD&C Act.  
198 However, if a person or entity downstream is the first to market that gas as a medical gas (e.g.,  
199 after re-processing an industrial gas into a medical gas for human or animal use), that person or  
200 entity must obtain a certification to lawfully market the designated medical gas.

201  
202 A person or entity that markets a medical gas but is neither the original manufacturer nor the  
203 original marketer of that gas should not submit a certification request, even if that person or  
204 entity is the first to market the gas in containers conforming to the requirements for labeling at  
205 576(a)(3)(A)(ii).<sup>11</sup> Such downstream persons or entities should, however, verify and document  
206 that the gas or gases they receive are from a source or sources that have a granted certification  
207 for the gas (see Part VI below).

208  
209 Requestors should submit separate certification requests for each designated medical gas they  
210 produce (e.g., one request for oxygen, another for nitrous oxide), but need only submit a single  
211 request for each gas regardless of whether the gas is manufactured in multiple facilities or by  
212 multiple methods.

213  
214 The certification process is the same for designated medical gases intended for human drug use  
215 and animal drug use. The attached form has a box for requestors to indicate whether they wish  
216 to market their gas for human use, animal use, or both. Upon grant of a certification, FDA will  
217 issue the requestor an NDA number, a NADA number, or both.

218  
219 Persons or entities that wish to market a medical gas that is a combination of one or more  
220 designated medical gases need not, and should not, seek certification for the combination of the  
221 two designated medical gases. Rather, they may lawfully market medically appropriate  
222 combinations of designated medical gases under the certification process so long as each  
223 designated medical gas is covered by a granted certification (see section 576(a)(3)(A)(i) of the  
224 FD&C Act).

225  
226 The certification process only applies to designated medical gases and only for the indications  
227 specified in section 576 of the FD&C Act.<sup>12</sup> A person or entity seeking to market a medical gas

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<sup>11</sup> We note that such downstream persons or entities commonly perform certain manufacturing or processing operations (e.g., combining gases or transfilling a gas from one container to another). Such persons or entities must comply with all applicable current good manufacturing practices (CGMPs) (see 21 CFR Parts 210 and 211) as well as all applicable drug registration and listing requirements (see section 510 of the FD&C Act and 21 CFR Part 207). In addition, should such downstream manufacturing or processing operations cause the product to fall outside the scope of the certification scheme (e.g., should they result in a single gas product that no longer meets the applicable compendial standard or a combination gas product that is not a medically appropriate combination of certified designated medical gases), the resulting product will not be considered to be covered by any upstream certification or certifications, and would have to be separately approved under the FD&C Act. See footnote 14 and accompanying text.

<sup>12</sup> See section 576(a)(3)(A)(i) of the FD&C Act.

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228 or combination of medical gases that falls outside the scope of this certification process should  
229 obtain approval of that medical gas or combination of medical gases under a different approval  
230 pathway (e.g., an NDA or a NADA under sections 505 and 512 of the FD&C Act along with the  
231 implementing regulations at 21 CFR Part 314 and 21 CFR Part 514).<sup>13</sup>

232

### **B. What information should be submitted?**

233

234 This section is organized to follow the format in the attached form.

235

#### *1. Requestor Information*

236

237 Section 576(a)(1)(B) requires the certification request to include the name and address of the  
238 sponsor. FDA also requests additional contact information for the person or entity requesting the  
239 certification (email address and phone number), along with the name, address, and other contact  
240 information of an authorized U.S. agent if applicable. FDA will use this information to  
241 communicate with the requestor as necessary.

242

#### *2. Type of Submission*

243

244 The requestor should indicate the type of submission as one of the following: Original  
245 Certification Request (for either new human or animal drugs, or both), Amendment to a Pending  
246 Certification Request, Resubmission, or Other.<sup>14</sup> For submissions other than original  
247 certification requests, the requestor should briefly describe the purpose of the submission (e.g.,  
248 an amendment to supply additional information regarding manufacturing facilities). Following  
249 receipt of an original certification request, FDA plans to provide the requestor an NDA and/or  
250 NADA number in an acknowledgment letter. The requestor should include their NDA and/or  
251 NADA number in all further submissions related to the gas to which that certification request  
252 applies.

253

#### *3. Description of Medical Gas*

254

255 Section 576(a)(1)(A) requires that the certification request include a description of the medical  
256 gas. This description must include the name of the gas and information sufficient to support that  
257 the gas “meets the standards set forth in an official compendium” (see section 575(1)).

258

#### *4. Facility Information*

259

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<sup>13</sup> The following products and/or indications fall outside the scope of the certification process: (1) any designated medical gas for any indication other than the indications listed in section 576(a)(3)(A)(i) or later added in accordance with section 576(a)(3)(A)(i)(VIII), (2) any other medical gas for any indication, or (3) any combination of medical gases other than medically appropriate combinations of certified designated medical gases for one or more of the indications specified at 576(a)(3)(A)(i) or later added in accordance with section 576(a)(3)(A)(i)(VIII).

<sup>14</sup> The “Other” category is intended as a catch-all for any submissions that do not fit into one of the other provided categories. For example, a sponsor would check “Other” to submit information concerning a new manufacturing facility in connection with a previously-granted certification.

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265 Section 576(a)(1)(C) requires that the certification request include the name and address of the  
266 facility or facilities where the medical gas is or will be manufactured. FDA requests that contact  
267 information be included for each facility involved in original manufacturing or processing of the  
268 designated medical gas. When the requestor is not the original manufacturer of the gas (if, for  
269 example, the original manufacturer produced the gas for industrial use), the requestor need only  
270 list the facilities involved in re-processing the gas into a designated medical gas. FDA also asks  
271 that the requestor briefly describe the manufacturing or processing activities performed at each  
272 facility so that FDA understands the role each plays in manufacturing or processing the gas.

273  
274 The requestor should include the Data Universal Numbering System (D-U-N-S) number for each  
275 facility, along with the facility's FDA Establishment Identifier (FEI) if one exists. If a D-U-N-S  
276 number has not been assigned, the facility may obtain one directly from Dun & Bradstreet  
277 (<http://www.dnb.com>) at no cost.

### *5. Additional Information*

280  
281 The requestor should affirm (by checking the appropriate box on the attached form) that the  
282 requestor's methods, facilities, and controls used for the manufacture, processing, and handling  
283 of the gas, as applicable, are adequate to ensure its identity, strength, quality, and purity (see  
284 sections 501(a)(2)(B) and 505(d) of the FD&C Act, and 21 CFR Parts 210 and 211). Pursuant to  
285 Section 576(a)(1)(D), the requestor must also provide any other information which the Secretary  
286 may, in the future, deem appropriate to determine whether the medical gas is a designated  
287 medical gas.

#### **C. How should a requestor submit the certification request?**

288  
289  
290  
291 FDA asks the requestor to submit the certification request by following the instructions on the  
292 attached form. As previously noted, the attached form should be used to indicate whether the  
293 requestor expects to market the designated medical gas for human use, animal use, or both.

#### **D. How should information in a certification request be updated or corrected?**

294  
295  
296  
297 If the original information submitted in connection with a certification request becomes  
298 incomplete or inaccurate at any time, including after the request has been granted, the requestor  
299 should resubmit its certification request, submitting both a complete new form and a cover letter  
300 clearly explaining the purpose of the submission and highlighting the updated or corrected  
301 information. Updated or corrected information to the information originally submitted on this  
302 form other than adding a new manufacturing facility can be submitted in this manner. If the  
303 update or change involves adding a new manufacturing facility requestors should notify the FDA  
304 of the change by submitting a "changes being effected" supplement under 21 CFR 314.70(c) or  
305 21 CFR 514.8(b)(3).<sup>15</sup> All other submissions must be made in accordance with 21 CFR 314.70  
306 or 21 CFR 514.8 as appropriate. The requestor should also update its registration and listing data  
307 as appropriate.

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<sup>15</sup> See 21 CFR 314.70(a)(3) and 21 CFR 514.8(b)(1)(iii).

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### **V. EVALUATING A CERTIFICATION REQUEST**

#### **A. Review of Request for Certification**

As provided in section 576(a)(2) of the FD&C Act, a certification request is deemed to be granted unless, within 60 days of filing, FDA finds that (1) the gas to which the request applies is not a designated medical gas, (2) the request does not contain the information required by section 576(a)(1) or otherwise lacks sufficient information to permit FDA to determine whether the gas is a designated medical gas, or (3) denying the request is necessary to protect the public health.

If the medical gas does not meet the applicable official compendial standards (e.g., the requestor fails to affirm that the medical gas meets the applicable compendial standards), FDA will not grant a certification request for such gas. FDA may find that it lacks sufficient information to determine whether the gas for which certification is sought is a designated medical gas if the available information, including the information submitted with the request, is insufficient to assure FDA that the gas meets the applicable compendial standards and that the requestor's methods, facilities, and controls used for the manufacture, processing, and handling of the gas, as applicable, are adequate to ensure its identity, strength, quality, and purity. FDA will not grant a certification request if it cannot determine whether the gas is a designated medical gas. Finally, FDA may conclude that denying the request is necessary to protect the public health.

In determining whether a request should be denied, FDA will consider information submitted with the request along with any other available, relevant information, including information obtained from state or federal officials, FDA inspection reports, or any other source.

#### **B. Communication with the Requestor**

FDA plans to send an acknowledgement letter to the requestor after receipt of a certification request.

FDA may contact the requestor to request additional information. If required information is not included in the request, and if FDA is not able to contact the requestor to obtain and evaluate the information within the 60 day review period, FDA may find that the request lacks sufficient information to permit a determination that the gas is a designated medical gas (see section 576(a)(2)(B) of the FD&C Act).

Unless, within 60 days of filing, FDA makes a finding that the certification request should not be granted, the certification request is deemed to be granted. See section 575(a)(2) of the FD&C Act. In this case, the designated medical gas will be granted a certification, and will have in effect an approved application under sections 505, 512, or both, as applicable, for the indications for use specified in 576(a)(3) of the FD&C Act, subject to all applicable post-approval requirements. FDA plans to issue a second letter to the requestor stating that the certification request has been granted. This letter will include an NDA and/or NADA number which the sponsor should include in all further submissions to the Agency.

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354 If FDA makes one of the findings listed at section 576(a)(2) of the FD&C Act, however, FDA  
355 will notify the requestor within 60 days of filing that the certification request has not been  
356 granted. In such an instance, FDA plans to issue a letter explaining its determination to the  
357 requestor. If the requestor chooses to re-submit its certification request, it should provide a  
358 written response to the deficiencies identified in FDA’s letter, along with the attached form.  
359

### **C. Revocation of Certification; Withdrawal or Suspension of Approval**

360  
361 Section 576(a)(4)(A) of the FD&C Act states that FDA may withdraw or suspend approval of a  
362 drug product, including a designated medical gas deemed under section 576 to have in effect an  
363 approved application under section 505 or 512 of the FD&C Act. In addition, FDA may revoke  
364 the grant of a certification if it determines that the certification request contained any material  
365 omission or falsification. See section 576(a)(4)(B) of the FD&C Act.  
366  
367

## **VI. ENFORCEMENT OF CERTIFICATION REQUIREMENT**

368  
369 All medical gases intended for human or animal drug use that are not certified or do not  
370 otherwise have an approved marketing application will be considered unapproved new drugs or  
371 unapproved new animal drugs and may be subject to enforcement action. This includes  
372 designated medical gases marketed for any indication other than those listed at section  
373 576(a)(3)(A)(i) of the FD&C Act  
374  
375

376 Sections 575 and 576 of the FD&C Act provide a streamlined mechanism for obtaining approval,  
377 and FDA expects original manufacturers or marketers of designated medical gases eligible for  
378 certification to obtain approvals for such gases through this certification process.

379 As noted in Part IV.A, a person or entity that markets a medical gas but is neither the original  
380 manufacturer nor the original marketer should not obtain a granted certification but should verify  
381 and document that the gas or gases they receive are from a certified source or sources.  
382 Documentation should include the name of the original manufacturer(s) or marketer(s) as well  
383 the applicable new drug application number or numbers associated with the gas, and should be  
384 verified by reference to the FDA database “Drugs@FDA,” a searchable database available at  
385 <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/> that contains a record of all granted  
386 certifications. Each downstream customer should obtain documentation from their immediate  
387 supplier. Proper certification by a supplier or suppliers should be verified initially for existing  
388 suppliers and for new suppliers as part of a vendor qualification process. Once a new vendor or  
389 existing supplier has been qualified initially and the certification of the gas or gases confirmed,  
390 this documentation can consist of an annual letter from the immediate supplier attesting or  
391 certifying that the gas was originally manufactured at one or more firms with granted  
392 certifications. The letter should contain the above-mentioned items of information for each  
393 certified original source. We recommend that this statement of certified original sources be  
394 updated to reflect any changes with each annual renewal.  
395

396 FDA does not plan to grant certification requests for carbon monoxide until a monograph for that  
397 medical gas is added to the USP or the NF. FDA does not intend to object to the marketing of  
398 carbon monoxide for use in lung diffusion testing as long as the product conforms to an

***Contains Nonbinding Recommendations***

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399 acceptable alternative compendial standard.<sup>16</sup> If and when a monograph entitled “Carbon  
400 Monoxide” is added to the USP or NF, original manufacturers and/or marketers of carbon  
401 monoxide should promptly submit a certification request.

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<sup>16</sup> See FDA’s Manual of Policies and Procedures, MAPP 5310.7, Acceptability of Standards from Alternative Compendia, available at <http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/ucm079841.pdf>.

# Request for Certification of Designated Medical Gas

## 1. Requestor Information

Requestor Name\*

### Requestor Address\*

Address 1

Address 2 (if applicable)

City

State/Province/Region

ZIP or Postal Code

Country (If not United States please provide contact information for authorized U.S. agent in "Contact Information" field below.)

### Contact Information (Enter address only if different from above.)

Name

Title

Address 1

Address 2 (if applicable)

City

State/Province/Region

ZIP or Postal Code

Country (if applicable)

Telephone Number

Email Address

Fax Number

## 2. Type of Submission (Select only one.)

- Original Certification Request to Market Gas for Human Drug Use       Original Certification Request to Market Gas for Animal Drug Use       Original Certification Request to Market Gas for Human and Animal Drug Use
- Amendment to Pending Certification Request       Resubmission
- Other (specify): \_\_\_\_\_

NDA or NADA Number (Does not apply to original certification request.): \_\_\_\_\_

Reason for Submission (Does not apply to original certification request.)

## 3. Description of Medical Gas\*

Select the medical gas to which this request applies (select only one). By checking one of the following boxes you indicate that the gas to which this request applies satisfies the compendial standard listed in connection with the gas.

- Oxygen, USP       Nitrogen, NF       Nitrous oxide, USP       Carbon dioxide, USP
- Medical Air, USP       Helium, USP

<b>4. Facility Information</b>		
Provide the following information regarding each facility involved in the manufacture and processing of the medical gas to which this request applies.		
Name of Facility*		
<b>Facility Address*</b>		
Address 1		
Address 2 (if applicable)		
City	State/Province/Region	ZIP or Postal Code
Country (if applicable)		
<b>Other Facility Information</b>		
Facility D-U-N-S Number	Facility FEI Number	
Briefly describe the manufacturing or processing performed at the above facility in connection with the gas to which this request applies.		
		<b>Add additional facility</b>
<b>5. Additional Information</b>		
Check the following box to indicate that your methods, facilities, and controls used for the manufacture, processing, and handling of the gas to which this request applies are adequate to ensure its identity, strength, quality, and purity. <input type="checkbox"/>		
Provide any other information you believe will assist FDA in evaluating your request.		
<b>6. Signature(s)</b>		
By my signature I hereby certify that the data and information in this submission have been reviewed and, to the best of my knowledge, are true and accurate. WARNING: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.		
<b>Applicant</b>		
Name and Title		
Signature of Applicant	Date of Request (mm/dd/yyyy)	
<b>Authorized U.S. Agent (if applicable)</b>		
Name and Title	Telephone Number	
Signature of Authorized U.S. Agent	Date (mm/dd/yyyy)	



This section applies only to requirements of the Paperwork Reduction Act of 1995.

**-DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF ADDRESS BELOW.-**

The burden time for this collection of information is estimated to average 2 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services  
Food and Drug Administration  
Office of Chief Information Officer  
Paperwork Reduction Act (PRA) Staff  
1350 Piccard Drive, Room 400  
Rockville, MD 20850

*"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."*

PROOF

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## Instructions for Submitting Request for Certification of Designated Medical Gas Using Form FDA 3864

**1. REQUESTOR INFORMATION:** The name and contact information of the legal person or entity submitting the certification request should be provided in the indicated areas. For non-U.S. requestors the name and contact information of the legal person or entity authorized to represent the requestor should be entered in the “Contact Information” field.

**2. TYPE OF SUBMISSION:** The submission type should be indicated by checking the appropriate box. If any box other than one of the three ‘original certification request’ boxes is checked an explanation should be provided in the “Reason for Submission” block (e.g., “Response to 02/15/13 Information Request Letter” or “Amendment to Supply Additional Information Regarding Manufacturing Facilities”). The NDA and/or NADA number should also be provided if known.

**Original Certification Request** – A certification request submitted by a person or entity to market a particular medical gas for human use, animal use, or both.

**Amendment to a Pending Certification Request** – Any submission to a pending certification request, including responses to Information Request Letters.

**Resubmission** – Any complete certification request submitted by a person or entity for a particular medical gas that has been previously denied certification.

**Other** – Any submission that does not fit in one of the other categories.

**3. DESCRIPTION OF MEDICAL GAS:** The requestor should affirm that the medical gas to which the request applies meets the applicable compendial standard.

**4. FACILITY INFORMATION:** Only a brief description sufficient to enable FDA to understand the role of each facility involved in the manufacture and processing of the gas to which the certification request applies need be provided in this section. For example, “production of [gas] by physical separation” or production of [gas] by purification.” If the D-U-N-S® Number for a facility has not been assigned, one may be obtained for no cost directly from Dun & Bradstreet (<http://www.dnb.com>). If an FDA Establishment Identifier (FEI) exists for the facility it should be included.

**5. ADDITIONAL INFORMATION:** The requestor should affirm that its methods, facilities, and controls used for the manufacture, processing, and handling of the gas, as applicable, are adequate to preserve the identity, strength, quality, and purity of the gas. If the requestor believes any other information would be useful for FDA to consider, it may provide that information in this section as well.

**6. SIGNATURE(S):** The form must be signed and dated. Ordinarily only one person should sign the form: the requestor, or the requestor’s attorney, agent, or other authorized official. However, if the person signing the request does not reside or have a place of business within the United States, the request should be countersigned by an attorney, agent, or other authorized official who resides or maintains a place of business within the United States.

**SUBMISSION:** Send three copies of the completed, signed Form FDA 3864 with three copies of a cover letter to: Central Document Room, 5901B Ammendale Road, Beltsville, MD 20705. The cover letter should clearly identify the nature of the submission (for example, Original Certification Request to Market Gas for Human and Animal Drug Use). The cover letter should also provide the NDA and/or NADA number if known.