

Guidance for Industry and FDA Staff

Premarket Approval Applications (PMA) for Absorbable Powder for Lubricating a Surgeon's Glove

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Food and Drug Administration
Center for Devices and Radiological Health**

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Division of Anesthesiology, General Hospital, Infection Control, and Dental Devices
Office of Device Evaluation**

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Preface

Public Comment

Written comments and suggestions may be submitted at any time for Agency consideration to the Division of Dockets Management, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. When submitting comments, please refer to the exact title of this guidance document. Comments may not be acted upon by the Agency until the document is next revised or updated.

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Guidance for Industry and FDA Staff

Premarket Approval Applications (PMA) for Absorbable Powder for Lubricating a Surgeon's Glove

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. Purpose

Absorbable powder for lubricating a surgeon's glove is a class III medical device (21 CFR § 878.4480, product code KGP). A person intending to market absorbable powder for lubricating a surgeon's glove must submit a PMA to FDA prior to its introduction into interstate commerce (21 CFR § 878.4480(c)). The regulations pertaining to the general content and format of PMA applications are in 21 CFR Part 814. This guidance document provides FDA's recommendations regarding information that applicants should submit in a premarket PMA for absorbable powder for lubricating a surgeon's glove. For more information on PMA approval, please see the PMA topic in **CDRH Device Advice** at <http://www.fda.gov/cdrh/devadvice/pma/>.

This guidance document does not apply to absorbable powder for lubricating an examination glove. Absorbable powder for lubricating an examination glove is considered a component of the examination glove (21 CFR § 880.6250) and is reviewed under a premarket notification for the examination glove.

FDA's guidance documents, including this guidance, 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

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use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

The Least Burdensome Approach

The issues identified in this guidance document represent those that we believe should be addressed before your device can be marketed. In developing the guidance, we carefully considered the relevant statutory criteria for Agency decision-making. We also considered the burden that may be incurred in your attempt to follow the guidance and address the issues we have identified. We believe that we have considered the least burdensome approach to resolving the issues presented in the guidance document. If, however, you believe that there is a less burdensome way to address the issues, you should follow the procedures outlined in **A Suggested Approach to Resolving Least Burdensome Issues**. It is available at: <http://www.fda.gov/cdrh/modact/leastburdensome.html>.

II. Background

On July 30, 1999, FDA issued a draft guidance for comment entitled “Medical Glove Guidance Manual,” (see <http://www.fda.gov/cdrh/dsma/135.html> for the draft guidance) and proposed the 1999 draft guidance serve as a special control for class II gloves. However, Chapter 4 of the 1999 draft guidance contained a section that discussed PMAs for absorbable powder for lubricating surgeon’s gloves. Because the section discussing PMAs for absorbable powder is not relevant to class II gloves, FDA is removing this section and issuing it as a separate guidance document. FDA did not receive any comments on this section of the 1999 draft guidance. Because the recommendations in this section were available in draft form for comment, FDA is issuing this guidance as a final document. As with any guidance, you may submit comments at any time.

Absorbable powder for lubricating a surgeon’s glove is a transitional device (42 FR 63472, Dec. 16, 1977). A transitional device is any device regulated as a drug before the enactment of the Medical Device Amendments of 1976 (Pub. L. 94-295) (the Amendments). Transitional devices are classified by statute into class III and are generally required to have an approved application for premarket approval, see section 520(1) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 360j(1)). Before the enactment of the Amendments, an approved New Drug Application (NDA) was required for absorbable powder for lubricating a surgeon’s glove (then known as desiccant and lubricant powder for surgical gloves). On June 24, 1988, FDA codified the statutory class III classification of absorbable powder for lubricating a surgeon's glove (21 CFR § 878.4480) (53 FR 23875).

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The information that follows represents FDA's recommendations for supporting the safety and effectiveness of absorbable powder for lubricating a surgeon's glove in a PMA application. **This information is intended as a supplement to other FDA publications on PMA applications and should not be construed as a replacement for those documents.** The Infection Control Devices Branch is available to answer any questions you may have about PMA applications for absorbable powder for lubricating a surgeon's glove.

The safe use of absorbable powder for lubricating a surgeon's glove is important in avoiding adverse reactions to the powder by the wearer and the patient. Comprehensive and scientifically sound criteria for the evaluation of absorbable powder are essential to help ensure that this device is safe and effective for its intended use when used according to its labeling. FDA recognizes the importance of providing applicants, and other interested parties, with the agency's criteria for evaluating absorbable powder for lubricating a surgeon's glove in order to facilitate the submission of PMAs, to maintain consistency of review, and to provide for a more efficient regulatory process.

III. Manufacturing Information

You must submit a complete description of the methods, facilities, and controls used in the manufacture, processing, packing, and storage of the device and include sufficient detail such that a person generally familiar with good manufacturing practices can make a knowledgeable judgment about the quality control used in manufacturing the device. 21 CFR § 814.20(b)(4)(v).

PMA approval is subject to an FDA inspection that finds the manufacturing facilities, methods, and controls in compliance with applicable requirements of the Quality Systems Regulation (21 CFR Part 820) (Section 515(d)(2)(C) of the Act).

IV. FDA Recognized Standards

If any part of the device design or testing relies on an FDA recognized standard, you should provide a declaration of conformity to the standard. Please note that this means testing must be completed before you submit a declaration of conformity to a recognized standard. (Section 514(c)(1)(B) of the Act.)

V. Device Description

You should provide a complete and detailed description of the physical and chemical properties and specifications of the absorbable powder in order to meet the requirements of 21 CFR § 814.20(b)(4).

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In the physical characterization, we recommend that you include information about the color, size, and distribution of the powder particles. In the chemical characterization, you should include the chemical composition of the powder and the chemical name, molecular formula, and quantity of each constituent, including impurities, unreacted cross-linking agents, and other chemical agents, processing additives, etc.

You should define the manufacturing specifications of the physical and chemical aspects of the powder. You should describe aspects of the powder that are described in the United States Pharmacopeia National Formulary (USP NF) XVII Monograph for Absorbable Dusting Powder, e.g., sedimentation and residue on ignition. If applicable, you should also specify the extent to which the starch is modified in the final product. For example, you should provide the upper and lower limits for the degree of cross-linking for a starch that has been chemically cross-linked.

You should provide a description of the packaging design and packaging materials.

VI. Sterilization Information

The manufacturer of surgeon's gloves sterilizes the gloves as part of the manufacturing process; consequently, the absorbable powder used on the gloves is sterilized as well at the same time. Therefore, we recommend that you identify the types of sterilization processes that are compatible with your absorbable powder. You should provide the cycle parameters and conditions for each sterilization method you have identified. You should provide the sterilization validation results, including all qualifications and verifications, for each of these methods.

The sterilization validation results should demonstrate that the absorbable powder meets specifications following sterilization by each method. If a cycle is based on a bioburden approach, then the results should reflect the controlled level of bioburden and periodic checks of bioburden. This should also be reflected in the quality control aspects of the manufacturing section.

Also, the results should demonstrate that the product packaging maintains a low bioburden in the powder during storage (shelf life stability). We recommend that you refer to the following standards for further details on sterilization validation methods:

- AAMI/ANSI/ISO 11134:1993 Sterilization of Health Care Products – Requirements for Validation and Routine Control – Industrial Moist Heat Sterilization.
- AAMI/ANSI/ISO 11135:1994 Medical Devices - Validation and Routine Control of Ethylene Oxide Sterilization.

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- AAMI/ANSI/ISO 11137:1994 Sterilization of Health Care Products – Requirements for Validation and Routine Control –Radiation Sterilization.

VII. Physical and Chemical Testing

You should describe the methods and provide the results of physical and chemical verification tests to show that the final finished powder meets the manufacturing specifications. For a corn starch-based absorbable powder, the product should meet the identification found in the Federal Register, May 25, 1971 (36 FR 9475), and current U.S.P. specifications for Absorbable Dusting Powder. In addition, you should provide a statement that the powder conforms to the U.S.P. specifications.

If the powder is modified, you should describe the methods you intend to use during the manufacturing process for monitoring the extent of the modification (e.g., cross-linking) to demonstrate conformity with the specification. If the modification cannot be measured using a direct method, you should provide an alternative method and the results to show that the modification correlates with the alternative measurement.

VIII. Non-clinical Studies

You should conduct all tests with samples of the final finished powder. A final finished powder is a powder that has been sterilized by the intended method(s) (e.g., steam, ethylene oxide, and/or gamma-irradiation). You should assess samples of the powder sterilized by each intended sterilization method. For each study, you should specify whether it was conducted in accordance with good laboratory practices (GLP) regulations (21 CFR Part 58) and explain any deviations.

1. Toxicological Studies

To ensure the safety of absorbable powder, you should submit a toxicological evaluation of the powder additives and all residues remaining in the final finished product. You should describe these ingredients and residues in the characterizations discussed in section **IV. Device Description**. The toxicity evaluation will assist FDA in evaluating the potential health risks to patients and users resulting from the presence of the residues.

You should address the toxicity of any agents that are added to the powder during the manufacturing process. You should identify the residues that are of concern and explain any residues that were excluded from the evaluation. You should provide evidence showing that the amount of each remaining residue of concern in the final finished powder is at a safe level. To evaluate the toxicity of the powder additives and/or any

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remaining toxic residues, we recommend that you review information from the following sources:

- animal toxicity studies sponsored by the manufacturers of the cross-linking agents and additives
- animal toxicity studies of the cross-linking agents and additives in the published scientific literature.

You should provide copies of all sources reviewed. If inadequate information is available from the manufacturers or the published literature, then you should conduct toxicity testing of the final finished powder. We recommend that you evaluate biocompatibility as described in the following two documents:

- AAMI/ANSI/ISO 10993-1:1997 - Biological Evaluation of Medical Devices – Evaluation and testing
- Use of International Standard ISO-10993, “Biological Evaluation of Medical Devices Part 1: Evaluation and Testing,” General Program Memorandum #G95-1, May 1, 1995. <http://www.fda.gov/cdrh/g951.html>.

For the user, the absorbable powder is a skin-contacting device. Therefore, we recommend that you conduct skin irritation and sensitization testing with the powder.

The powder contacts not only the skin of the person wearing the glove, but also may deposit at the surgical site, such as in the peritoneum and the blood stream, and may be in contact with the tissue for an extended period of time. Therefore, we recommend that you consider the following additional tests if the toxicity of the cross-linking agents or other additives cannot be addressed with the manufacturer’s and published scientific literature:

- systemic toxicity
- subchronic toxicity
- genotoxicity, including one bacterial and two mammalian cell assays
- hemocompatibility.

The definition of an absorbable powder for lubricating a surgeon’s glove states that the device is absorbable through biological degradation (21 CFR § 878.4480). Therefore, you should demonstrate through testing that the biodegradability of your absorbable powder is comparable to that of unmodified corn starch (see Bioabsorbability Studies below). You do not need to conduct implantation, chronic toxicity, or carcinogenicity

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tests, unless special circumstances arise.

We recommend that you refer to the ISO 10993 standard for further details on biocompatibility testing of medical devices. The ISO 10993 standard also references published guidelines and methods for conducting these tests. You should provide a complete description of any test methods you use which are not described in the standard.

2. Bioabsorbability Studies

Powder from gloves may lead to a foreign body reaction and the formation of granulomas if the powder is not degraded and absorbed adequately by the body (FDA Medical Glove Powder Report, January 1997, U.S. Food and Drug Administration, Center for Devices and Radiological Health, <http://www.fda.gov/cdrh/glvpwd.html>). Digestive enzymes will degrade the cornstarch powder; however, the particle size and the nature of modifications (e.g., cross-linking) to the powder will affect the rate at which it is degraded. The larger the particle and the slower the rate of degradation, the greater the risk of granuloma formation. Therefore, we recommend that you provide test data for *in vivo* animal bioabsorbability testing to establish that any modification, such as cross-linking, made to the natural starch does not significantly alter the biodegradability of the starch.

Alternatively, you may conduct *in vitro* testing of the modified powder for susceptibility to digestive enzymes, such as amylase. You should compare the rate of enzymatic degradation of the final finished product (i.e., modified starch powder) against the unmodified starch and talc by amylase. Unmodified starch is easily digested by the enzyme and serves as a positive control. Talc is resistant to degradation and serves as a negative control. If the difference in the rate of degradation between the modified and unmodified starch is insignificant, then you may conclude that the biodegradability of the modified powder produced by the new process is comparable to that of unmodified starch. Such a result would suggest that the risk of granuloma formation or a foreign body reaction is no greater for the modified starch than for the unmodified starch. If the enzyme degradation data are inadequate to resolve concerns about the safety of the powder, then you should conduct *in vivo* animal bioabsorbability testing.

We recommend that you refer to the published literature for information about the appropriate test methods. You should provide a complete description of the test methods used. You should also provide justification for the test sample size and a statistical analysis of the data. You may request FDA's comments regarding test protocols prior to initiation of the tests. However, FDA's comments and suggestions regarding test methods can not ensure that the final test protocol or results will be adequate.

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IX. Clinical Studies

Clinical studies are not necessary to support the safety and effectiveness of a powder that meets the Absorbable Dusting Powder USP monograph. The Infection Control Devices Branch is available to answer any questions you may have about clinical studies.

X. Labeling

You must submit copies of all proposed labeling in accordance with 21 CFR §814.20(b)(10). The labeling must comply with 21 CFR Part 801.

We recommend that you include the methods of sterilization that are compatible with the absorbable powder, along with the cycle parameters and conditions for each method.

Because manufacturing processes have improved dramatically in the last 30 years, substantially reducing the amount of powder on surgeon's gloves, we no longer advise manufacturers to include either of the labeling statements announced in the Federal Register on May 25, 1971 (36 FR 9475), and excerpted below:

“**Caution:** Powder should be removed from the gloves after donning by wiping gloves thoroughly with a sterile wet sponge, sterile wet towel, or other effective method.”

or

“**Caution:** After donning, remove powder by wiping gloves thoroughly with a sterile wet sponge, sterile wet towel, or other effective method.”

XI. Environmental Assessment

We believe that these devices qualify for an exclusion from an environmental assessment according to 21 CFR § 814.20(b)(11) as described under 21 CFR § 25.34(d). However, you should request an exclusion for your PMA and provide justification that establishes that the requested action is within the excluded category and meets the criteria for the applicable exclusion.