4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 15

[Docket No. FDA-2012-N-1148]

FDA Actions Related to Nicotine Replacement Therapies and Smoking-Cessation Products; Report to Congress on Innovative Products and Treatments for Tobacco Dependence; Public Hearing; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public hearing; request for comments.

SUMMARY: The Food and Drug Administration (FDA) is announcing a 1-day public hearing to obtain input on certain questions related to the implementation of the Federal Food, Drug, and Cosmetic Act (the FD&C Act), as amended by the Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act). This public hearing is being held to obtain comments from the public on FDA consideration of applicable approval mechanisms and additional indications for nicotine replacement therapies (NRTs), and to request input on a report to Congress examining the regulation and development of innovative products and treatments for tobacco dependence.

DATES: The public hearing will be held on December 17, 2012, 8 a.m. to 5 p.m. Individuals who wish to present at the public hearing must register by December 6, 2012. Section III of this document provides attendance and registration information. Electronic or written comments will be accepted after the public hearing until January 2, 2013.

ADDRESSES: The public hearing will be held at FDA's White Oak Campus, 10903 New Hampshire Ave., Bldg. 31, rm. 1503, Silver Spring, MD 20993. Individuals who wish to present at the public hearing must register by December 6, 2012, and provide complete contact information, including name, title, affiliation, address, email, and phone number (see section III of this document for further information).

Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Identify comments with the docket number found in brackets in the heading of this document.

Transcripts of the public hearing will be available for review at the Division of Dockets Management and on the Internet at http://www.regulations.gov approximately 30 days after the public hearing (see section VI of this document).

A live Web cast of this public hearing may be seen at https://collaboration.fda.gov/Section918 on the day of the public hearing. A video record of the public hearing will be available at the same Web address for 1 year.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing a 1-day public hearing to obtain input on certain questions related to the implementation of section 918 of the FD&C Act (21 U.S.C. 387r), as amended by the Tobacco Control Act (Public Law 111–31). Section 918 has two parts. Under Section 918(a), which is primarily focused on NRTs, the Secretary of the Department of Health and Human Services (the Secretary of HHS) is required to consider certain new approval mechanisms and additional indications for NRTs. Several NRTs, including nicotine-containing gums, patches, and lozenges, are already marketed for smoking cessation. Under section 918(b), a broader range of products is implicated. Section 918(b) requires that the Secretary of HHS, after consultation with recognized scientific, medical, and public health experts, submit a report to Congress examining how best to regulate, promote, and encourage the development of "innovative products and treatments (including nicotine-based and non-nicotine-based products and treatments)" to better achieve the following three goals: (1) Total abstinence from tobacco use, (2) reductions in consumption of tobacco, and (3) reductions in the harm associated with continued tobacco use. The purpose of this public hearing is to create a forum for interested stakeholders to provide input regarding FDA's fulfillment of the requirements set forth in section 918, including on the following issues, among others: (1) The use of fast-track and accelerated approval authorities for smoking-cessation products, including NRTs; (2) the potential for extended use of NRTs (beyond currently approved durations of use) for the treatment of tobacco dependence; (3) the potential for additional indications for NRTs, including for craving relief or

relapse prevention; and (4) how best to regulate "innovative products and treatments" targeted at tobacco users in order to achieve abstinence from tobacco use, reductions in consumption of tobacco, and reductions in the harm associated with continued tobacco use. FDA will consider the information it obtains from the public hearing in its implementation of the requirements of section 918, including in drafting the report to Congress required by section 918(b).

II. Purpose and Scope of the Public Hearing

The purpose of this 21 CFR part 15 hearing is to receive information and comments from a broad group of stakeholders, including manufacturers, interested industry and professional organizations, the public health community, individuals affected by tobacco dependence, researchers, health care professionals, and the public, regarding implementation of section 918 of the FD&C Act. FDA is also consulting directly with other Federal Agencies and third parties, as contemplated by section 918.

FDA is particularly interested in obtaining information and public comment on the issues listed in sections II.A and II.B of this document, although comments related to any issues regarding implementation of section 918 are welcome.

A. Section 918(a): FDA Actions Related to NRTs and Smoking-Cessation Products

Fast-Track Status for Smoking-Cessation Products, Including NRTs.

Section 918(a)(1) of the FD&C Act provides that the Secretary of HHS must, "at the request of the applicant, consider designating products for smoking cessation, including nicotine replacement products as fast track research and approval products within the meaning of section 506" of the FD&C Act (21 U.S.C. 356).

Accelerated approval and fast track designation are available under section 506 of the FD&C Act and FDA regulations,[1] and these provisions have been used on a case-by-case basis for drug candidates that are intended to treat "a serious or life-threatening condition" and that have the potential to fill an unmet medical need. The Food and Drug Administration Safety and Innovation Act (FDASIA), which was enacted in July 2012, amends section 506 to define "breakthrough therapy"[2] and provide that certain expedited review processes may be available to any drug candidate intended to treat a serious or life-threatening disease or condition, whether alone or in combination with other drugs, provided that the drug candidate has the potential to fill an unmet medical need.

FDA seeks comment on the following issues related to section 918(a)(1) of the FD&C Act:

1.1. How can FDA best use its authorities under section 506 of the FD&C Act, as amended by FDASIA (including the designation of products as "fast track products" and as "breakthrough therapies"), to facilitate expedited review and accelerated approval for smoking-cessation products?

1.2. Under what circumstances should a smoking-cessation product candidate be considered to fill an unmet medical need under section 506, in light of the existing products for smoking cessation?

1.3. What kind of preliminary clinical evidence might support the designation of a smoking-cessation product candidate as a "breakthrough therapy" under section 506?

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[1] See 21 CFR part 314, subpart H, and 21 CFR part 601, subpart E.

[2] A "breakthrough therapy" is a drug intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, where "preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on 1 or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development." 21 U.S.C. 356(a)(1).

Extended use of NRTs for treatment of tobacco dependence. Section 918(a)(2) of the FD&C Act provides that the Secretary of HHS must "consider approving the extended use of nicotine replacement products (such as nicotine patches, nicotine gum, and nicotine lozenges) for the treatment of tobacco dependence." The NRTs referenced in this provision are currently labeled as aids to smoking cessation with a course of treatment generally lasting 10-12 weeks, depending on the product. FDA's understanding is that "extended use" as used in section 918(a)(2) refers to use beyond that period of time, for the treatment of tobacco dependence.

On October 26 and 27, 2010, FDA held a public workshop entitled "Risks and Benefits of Long-Term Use of Nicotine Replacement Therapy Products." The questions explored in that workshop overlap with the issues raised in section 918(a)(2) of the FD&C Act. Although FDA does not seek to duplicate the discussion held at the October 2010 workshop, FDA is interested in receiving any new or additional information that might be relevant to the extended use of NRTs for tobacco dependence.

FDA seeks comment on the following issues related to section 918(a)(2) of the FD&C Act:

2.1. What evidence is available to support the approval of NRTs for extended use to maintain abstinence in individuals who have quit?

2.2. What evidence is available to support the approval of NRTs for extended use to achieve cessation (quitting)?

2.3. With regard to both of the above indications, does the evidence implicate specific populations?

Additional indications for NRTs, such as craving relief and relapse prevention. Section 918(a)(3) of the FD&C Act provides that the Secretary of HHS must "review and consider the

evidence for additional indications for nicotine replacement products, such as for craving relief or relapse prevention." As noted previously, the NRTs referenced in this provision are currently indicated as aids to smoking cessation. In the studies that were carried out to demonstrate efficacy, the endpoint was smoking cessation. These products aid cessation by relieving withdrawal symptoms, including cravings, that smokers may experience in the process of quitting. However, no currently approved NRT is indicated for craving relief outside of the context of quitting; nor is any currently approved NRT indicated for relapse prevention.

FDA seeks comment on the following issues related to section 918(a)(3) of the FD&C Act:

3.1. If an additional indication is sought for an approved NRT in which craving relief itself is the endpoint of efficacy studies:

a. How can the concept of "craving" be adequately characterized to support a potential indication for craving relief?

b. Craving can occur in the context of acute withdrawal or long after a former smoker has quit (the latter may be described as "provoked" or "cue-induced" craving). Have both types of craving been adequately characterized to support a potential indication for craving relief?

c. Are there scientifically acceptable study designs for establishing efficacy for craving relief that use:

i. Established instruments to measure patient-reported outcomes?

ii. Analytical methods that address the degree of craving relief that should be considered clinically significant?

3.2. If an additional indication is sought for an approved NRT for relapse prevention:

a. How should "relapse" be defined and measured?

b. How should the population of individuals at risk of relapse be defined?

3.3. Are there other additional indications that might be sought for approved NRT products?

B. Report to Congress on How Best to Regulate Innovative Products and Treatments to Achieve Abstinence From Tobacco Use, Reductions in the Consumption of Tobacco, and Reductions in the Harm Associated With Continued Tobacco Use

Section 918(b) of the FD&C Act requires that the Secretary of HHS, after consultation with recognized scientific, medical, and public health experts, submit to Congress a report that examines how best to regulate, promote, and encourage the development of "innovative products and treatments (including nicotine-based and non-nicotine-based products and treatments) to better achieve, in a manner that best protects and promotes the public health – (A) total abstinence from tobacco use; (B) reductions in consumption of tobacco; and (C) reductions in the harm associated with continued tobacco use." The report to Congress must include the recommendations of the Secretary of HHS on how FDA should coordinate and facilitate the exchange of information on these "innovative products and treatments" among relevant offices and Centers within FDA and within the National Institutes of Health, the Centers for Disease Control and Prevention, and other relevant Agencies such as the Substance Abuse and Mental Health Services Administration.

One question raised by section 918(b) of the FD&C Act is how FDA should regulate specific "innovative products and treatments" that make claims in the three categories identified. "Abstinence from tobacco use" may be understood to include non-initiation of tobacco use (never starting to use) as well as cessation of tobacco use (a user successfully quitting). Product

claims in this category might therefore include claims to prevent or inhibit initiation as well as claims to bring about cessation.

A claim to reduce consumption of tobacco might, for example, suggest that the product would cause users to smoke fewer cigarettes or otherwise consume less tobacco. A claim to reduce the harms associated with continued tobacco use might, for example, suggest that the user could continue consuming tobacco as desired without experiencing one or more of the harmful effects of tobacco use.

Section 918(b) also raises a question as to how FDA and other HHS Agencies can implement regulation and policy with regard to the "innovative products and treatments" referenced in the statute to bring about the three effects identified--abstinence, reductions in consumption, and reductions in the harm associated with continued use--as broader outcomes, in a manner that best protects and promotes the public health.

FDA seeks comment on the following issues related to these provisions of section 918(b):

4.1. What kinds of innovative products and treatments designed to achieve any of the above three purposes--abstinence from tobacco use, reduction in tobacco consumption, and reduction in the harm associated with continued use--might be developed to meet the criteria for marketing under applicable legal authorities?

4.2. With regard to the "abstinence" category, what innovative products and treatments might be developed to better achieve either cessation or non-initiation? What are the established methods for measuring the prevention or inhibition of initiation?

4.3. With regard to innovative products and treatments for "reduction in consumption of tobacco,"

a. How can the reduction best be measured?

b. If the reduction is associated with a certain goal or benefit:

i. What evidence is available to indicate that the reduction in consumption will bring about that goal or achieve that benefit?

ii. What degree and duration of reduction are necessary to achieve that goal or benefit?

4.4. With regard to innovative products and treatments for "reduction in the harm associated with continued tobacco use":

a. How should the "harm" be identified and measured?

b. Is there a range of harms that might be addressed, and if so, which are the most important to address?

4.5. With regard to innovative products and treatments making claims in any of the three categories identified in section 918(b), what barriers exist to development and marketing approval?

4.6 In regulating the innovative products and treatments referenced in section 918(b), how can FDA and other HHS Agencies act to ensure that the three effects mentioned in section 918(b)--total abstinence from tobacco use, reductions in consumption of tobacco, and reductions in the harm associated with continued tobacco use--are achieved as broader outcomes, in a manner that best protects and promotes the public health?

4.7. How can these broader outcomes be taken into account in FDA's premarket evaluation of new product candidates?

III. Attendance and Registration

The FDA Conference Center at the White Oak location is a Federal facility with security procedures and limited seating. Attendance is free and will be on a first-come, first-served basis.

Individuals who wish to present at the public hearing must register by December 6, 2012, and provide complete contact information, including name, title, affiliation, address, email, and phone number. Those without email access may register by contacting Ayanna Augustus (see FOR FURTHER INFORMATION CONTACT). FDA has included questions for comment in section II of this document. You should identify the number of each question you wish to address in your presentation, so that FDA can consider that in organizing the presentations. Individuals and organizations with common interests should consolidate or coordinate their presentations and request time for a joint presentation. FDA will do its best to accommodate requests to speak and will determine the amount of time allotted for each oral presentation, and the approximate time that each oral presentation is scheduled to begin. FDA will notify registered presenters of their scheduled times, and make available an agenda at http://www.fda.gov/Drugs/NewsEvents/ucm324938.htm approximately 1 week prior to the public hearing. Once FDA notifies registered presenters of their scheduled times, presenters should submit to FDA an electronic copy of their presentation to Section918PublicMeeting@fda.hhs.gov by December 10, 2012.

If you need special accommodations because of a disability, please contact Ayanna Augustus (see FOR FURTHER INFORMATION CONTACT) at least 7 days before the meeting.

A live Web cast of this public hearing may be seen at https://collaboration.fda.gov/Section918 on the day of the public hearing. A video record of the public hearing will be available at the same Web address for 1 year.

IV. Notice of Hearing Under 21 CFR Part 15

The Commissioner of Food and Drugs is announcing that the public hearing will be held in accordance with part 15 (21 CFR part 15). The hearing will be conducted by a presiding officer, who will be accompanied by senior management and technical experts from various offices within FDA.

Under § 15.30(f), the hearing is informal and the rules of evidence do not apply. No participant may interrupt the presentation of another participant. Only the presiding officer and panel members may question any person during or at the conclusion of each presentation. Public hearings under part 15 are subject to FDA's policy and procedures for electronic media coverage of FDA's public administrative proceedings (part 10 (21 CFR part 10, subpart C)). Under § 10.205, representatives of the electronic media may be permitted, subject to certain limitations, to videotape, film, or otherwise record FDA's public administrative proceedings, including presentations by participants. The hearing will be transcribed as stipulated in § 15.30(b) (see section VI of this document). To the extent that the conditions for the hearing, as described in this document, conflict with any provisions set out in part 15, this document acts as a waiver of those provisions as specified in § 15.30(h).

V. Request for Comments

Regardless of attendance at the public hearing, interested persons may submit either electronic or written comments to the Division of Dockets Management (see ADDRESSES). It is no longer necessary to send two copies of mailed comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

VI. Transcripts

Transcripts of the public hearing will be available for review at the Division of Dockets Management (see ADDRESSES) and on the Internet at http://www.regulations.gov approximately 30 days after the public hearing. A transcript will also be made available in either hard copy or on CD-ROM, upon submission of a Freedom of Information request. Written requests should be sent to the Division of Freedom of Information (ELEM-1029), Food and Drug Administration, 12420 Parklawn Dr., Element Bldg., Rockville, MD 20857.

Dated: November 21, 2012.

Leslie Kux,

Assistant Commissioner for Policy.

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