Certification Process for Designated Medical Gases

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact CDER at CDER-Quality-Policy@fda.hhs.gov or CVM at AskCVM@fda.hhs.gov.

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

February 2026
Administrative/Procedural

Revision 2

Certification Process for Designated Medical Gases

Guidance for Industry

Additional copies are available from:

Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
Phone: 855-543-3784 or 301-796-3400
Email: druginfo@fda.hhs.gov
https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs

and/or

Policy and Regulations Staff
Center for Veterinary Medicine
Food and Drug Administration
5001 Campus Dr., College Park, MD 20740-3835
https://www.fda.gov/animal-veterinary/guidance-regulations/guidance-industry

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

February 2026
Administrative/Procedural

Revision 2

Contains Nonbinding Recommendations

Draft — Not for Implementation

TABLE OF CONTENTS

I. INTRODUCTION 1

II. BACKGROUND 2

III. THE CERTIFICATION OF DMGS 3

IV. THE CURRENT LIST OF DMGS 4

V. SUBMITTING A REQUEST FOR CERTIFICATION 6

A. Who Must Submit a Request for Certification? 6

B. What Information Must Be Submitted? 8

1. Applicant Information 8
2. Type of Submission 8
3. Description of Medical Gas 8
4. Facility Information 9
5. Certification of Adequate Manufacture, Processing, Packaging, and Holding of DMG 9
6. Additional Information 9

C. How Must an Applicant Submit the Certification Request? 9

D. How Must Information in a Certification Request Be Updated or Corrected? 10

E. What if a Certification Request Is No Longer Wanted? 10

VI. EVALUATING A CERTIFICATION REQUEST 10

A. Review of Request for Certification 10

B. Communication With the Applicant 11

VII. CHANGES TO A GRANTED CERTIFICATION 12

A. Supplements 12

B. Change in Ownership 12

VIII. ANNUAL REPORT 12

IX. WITHDRAWAL OR REVOCATION OF APPROVAL 13

A. Withdrawal of Approval 13

B. Revocation of Certification 14

Certification Process for Designated Medical Gases Guidance for Industry[1]

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

This guidance explains how the Food and Drug Administration (FDA) administers the certification process and describes the annual reporting requirements for designated medical gases (DMGs). Specifically, the guidance discusses what products qualify as DMGs, who must submit a certification request, what information must be submitted, and how FDA will evaluate and act on the request.[2]

On June 18, 2024, FDA established new and revised regulations tailored to medical gases,[3] including DMG certification requirements codified in part 230 (21 CFR part 230). Before these requirements were implemented, recommendations for DMG certification were described in draft guidance. This guidance revises and replaces the draft guidance for industry *Certification Process for Designated Medical Gases* (November 2015) and is being issued to reflect the new requirements for DMG certification.

This guidance does not discuss how FDA will designate gases in addition to those listed in section II., Background[4] or expand the indications for use for DMGs beyond those specified at section 576(a)(3)(A)(i) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360ddd-1(a)(3)(A)(i)).

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

[1] This guidance has been prepared by the the Office of Pharmaceutical Quality in the Center for Drug Evaluation and Research in cooperation with the Center for Veterinary Medicine at the Food and Drug Administration.

[2] See section 576 of the FD&C Act and 21 CFR part 230, subpart B.

[3] See 89 FR 51738.

[4] See section 575(1)(H) of the FD&C Act (21 U.S.C. 360ddd(1)(H)).

II. BACKGROUND

Title XI, Subtitle B of the Food and Drug Administration Safety and Innovation Act (Public Law 112-144) added sections 575, 576, and 577 to the FD&C Act (21 U.S.C. 360ddd, 360ddd-1, and 360ddd-2), creating a new certification process for approval of DMGs. Section 575(1) of the FD&C Act defines *DMG* to include oxygen, nitrogen, nitrous oxide, carbon dioxide, helium, medical air, and carbon monoxide that meet the standards set forth in an official compendium. Section 576 of the FD&C Act establishes a pathway for any person who seeks to initially introduce or deliver for introduction a DMG into interstate commerce to file a request for certification of a medical gas as a DMG for certain indications specified in the statute. At this time, DMGs may be certified only for the following indications:

- Oxygen for treatment or prevention of hypoxemia or hypoxia
- Nitrogen for use in hypoxic challenge testing
- Nitrous oxide for analgesia
- Carbon dioxide for use in extracorporeal membrane oxygenation therapy or respiratory stimulation
- Helium for treatment of upper airway obstruction or increased airway resistance
- Medical air to reduce the risk of hyperoxia
- Carbon monoxide for use in lung diffusion testing

A DMG for which a certification is granted is deemed to have in effect an approved application under section 505 of the FD&C Act (human drugs) (21 U.S.C. 355), section 512 of the FD&C Act (animal drugs) (21 U.S.C. 360b), or both, depending on the type of certification requested and granted. Regulations for obtaining certification of a DMG under section 576 of the FD&C Act are set forth in part 230.

Until a certification has been granted, anyone marketing a medical gas for human or animal use without an approved application under section 505 or section 512 of the FD&C Act is marketing an unapproved new drug and may be subject to enforcement action.[5] This includes DMGs marketed for any indication other than those listed in section 576(a)(3)(A)(i) of the FD&C Act. Persons wishing to market DMGs for the indication or indications specified in section

[5] See sections 505(a) and 512(a)(1)(A) of the FD&C Act. See also section V., Submitting a Request for Certification regarding who must request a certification and section IV., The Current List of DMGs regarding the marketing of carbon monoxide for use in lung diffusion testing.

576(a)(3)(A)(i) of the FD&C Act must request certification from FDA.[6] Gases not intended for human or animal use (e.g., gases intended for industrial applications or nondrug medical applications such as calibration gases), do not fall within the definition of *medical gas* provided in section 575(2) of the FD&C Act, and are not subject to the certification process under part 230 and described in this guidance.

III. THE CERTIFICATION OF DMGs

As noted in section II., Background, any person who seeks to initially introduce or deliver for introduction a DMG into interstate commerce may file a request for certification of a medical gas as a DMG.[7] A certification request is deemed to be granted unless, within 60 calendar days of filing, FDA makes a finding justifying denial of the request.[8] Specifically, FDA will deny a submission if the Agency finds that:

> (1) [t]he medical gas that is the subject of the submission is not a [DMG]; (2) [t]he submission does not contain the required information or otherwise appears to lack sufficient information to determine that the medical gas is a [DMG]; (3) [t]he applicant's methods, facilities, and controls used for the manufacture, processing, and handling of the [DMG], as applicable, are not adequate to ensure its safety, identity, strength, quality, and purity; or (4) [d]enying the request is otherwise necessary to protect the public health.[9]

A DMG for which a certification is granted is deemed to have in effect an approved application under section 505 (for gases intended for human use) or section 512 (for gases intended for animal use) of the FD&C Act (or both) for the indications listed in section II., Background of this guidance, and is subject to all applicable postapproval requirements.[10] The approval applies to the DMG alone or in combination, as medically appropriate, with one or more other certified DMGs.[11]

Section 576(a)(3)(A)(ii) of the FD&C Act provides that the labeling requirements in sections 503(b)(4) and 502(f) of the FD&C Act (21 U.S.C. 353(b)(4) and 352(f)) are deemed to have been met for a DMG if the labeling on final use containers for the medical gas bears "(I) the information required by section 503(b)(4); (II) a warning statement concerning the use of the

---

[6] See § 230.50(a). Those seeking to market any other medical gas, or seeking to market a DMG (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 DMG, nor 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 or a new animal drug application). See also section V.A., Who Must Submit a Request for Certification?

[7] See section 576(a)(1) of the FD&C Act.

[8] See section 576(a)(2) of the FD&C Act.

[9] See § 230.100(b).

[10] See section 576(a)(3)(A)(i) of the FD&C Act.

[11] See section 576(a)(3)(A)(i) of the FD&C Act.

medical gas as determined by the Secretary by regulation; and (III) appropriate directions and warnings concerning storage and handling." With regard to the warning statement referred to in section 576(a)(3)(A)(ii)(II) of the FD&C Act, warning statements applicable to DMGs can be found in § 201.161(a) (21 CFR 201.161(a)).

Section 576 of the FD&C Act further provides that, in the case of oxygen provided for certain uses specified at 576(b)(2)(B) of the FD&C Act, the requirements of section 503(b)(4) of the FD&C Act shall be deemed to have been met if the labeling bears a warning that oxygen can be used for emergency use only, and that for all other medical applications a prescription is required. Accordingly, oxygen may be provided without a prescription for the uses listed at section 576(b)(2)(A) of the FD&C Act and must bear a warning statement in accordance with section 576(b)(2)(B) of the FD&C Act and § 201.161(a)(1).

IV. THE CURRENT LIST OF DMGs

Section 575(1) of the FD&C Act provides that oxygen, nitrogen, nitrous oxide, carbon dioxide, helium, medical air, and carbon monoxide are *DMGs* if they "meet[] the standards set forth in an official compendium."[12] The United States Pharmacopeia and National Formulary (USP-NF) is the applicable compendium for DMGs.

Based on the statutory language and the current language in the official compendium,[13] FDA considers the following to be the current list of the gases that constitute DMGs for which a certification can be sought:[14]

- Oxygen that conforms to the requirements and standards set forth in the USP monograph for Oxygen[15]

[12] See section 201(j) of the FD&C Act (21 U.S.C. 321(j)).

[13] Persons marketing a DMG must comply with a monograph in an official compendium (see section 501(b) of the FD&C Act (21 U.S.C. 351(b))), including when there are any changes to that monograph. Persons marketing a DMG are responsible for remaining up to date on any changes to relevant monographs.

[14] Section 575(1)(H) of the FD&C Act authorizes the Secretary to add other gases to the list of DMGs. The Secretary has not taken any such action at this time. As noted in section I., Introduction, this guidance does not discuss how FDA plans to implement this authority.

[15] See section 575(1)(A) of the FD&C Act. Note that the USP monograph for Oxygen states that "Oxygen contains not less than 99.0 percent of oxygen (O_2) by volume." There is another USP monograph for Oxygen 93 Percent. Oxygen 93 Percent is different from Oxygen and does not fall within the meaning of section 575(1)(A) of the FD&C Act. Thus, FDA considers only products that conform to the Oxygen monograph to be "oxygen that meets the standards set forth in an official compendium."

- Nitrogen that conforms to the requirements and standards set forth in the NF monograph for Nitrogen[16]

- Nitrous oxide that conforms to the requirements and standards set forth in the USP monograph for Nitrous Oxide[17]

- Carbon dioxide that conforms to the requirements and standards set forth in the USP monograph for Carbon Dioxide[18]

- Helium that conforms to the requirements and standards set forth in the USP monograph for Helium[19]

- Medical air that conforms to the requirements and standards set forth in the USP monograph for Medical Air[20]

In addition, the gases listed above must conform to any other applicable requirements in the USP-NF to meet the standards set forth in an official compendium and be considered a DMG.[21]

Carbon monoxide that meets the standards set forth in an official compendium is a DMG. However, there is currently no monograph in the USP-NF for carbon monoxide. Therefore, FDA does not plan to grant certification requests for carbon monoxide. FDA does not intend to object to the marketing of carbon monoxide for use in lung diffusion testing pending its inclusion in the USP-NF, as long as the product conforms to the European Pharmacopoeia monograph for carbon monoxide, monograph 2408 (01/2011:2408 corrected 7.2). As of issuance of this guidance, FDA is not aware of other carbon monoxide monographs. If the European Pharmacopoeia monograph is revised or another non-USP-NF monograph is developed that is equivalent to or better than the referenced European Pharmacopoeia monograph,[22] FDA would

[16] See section 575(1)(B) of the FD&C Act. Note that the NF monograph for Nitrogen states that "Nitrogen contains not less than 99.0 percent, by volume, of nitrogen (N_2)." The NF also contains a monograph for Nitrogen 97 Percent. Nitrogen 97 Percent is different from Nitrogen and does not fall within the meaning of section 575(1)(B) of the FD&C Act. Thus, FDA considers only products that conform to the Nitrogen monograph to be "nitrogen that meets the standards set forth in an official compendium."

[17] See section 575(1)(C) of the FD&C Act.

[18] See section 575(1)(D) of the FD&C Act.

[19] See section 575(1)(E) of the FD&C Act.

[20] See section 575(1)(G) of the FD&C Act.

[21] See section 575(1) of the FD&C Act.

[22] For purposes of this guidance, equivalent standards have the same acceptance criteria and make use of analytical procedures based on similar principles (e.g., chromatographic, spectroscopic, titration) and performance characteristics (e.g., specificity, accuracy, precision). A standard can be considered better than a corresponding standard for a number of reasons, including narrower ranges for acceptance criteria or superior performance of the analytical procedure (e.g., improved specificity, greater accuracy).

not object to the marketing of carbon monoxide for use in lung diffusion testing as long as the product conforms to such standard. If and when a monograph for carbon monoxide is added to the USP-NF, original manufacturers of carbon monoxide will be required to submit a certification request. In addition, future applicants must conform to the requirements and standards set forth in such a monograph as well as any other applicable requirements in the USP-NF for the product to be considered a DMG.[23]

As explained above, FDA does not intend to object to carbon monoxide being marketed for use in lung diffusion testing without an approved certification; however, registrants[24] must still list such products with FDA in accordance with 21 CFR part 207, subpart D.

V. SUBMITTING A REQUEST FOR CERTIFICATION

FDA expects all persons who initially introduce or deliver for introduction a DMG into interstate commerce to obtain a granted certification.[25] To facilitate the certification process, FDA has developed Form FDA 3864 (Request for Certification of Designated Medical Gas) for applicants to use when requesting certification.[26]

A. Who Must Submit a Request for Certification?

Any person who seeks to initially introduce or deliver for introduction a DMG into interstate commerce must request a certification as required by § 230.50(a)(1) (21 CFR 230.50(a)(1)). In most cases, the applicant will be the original manufacturer of the gas, that is, the person who initially produces the gas by chemical reaction, physical separation, compression of atmospheric air, or other means. In some instances, original manufacturers may produce gases solely for industrial or other nonmedical uses. Such manufacturers are not subject to the certification requirements in the FD&C Act. However, if a person downstream is the first to market that gas as a medical gas (e.g., after reprocessing an industrial gas into a medical gas for human or animal use), that person must obtain a certification to lawfully market the DMG.

A person who markets a DMG but is neither the original manufacturer nor the original marketer of the DMG should not submit a certification request, even if that person is the first to market the DMG in containers conforming to the labeling requirements at section 576(a)(3)(A)(ii) of the

[23] See section 575(1)(F) of the FD&C Act.

[24] For the definition of *registrant*, see 21 CFR 207.1.

[25] See generally section 505(a) of the FD&C Act for human drugs and sections 501(a)(5) and 512(a)(1)(A) of the FD&C Act (21 U.S.C. 351(a)(5) and 360b(a)(1)(A)) for animal drugs.

[26] Form FDA 3864 fulfills the certification request requirements under section 576(a)(1) of the FD&C Act and § 230.50 and is available at https://www.fda.gov/media/186745/download. Instructions for completing Form FDA 3864 are available at https://www.fda.gov/media/186742/download.

FD&C Act and § 201.161(a).[27] Such downstream persons should, however, verify and document that the gas or gases they receive are from a source or sources that have a granted certification for the gas. See § 213.82(a)(2) (21 CFR 213.82(a)(2)) for requirements for the receipt and storage of incoming DMGs. In accordance with § 213.82(a)(1)(vi), the applicable new drug application (NDA) number, new animal drug application (NADA) number, or both associated with the gas should be verified by reference to the FDA databases Drugs@FDA for gases intended for human use and Animal Drugs@FDA for gases intended for animal use.[28] Downstream persons subject to the registration and listing requirements of part 207 should use the NDA number, NADA number, or both when listing their products with FDA. A consumer or healthcare provider, such as a medical transport service or hospital, administering a certified DMG for human or animal use should not submit a certification request. Similarly, a person marketing a gas not intended for medical use in humans or animals should not submit a certification request.

Applicants must submit separate certification requests for each DMG they produce (e.g., one request for oxygen and another for nitrous oxide),[29] but need only submit a single request for each gas regardless of whether the gas is manufactured in multiple facilities or by multiple methods.

The certification process is the same for DMGs intended for human use and animal use. Form FDA 3864 has a box for applicants to indicate whether they wish to market their gas for human use, animal use, or both. Upon receipt of a certification request, FDA will issue the applicant an NDA number, a NADA number, or both. Assignment of an NDA number, a NADA number, or both does not constitute a decision on the request. FDA will issue a separate letter to the applicant notifying the applicant that the certification request has either been deemed granted or denied.

Persons who wish to market a medical gas that is a combination of one or more certified DMGs need not, and should not, seek certification for the combination of the DMGs. Rather, they may lawfully market medically appropriate combinations of DMGs under the certification process so long as each DMG is covered by a granted certification.[30]

---

[27] We note that such downstream persons commonly perform certain manufacturing or processing operations (e.g., combining gases or transfilling a gas from one container to another). Such persons must comply with all applicable requirements, including those related to current good manufacturing practice (see part 213 (21 CFR part 213)), drug registration and listing (see section 510 of the FD&C Act (21 U.S.C. 360) and 21 CFR part 207), and labeling (see 21 CFR part 201). 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 DMGs), 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.

[28] Drugs@FDA and Animal Drugs@FDA are searchable databases that contain, among other things, a record of all granted certifications and are available at https://www.fda.gov/drugsatfda and https://animaldrugsatfda.fda.gov/, respectively.

[29] See § 230.50(b)(3).

[30] See section 576(a)(3)(A)(i) of the FD&C Act.

The certification process only applies to DMGs and only for the indications specified in section 576 of the FD&C Act and described in section II., Background of this guidance.[31] A person seeking to market a medical gas or combination of medical gases that falls outside the scope of this certification process should obtain approval of that medical gas or combination of medical gases under a different approval pathway (e.g., an NDA or a NADA under section 505 or section 512 of the FD&C Act, respectively).

B. What Information Must Be Submitted?

This section is organized to follow the format of Form FDA 3864.

1. Applicant Information

Section 576(a)(1)(B) of the FD&C Act requires the certification request to include the name and address of the applicant. Section 230.50(b)(1) also requires additional contact information for the person requesting the certification (telephone number and email address), along with the name and address of an authorized U.S. agent, if applicable. FDA will use this information to communicate with the applicant as necessary.

2. Type of Submission

The applicant must indicate the type of submission as one of the following: (1) Original Certification Request (for either new human or animal drug, or both), (2) Amendment to a Pending Certification Request, (3) Resubmission, (4) Supplement to a Granted Certification Request, or (5) Other.[32,33] For submissions other than original certification requests, the applicant should briefly describe the reason for the submission (e.g., an amendment to supply additional information regarding manufacturing facilities). Following receipt of an original certification request, FDA will provide the applicant an NDA and/or NADA number in an acknowledgment letter. The applicant should include their NDA and/or NADA number in all further submissions related to the certification request.

3. Description of Medical Gas

Section 576(a)(1)(A) of the FD&C Act requires that the certification request include a description of the medical gas. This description must include the name of the gas, and the applicant must certify (by signing section 7 of Form FDA 3864) that the gas "meets the standards set forth in an official compendium."[34] For example, an applicant for carbon dioxide must

[31] Ibid.

[32] See § 230.50(b)(2).

[33] 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, an applicant would check Other when submitting a request to withdraw a certification.

[34] See § 230.50(b)(3).

certify that its DMG meets all the standards set forth in the USP monograph for Carbon Dioxide, which includes methods and acceptance criteria for identification, assay, impurities, and specific tests, as well as any other applicable requirements in the USP-NF.

4. Facility Information

Section 576(a)(1)(C) of the FD&C Act requires that the certification request include the name and address of the facility or facilities where the DMG is or will be manufactured. When the applicant is not the original manufacturer of the gas (if, for example, the original manufacturer produced the gas for industrial use), the applicant need only list the facilities involved in reprocessing the gas into a DMG. The applicant must also briefly describe the manufacturing or processing activities performed at each facility so that FDA understands the role each plays in manufacturing or processing the gas.[35]

The applicant must include each facility's FDA Establishment Identifier, if one exists, and the Unique Facility Identifier (UFI).[36] FDA's preferred UFI for facilities is the Data Universal Numbering System (DUNS) number. If a DUNS number has not been assigned, the facility may obtain one directly from Dun & Bradstreet (http://www.dnb.com) at no cost.

5. Certification of Adequate Manufacture, Processing, Packaging, and Holding of DMG

The applicant must affirm (by checking the box in section 5 of Form FDA 3864) that the applicant's methods, facilities, and controls used for the manufacture, processing, packing, and holding of the gas, as applicable, are adequate to ensure its identity, strength, quality, and purity.[37]

6. Additional Information

Section 576(a)(1)(D) of the FD&C Act requires that the certification request include any other information deemed appropriate by the Secretary to determine whether the medical gas is a DMG. Under § 230.50(b)(6), the applicant may also provide other information that the applicant believes will assist FDA in evaluating the request.

C. How Must an Applicant Submit the Certification Request?

The applicant must submit the certification request by following the instructions on Form FDA 3864.[38] FDA encourages submission of certification requests through the CDER NextGen Portal at https://edm.fda.gov.

---

[35] See § 230.50(b)(4).

[36] Ibid.

[37] See sections 501(a)(2)(B), 505(d), and 512(d)(1) of the FD&C Act and part 213.

[38] See footnote 26.

D. How Must Information in a Certification Request Be Updated or Corrected?

If the original information submitted in connection with a certification request becomes incomplete or inaccurate while the submission is pending, an applicant can submit an amendment in accordance with § 230.50(b)(2)(ii) to revise existing information or provide additional information, including responses to Information Request Letters. If a certification request is denied, an applicant can choose to resubmit the submission. Under § 230.50(b)(2)(iii), the applicant must provide a complete submission that includes a written response to the deficiencies identified in FDA's denial letter, along with other information required for certification requests. For either an amendment or resubmission, the applicant should use the NDA and/or NADA numbers assigned when the original certification request was filed in all further submissions to the Agency.

E. What if a Certification Request Is No Longer Wanted?

An applicant may notify FDA that it withdraws its certification request at any time prior to the certification being deemed granted.[39] Withdrawal of a certification request does not preclude refiling. If a certification request is withdrawn, FDA will retain the certification request, and, if the applicant requests a copy via a Freedom of Information Act request, FDA will provide the requested copy pursuant to the fee schedule in FDA's public information regulations.[40]

VI. EVALUATING A CERTIFICATION REQUEST

A. Review of Request for Certification

As described in section 576(a)(2) of the FD&C Act, a certification request is deemed to be granted unless, within 60 calendar days of filing, FDA makes a finding justifying denial of the request. Specifically, FDA will deny a submission if the Agency finds that:

> (1) [t]he medical gas that is the subject of the submission is not a [DMG]; (2) [t]he submission does not contain the required information or otherwise appears to lack sufficient information to determine that the medical gas is a [DMG]; (3) [t]he applicant's methods, facilities, and controls used for the manufacture, processing, and handling of the [DMG], as applicable, are not adequate to ensure its safety, identity, strength, quality, and purity; or (4) [d]enying the request is otherwise necessary to protect the public health.[41]

If the medical gas does not meet the applicable official compendial standards (e.g., the applicant fails to affirm that the medical gas meets the applicable compendial standards), FDA will not grant a certification request for such gas. FDA will also not grant a certification request if the

[39] See § 230.65.

[40] See 21 CFR 20.45.

[41] See § 230.100(b).

Agency finds that it lacks sufficient information to determine whether the gas for which certification is sought is a DMG, 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 applicant's methods, facilities, and controls used for the manufacture, processing, packaging, and holding of the gas, as applicable, are adequate to preserve its safety, identity, strength, quality, and purity. 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.[42]

B. Communication With the Applicant

FDA will send an acknowledgement letter to the applicant after receipt of a certification request.

Within 60 calendar days of filing of a submission, FDA may contact the applicant to request additional information. Upon receipt of an amendment to a pending certification request, the 60-day review period will restart to allow FDA sufficient time to review new information. If the required information is not included in the request, or if FDA is not able to contact the applicant 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 DMG and deny the submission.[43]

Unless, within 60 calendar days of filing of a submission, FDA makes a finding that the certification request should not be granted, the certification request is deemed to be granted.[44] In this case, the DMG will be deemed to have in effect an approved application under section 505 of the FD&C Act, section 512 of the FD&C Act, or both, as applicable, for the indications for use specified in section 576(a)(3)(A)(i) of the FD&C Act, subject to all applicable postapproval requirements. FDA will issue a letter to the applicant stating that the certification request has been deemed granted.

If FDA makes one of the findings listed in § 230.100(b), however, FDA will notify the applicant within 60 calendar days of filing that the certification request has been denied. In such an instance, FDA will issue a letter to the applicant explaining the basis for the denial determination. If the applicant chooses to resubmit the certification request, the applicant must provide a written response to the deficiencies identified in FDA's letter, along with a new Form FDA 3864.[45]

[42] See § 230.100(a).

[43] See section 576(a)(2)(B) of the FD&C Act and § 230.100(c).

[44] See section 575(a)(2) of the FD&C Act and § 230.105.

[45] See § 230.50(b)(2)(iii).

VII. CHANGES TO A GRANTED CERTIFICATION

A. Supplements

If the original information submitted in connection with a certification request becomes incomplete or inaccurate at any time after the request has been deemed granted, the applicant must submit a supplement that includes a new certification request with updated information.[46] Examples of changes that require a supplement include, but are not limited to, the addition of a new facility manufacturing the DMG, a change in contact information, or a change in the corporate name. FDA also recommends submitting a cover letter with a new Form FDA 3864 clearly explaining the purpose of the submission and highlighting the updated information. The updated information must be submitted no later than 30 calendar days after the date the change occurred.[47] The applicant must also update the associated registration and listing data as appropriate to comply with section 510 of the FD&C Act (21 U.S.C. 360) and 21 CFR part 207.

B. Change in Ownership

If a DMG certification that has been deemed granted undergoes a change in ownership (e.g., due to a merger or acquisition), an applicant may transfer ownership of the certification. At the time of transfer, the new and former owners are required to submit certain information to FDA.[48] The former owner is required to submit a letter or other document explaining that all rights to the certification have been transferred to the new owner. The new owner is required to submit a supplement under § 230.70 signed by the new owner describing any changes in the conditions in the granted certification, and a letter or other document identifying the date the transfer of ownership is effective.

VIII. ANNUAL REPORT

After a certification request is deemed granted, the applicant must submit an annual report each year within 60 calendar days of the new calendar year.[49] Under § 230.80(b), the annual report must contain, for the prior calendar year, the following information in the order listed:

- Summary: A brief summary of significant new information that might affect the safety, effectiveness, or labeling of the DMG, including any actions the applicant has taken or intends to take as a result of this new information.

- Distribution data: Information including the National Drug Code (NDC) numbers, the quantities distributed for domestic use, and the quantities distributed for foreign use.

[46] See § 230.70(a).

[47] See § 230.70(b).

[48] See § 230.72.

[49] See § 230.80(a).

Disclosure of financial or pricing data is not required.[50]

- Administrative changes: Any changes to the applicant's name or contact information. Note that under § 230.70, this information must also be submitted in a supplement no later than 30 calendar days after the change occurred.

- Current facilities: A list of current facilities where the DMG is initially produced, and a list of facilities that were used since the previous annual report (or since the certification was deemed granted) but are no longer in use.

The applicant must submit a signed, completed annual report form.[51] FDA has developed Form FDA 5025 (Annual Report for Designated Medical Gas) for applicants to use.[52]

IX. WITHDRAWAL OR REVOCATION OF APPROVAL

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

A. Withdrawal of Approval

The grounds for which FDA will initiate the withdrawal process are described in § 230.150(a). FDA will notify the applicant and afford an opportunity for a hearing on a proposal to withdraw approval of the application under the procedure in 21 CFR 314.200, 21 CFR 514.200, or both, as applicable, for any of the grounds for withdrawal listed in § 230.150(a)(1). The Agency may

[50] Please note that the requirement to submit distribution data in annual reports under § 230.80(b)(2) is separate from the reporting requirements for listed drugs and biological products under section 510(j)(3) of the FD&C Act. FDA considers the requirement to submit distribution data in annual reports under § 230.80(b)(2) to have been met if: (1) the registrant of establishments identified in the application submits a timely and complete report under section 510(j)(3) of the FD&C Act; (2) the registrant of establishments identified in the application includes in its section 510(j)(3) report the amount of listed drug product (organized by NDC number) that was distributed for foreign use during the reporting period (in addition to the amount distributed in the United States); (3) the applicant's annual report provides the date(s) of the report(s) submitted under section 510(j)(3) of the FD&C Act that includes the domestic and foreign distribution information; and (4) the applicant's annual report submitted under § 230.80 contains all other information required in § 230.80(b). For more information on the requirements of section 510(j)(3) of the FD&C Act, see the guidance for industry *Reporting Amount of Listed Drugs and Biological Products Under Section 510(j)(3) of the FD&C Act* (February 2024). We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[51] See footnote 49.

[52] Form FDA 5025 fulfills the annual report requirements under § 230.80 and is available at https://www.fda.gov/media/186748/download. Instructions for completing Form FDA 5025 are available at https://www.fda.gov/media/186749/download.

notify the applicant and afford an opportunity for such a hearing for any of the grounds for withdrawal listed in § 230.150(a)(2).

Under § 230.150(a)(3), FDA will withdraw approval of an application if the applicant requests the withdrawal because the DMG subject to the application is no longer being marketed, provided none of the conditions listed in § 230.150(a)(1) and (2) apply. An applicant that wishes to withdraw its application should submit a new Form FDA 3864 and check *Other* as the type of submission. In the text box, the applicant should note that they are submitting a withdrawal request. FDA will send an acknowledgement letter to the applicant upon receipt of the request for withdrawal. FDA will consider the withdrawal request to be a waiver of an opportunity for hearing, and such withdrawal would be without prejudice to refiling.

Under § 230.150(a)(4), FDA may notify an applicant that it believes a potential problem associated with a DMG is sufficiently serious that the DMG should be removed from the market and may ask the applicant to waive the opportunity for hearing otherwise provided for under § 230.150, to permit FDA to withdraw approval of the application for the product, and to remove voluntarily the product from the market. If the applicant agrees, FDA will not make a finding under § 230.150(a)(1) or (2), but will withdraw approval of the application in a notice published in the *Federal Register* that contains a brief summary of FDA's and the applicant's views of the reasons for withdrawal.

Under § 230.150(a)(5), if FDA withdraws an approval, FDA will publish a notice in the *Federal Register* announcing the withdrawal of approval and the effective date.

B. Revocation of Certification

In accordance with § 230.150(b), FDA may revoke the grant of a certification if FDA determines, after providing the applicant with notice and opportunity for an informal hearing in accordance with 21 CFR part 16, that the request for certification contains any material omission or falsification.