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Regulatory Considerations for Microneedling Devices

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

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For questions about this document, contact the Office of Device Evaluation, Division of Surgical Devices, at (301) 796-6970.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Preface

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Regulatory Considerations for Microneedling Devices

Draft Guidance for Industry and Food and Drug Administration Staff

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic.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 or Office responsible for this guidance as listed on the title page.

I. Introduction

This draft guidance is being issued to assist industry in understanding when a microneedling product is a device as defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. § 321(h), and is therefore subject to the device requirements under the FD&C Act and its implementing regulations. This document also provides clarity on the regulatory pathway to market for microneedling devices.

FDA's guidance documents, including this draft guidance, do not establish legally enforceable responsibilities.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 use of the word *should* in Agency guidance means that something is suggested or recommended, but not required.

II. Scope

This draft guidance addresses certain "microneedling products," which is a generic term that encompasses instruments with common technological features that include an array of needles, "micro-protrusion" tips, or pins, which can be blunt or sharp, and of varying lengths. The

needles[1] are incorporated into the body of an instrument that facilitates rolling or stamping of these needles across or into the skin. For example, the needles may be attached to a cylinder that is rolled across the skin, attached perpendicular to a flat surface which is applied to the skin in a "stamping" fashion, or arranged in an array on the tip of a pen-shaped instrument. The application of needles to skin may be done manually, or motorized where the depth and speed of penetration of needles into the skin can be controlled. Other generic terms used to describe microneedling products include: microneedling or needling instruments, needlers, dermal rollers, microneedle rollers, microneedle stamps, dermal stamps, and variations thereof.

Microneedling products have a wide range of intended uses from facilitating skin exfoliation, improvement of the appearance of skin to treatment of scars, wrinkles, and other skin conditions (e.g., acne). In addition, these products may be indicated for single use or multiple use for a single or multiple users, and include, or have available separately, cleaning solutions, additional needle cartridges, and/or additional tips.

Microneedling products have also been promoted with topically applied substances such as creams, ointments, gels, vitamin solutions, drugs, or blood products (e.g., platelet-rich-plasma), which are either packaged together with the microneedling product or available separately where the microneedling product provides instructions for use with such topical products. Such microneedling products may be combination products under 21 CFR 3.2(e), which would be regulated by the Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), and/or the Center for Devices and Radiological Health (CDRH). Microneedling combination products are outside the scope of this guidance; manufacturers of such combination products should contact the Agency for additional information regarding the regulation of these products.[2]

Acupuncture needles, hypodermic needles or other needles for injection, tattoo machine needles, and needle probes that emit any type of energy (e.g., radio-frequency needles) or deliver any type of energy to a patient (e.g., LASER, ultrasound) are also outside the scope of this guidance.

Certain microneedling products are devices, whereas others are not. See sections IV and V for more information. In addition, FDA is not aware of any microneedling devices that are preamendment devices (i.e., available before the enactment of the Medical Device Amendments of 1976) and FDA has not yet classified these devices. See section VI for more information on the De Novo classification process.

Microneedling devices are different than dermabrasion devices. Dermabrasion devices are classified as class I devices under 21 CFR 878.4800 (manual) and 21 CFR 878.4820 (motorized)

[1] For the purposes of this draft guidance document, the term "needles" refers to any configuration of needles, "micro-protrusion" tips, or pins.

[2] For information on combination products, please refer to the Office of Combination Products webpage at http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/OfficeofScienceandHealthCoordination/ucm2018184.htm.

and are exempt from the premarket notification (510(k)) process under section 510(k) of the FD&C Act, 21 U.S.C. § 360(k), and 21 CFR part 807, subpart E, subject to the limitation in 21 CFR 878.9. According to CDRH's 1999 guidance document, "Guidance for Dermabrasion Devices" (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073789.pdf), dermabrasion devices are defined as "devices with indications for general dermabrasion, scar revision, acne scar revision, and tattoo removal." Dermabrasion devices utilize abrasion substrates such as brushes, rasps, and burrs that are intended to abrade and remove layers of the skin via shear forces. In contrast, microneedling devices utilize a substrate of needles. Although dermabrasion devices and microneedling devices may have the same or similar intended uses, as identified above, microneedling devices have technological characteristics and operate via modes of action that are different from those of dermabrasion devices that raise different questions of safety and effectiveness. In addition, microneedling devices may have intended uses that are different from those of dermabrasion devices.

III. Definitions

The following definitions are intended to be used within the context of this draft guidance and are not applicable to any context beyond this document.

Stratum corneum: The stratum corneum is the superficial or outer layer of the epidermis, consisting of several layers of flat, keratinized, non-viable, peeling cells. The stratum corneum is a dead cell layer of skin, as opposed to living layers of skin.

Exfoliation: Exfoliation is the detachment and shedding of superficial dead cells of the epidermis, i.e., the stratum corneum.

Living layers of skin: Living layers of skin are layers of live cells and surrounding tissues (e.g., connective tissue) within the epidermis, dermis, and subcutis, including hair follicles and glandular structures. Living layers of skin exclude the stratum corneum.

Dermabrasion: Dermabrasion is the abrading or eroding of skin via shear forces with abrasive substrates such as brushes, rasps, corundum, and burrs.

IV. Microneedling Products That Are Devices

A. Statutory Definition of a Device

Under section 201(h) of the FD&C Act, a device is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory which is:

- intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, or

- intended to affect the structure or any function of the body of man,

and which does not achieve its primary intended purposes through chemical action within or on the body of man and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

Whether a microneedling product is a device, in part, depends on whether it is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, or intended to affect the structure or any function of the body. A product's intended use refers to the "objective intent" of those legally responsible for the labeling of a product,[3] which is determined by their expressions or may be determined by considering the circumstances surrounding the distribution of a product.[4] This objective intent may be shown, for example, by the claims made by a firm of a microneedling product, and from other relevant sources.

B. Determining Whether a Microneedling Product Is a Device

FDA may take into account the following, among other relevant sources, in determining whether a microneedling product is a device under the FD&C Act:

1. Firm's Claims

FDA may consider the written or oral statements in any label, labeling, advertising, and/or promotion of a microneedling product by or on behalf of a firm in determining whether a microneedling product is intended to cure, mitigate, treat or prevent disease or affect the structure or function of the body. Further, FDA considers claims that indicate penetration or some effect beyond the stratum corneum into living layers of skin by such products to be evidence of a firm's intent to affect the structure or function of the body. The stratum corneum is a dead layer of skin that is naturally shed through the desquamation process. Therefore, claims regarding the removal of the stratum corneum are not considered an intent to affect the structure or function of the body. In contrast, explicitly or implicitly claiming that a microneedling product penetrates living layers of skin (e.g., epidermis and dermis), would be an intent to affect the structure or function of the body. The following are examples of claims associated with microneedling products that meet the device definition:

- Treats scars (e.g., acne scars, atrophic scars, hypertrophic scars, burn scars)
- Treats wrinkles and deep facial lines
- Treats cellulite and stretch marks

[3] For the purposes of this guidance document, the term "firm" is used to refer to "persons legally responsible for the labeling of devices" under 21 CFR 801.4 as a convenience throughout the guidance.

[4] See 21 CFR 801.4.

- Treats dermatoses
- Treats acne
- Treats alopecia (hair loss)
- Stimulates collagen production
- Stimulates angiogenesis
- Promotes wound healing

2. Device Design and Technological Characteristics/Features

In addition to examining a firm's claims, FDA may consider the design and technological characteristics/features of a microneedling product as a relevant source of information regarding intended use. Specifically, FDA considers needle penetration beyond the stratum corneum as a result of the design or technology of a microneedling product as evidence that it may be intended to "affect the structure or any function of the body." In considering the design and technology of these products, FDA evaluates the following:

- Needle length and arrangement and whether the specifications facilitate penetration into living layers of skin
- Needle sharpness and whether that facilitates penetration into living layers of skin
- Degree of control of manual or motorized microneedling products over the movement of needles and depth of penetration into living layers of skin

V. Microneedling Products That Are Not Devices

Microneedling products which are not intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease, and which are not intended to affect the structure or any function of the body, are not devices under the FD&C Act. For example, generally, microneedling products that do not penetrate living skin (e.g., epidermal and dermal layers of the skin) and claim only to do the following would not be devices:

- facilitate exfoliation of the skin (i.e., disruption of the stratum corneum)
- improvement in the appearance of skin
- give skin a smoother look and feel
- give skin a luminous look

In general, such microneedling products would not be devices; however the products may still be subject to other requirements of the FD&C Act or other Federal statutes or regulations administered by other Federal agencies.

VI. Classification of Microneedling Devices

At the time of issuance of this draft guidance, microneedling devices do not fall within any classification regulation, and there is no legally marketed predicate device upon which to base a

determination of substantial equivalence. Such devices are of a new type that FDA has not previously classified based on the criteria at section 513(a)(1) of the FD&C Act, 21 U.S.C. § 360c(a)(1), and are statutorily classified into class III by operation of section 513(f)(1) of the FD&C Act. However, FDA believes that these devices may be suitable for classification under section 513(f)(2) of the FD&C Act, also referred to as the De Novo classification process. This process provides a pathway to class I or class II classification for low-moderate risk devices for which general controls or general and special controls provide a reasonable assurance of safety and effectiveness, but for which there is no legally marketed predicate device. Under section 513(f)(2)(A)(ii) of the FD&C Act, a manufacturer of a microneedling device may request FDA to classify its device based on the criteria set forth in section 513(a)(1) of the FD&C Act without first submitting a 510(k). If a De Novo request is granted for a microneedling device, the specific device and device type would be classified in class I or II, and may be marketed immediately and serve as a predicate for future devices. For additional information, please visit FDA's webpage at http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHTransparency/ucm232269.htm.

VII. Questions and Answers

1) What are examples of microneedling products that would be devices?

As discussed above, microneedling products are regulated as devices if they are intended to diagnose disease or other conditions, or cure, mitigate, treat, or prevent disease, or to affect the structure or function of the body. The following are examples of microneedling products that would be regulated as devices:

a) A manual microneedling product with short, blunt needles where the firm makes claims that the product is intended to exfoliate, give skin a luminous look, stimulate collagen production, and treat wrinkles

In spite of the exfoliation and "give skin a luminous look" claims in this first example, the firm also makes claims that the microneedling product is intended to stimulate collagen production and treat wrinkles (i.e., affect the structure or function of skin); therefore, the product would be subject to FDA regulation as a device.

b) A motorized microneedling product with sharp needles that penetrate living layers of the skin, where the firm makes claims that the product is intended to make skin smoother by penetrating the skin to stimulate healing response and formation of new tissue

This second example illustrates how FDA considers the technology and design of a microneedling product, in conjunction with statements by the firm to determine whether the product is a device. Here, the microneedling product is intended to affect the structure and function of the body. Although making skin smoother may not necessarily require an effect on the structure or function of the body, such as through the removal or disruption of the

stratum corneum, the firm makes claims that the product here is intended to penetrate living layers of the skin and designed the product to achieve this effect, and therefore it would be subject to FDA regulation as a device.

2) What are examples of microneedling products that would not be devices?

As discussed above, microneedling products which are not intended to diagnose disease or other conditions, or cure, mitigate, treat or prevent disease and which are not intended to affect the structure or any function of the body are not devices. For example, the following products would not be devices:

a) A microneedling product with short, blunt needles or "micro-protrusion" tips that do not penetrate living layers of skin and for which the firm claims that the product is intended to facilitate skin exfoliation

b) A microneedling product with short, densely packed needles that are not designed to penetrate living layers of skin and for which the firm claims that the product is intended to give skin a smoother look and feel

In both of these examples, the products would not be devices. In these examples, the microneedling products are intended to be used to facilitate skin exfoliation and to give skin a smoother look and feel. Furthermore, the products are designed such that they would not penetrate living layers of skin due to the needle length, blunt needle tips, and/or densely packed needles.

3) I have determined my microneedling product is a device regulated by CDRH. What are my next steps?

At the time of issuance of this draft guidance, there is no existing classification regulation for microneedling devices. However, FDA believes that these devices may obtain marketing authorization as class I or class II devices under the De Novo classification process (see section VI, above).

To facilitate review, the De Novo request should include all necessary information to demonstrate a reasonable assurance of the safety and effectiveness of the device. The De Novo request should identify the benefits and risks of the device and the general controls or general and special controls needed to assure safety, such as mitigation measures to any identified risks to health, and effectiveness. Data should be provided which demonstrate that general controls or general and special controls support a classification of class I or class II. Based on currently available information, FDA considers risks associated with microneedling devices to include infection, nerve and blood vessel damage, disease transmission between users, scar formation, hyperpigmentation, skin inflammation, allergic reactions, and skin irritation. Additional risks may be identified depending on the technological characteristics and intended uses of the specific microneedling device.

The following information should be considered for inclusion in your De Novo request. This list is not intended to be comprehensive regarding the content to include in a De Novo request for a microneedling device. Additional information and testing data may be needed depending on the technological characteristics and intended uses of the specific microneedling device.

a) Information regarding the technological characteristics and performance of your device, including, but not limited to:

   i) Representative engineering drawing(s), schematics, illustrations and/or figures of the device that are clear, legible, labeled, and include dimensions

   ii) Consumables and disposable items included with the device, including additional or extra needle heads, sleeves, etc.

   iii) Needle characteristics, including materials, length, adjustability, sharpness, and geometry

   iv) Biocompatibility information; see FDA's guidance document "Use of International Standard ISO-10993-1, 'Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process'" (http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm348890.pdf)

   v) Proposed labeling for your device, including package labeling and instructions for use

   vi) Usability testing of your device with an appropriate user population; see FDA's guidance document "Applying Human Factors and Usability Engineering to Medical Devices" (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm259760.pdf)

   vii) Sterilization information; see FDA's guidance document "Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile" (http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm109897.pdf)

   viii) Cleaning or disinfection information, if the device is reusable; see FDA's guidance document "Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling" (http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm253010.pdf)

   ix) If applicable, information regarding the motorized components or aspects of your device, including testing to mitigate risks associated with the mechanism of use (e.g., electrical safety, fluid ingress, electromagnetic compatibility)

   x) If applicable, information regarding software; see FDA's guidance document "Guidance for the Content of Premarket Submissions for Software Contained in

Medical Devices" (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089593.pdf)

b) Clinical data may be necessary to demonstrate a reasonable assurance of the safety and effectiveness of a microneedling device. We recommend considering the following when designing a clinical study:

i) The clinical study protocol should ensure that enrolled subjects are representative of the clinical population that the device is intended to treat. This should be reflected in the inclusion and exclusion criteria developed for the study.

ii) Safety data should be collected to support the safe use of the device. Such data should characterize the risks of infection, nerve and blood vessel damage, scar formation, hyperpigmentation, skin inflammation, allergic reactions, skin irritation, and other potential adverse events related to the use of the device.

iii) The proposed primary effectiveness endpoint should be developed to support the proposed indications for use for your device. Effectiveness should be measured using a method that minimizes subjectivity or bias. FDA recommends use of validated measurement tools to assess device effectiveness.

iv) The follow-up period should ensure a reasonable assessment of the short-term and long-term safety and effectiveness of the device.

Given the risks associated with these devices, consideration should be given as to whether the clinical study will be a Significant Risk device study. For additional information, please see the guidance document "Significant Risk and Nonsignificant Risk Medical Device Studies" (http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126418.pdf).

As a resource for designing clinical studies, FDA recommends reviewing the guidance document "Design Considerations for Pivotal Clinical Investigations for Medical Devices" (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM373766.pdf).

If you have further questions regarding a proposed De Novo request, you may contact FDA via the Pre-Submission process. For more information regarding the Pre-Submission program, please refer to the guidance document "Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff" (http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm311176.pdf).