Sunscreen Innovation Act: Withdrawal of a 586A Request or Pending Request

Guidance for Industry

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

October 2016
OTC

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Contains Nonbinding Recommendations

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Guidance for Industry[1]

This guidance represents 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 office responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance addresses the process for (1) withdrawal of a request submitted under section 586A (586A request)[2] of the Federal Food, Drug, and Cosmetic Act (FD&C Act), as amended by Public Law 113-195 (also referred to as the Sunscreen Innovation Act or SIA)[3] and (2) withdrawal of a pending request, as defined under section 586(6) of the FD&C Act.[4] The recommendations in this guidance apply to 586A requests and pending requests that seek a determination from FDA of whether a nonprescription sunscreen active ingredient[5] or a combination of nonprescription sunscreen active ingredients is generally recognized as safe and

[1] This guidance has been prepared by the Office of Regulatory Policy in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration.

[2] A *586A request* is a request submitted to FDA for a determination of whether a nonprescription sunscreen active ingredient or a combination of nonprescription sunscreen active ingredients, for use under specified conditions, is generally recognized as safe and effective (GRASE) and should be included in the sunscreen OTC monograph (section 586A of the FD&C Act (21 U.S.C. 360fff-1)).

[3] 21 U.S.C. Ch. 9 Sub. 5 Part 1, enacted November 26, 2014.

[4] Section 586(6) of the FD&C Act defines a *pending request* to mean a request for a nonprescription sunscreen active ingredient submitted under § 330.14 (21 CFR 330.14) for consideration for inclusion in the OTC monograph that was determined to be eligible for review and for which safety and effectiveness data were submitted prior to the enactment of the SIA (section 586(6) of the FD&C Act (21 U.S.C 360fff(6)). These pending requests were submitted as time and extent applications (TEAs) under § 330.14 of FDA's regulations.

[5] A *sunscreen* as defined in the SIA means a drug containing one or more sunscreen active ingredients (section 586(9) of the FD&C Act (21 U.S.C. 360fff(9))), and the term *sunscreen active ingredient* means an active ingredient that is intended for application to the skin of humans for purposes of absorbing, reflecting, or scattering ultraviolet radiation (section 586(10) of the FD&C Act (21 U.S.C. 360fff(10))).

effective (GRASE) for use under specified conditions and should be included in the over-the-counter (OTC) sunscreen drug monograph.

The SIA, enacted on November 26, 2014, added new section 586D(a)(1) to the FD&C Act (21 U.S.C. 360fff-4(a)(1)), which directs FDA to issue draft and final guidance on the process by which a request under section 586A or a pending request is withdrawn.[6] This guidance is organized as follows:

- Section II provides background information on the sunscreen OTC monograph process and the new procedures under the SIA (the SIA process) for reviewing 586A requests and pending requests for nonprescription sunscreen active ingredients.[7]

- Section III addresses the general withdrawal process for a 586A request or pending request. At certain stages of the SIA process, the sponsor[8] who submitted a 586A request or pending request might seek to have it withdrawn, or the request may be withdrawn due to the sponsor's failure to act on the request and failure to respond to communications from FDA.

- Section IV addresses the effect of this withdrawal process on key phases of the SIA process.

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.

II. BACKGROUND

A. Regulation of Sunscreen Products

All sunscreens are regulated as drugs in the United States under one of two processes:

- The new drug approval process described in part 314 (21 CFR part 314)

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[6] The draft guidance was issued in November 2015 (80 FR 72970, Nov. 23, 2015).

[7] We have previously published *Federal Register* notices about rulemaking actions for OTC sunscreen monograph products and about actions taken under the SIA. This information can be found on our "Status of OTC Rulemakings" and "Sunscreens" Web sites, respectively. See http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Over-the-CounterOTCDrugs/StatusofOTCRulemakings/default.htm and http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingOver-the-CounterMedicines/ucm239463.htm.

[8] A *sponsor* under the SIA is a person that has submitted a 586A request, a pending request, or any other application subject to the SIA (section 586(8) of the FD&C Act (21 U.S.C. 360fff(8))).

- The OTC drug monograph process (also known as the OTC Drug Review) described in part 330 (21 CFR part 330), as supplemented by the SIA

Products regulated under the new drug approval process may not be marketed without FDA's prior review and approval of a new drug application (NDA) or abbreviated new drug application (ANDA) for each product.[9] Products marketed under the OTC drug monograph process are not individually reviewed and approved prior to marketing. Instead, OTC drug monographs categorize drugs by therapeutic categories, such as sunscreens. For each category, a monograph establishes conditions under which any drug that satisfies those conditions and FDA's general regulations for OTC drugs is considered to be GRASE and not misbranded when used under the conditions prescribed, recommended, or suggested in the drug's labeling.[10]

Active ingredients that were used in U.S.-marketed sunscreens before the OTC Drug Review began are eligible to be included in the OTC sunscreen monograph. An active ingredient or other condition that is ineligible for inclusion in the OTC monograph system is subject to the new drug approval process.

In 2002, before the SIA was enacted, FDA published the "time and extent application" (TEA) regulation in 21 CFR 330.14. The TEA regulation (§ 330.14(c)) has provided a process through which any person may request that FDA amend an existing OTC drug monograph to include an active ingredient or other OTC drug condition, including one not previously marketed in the United States before the OTC Drug Review began.

For OTC sunscreens, the SIA process supplements FDA's TEA regulation (§ 330.14). The SIA amended the FD&C Act in part by providing new procedures for establishing that nonprescription sunscreen active ingredients or combinations of nonprescription sunscreen active ingredients are GRASE and not misbranded when used under the conditions specified in a final sunscreen order (GRASE determination).[11] Active ingredients that are determined to be GRASE under specified conditions of use in a final sunscreen order may be used in U.S.-marketed sunscreens without first obtaining an approved NDA or ANDA. Because the monograph and SIA processes are public, anyone, not just the sponsor who originated the request, may submit data during public comment periods.

As with the TEA process, the SIA process calls for an initial eligibility determination, followed by submissions of safety and efficacy data, and a GRASE determination phase. However, the SIA process also requires FDA to make a filing determination[12] and to make proposed and final GRASE determinations in the form of orders rather than the rulemaking required by the TEA

[9] See sections 505(a) and 301(d) of the FD&C Act (21 U.S.C. 355(a) and 331(d)).

[10] 21 CFR part 330.

[11] Section 586C of the FD&C Act (21 U.S.C. 360fff-3).

[12] The filing determination requires FDA to determine whether the safety and efficacy data submitted to support a GRASE determination are appropriately formatted and sufficiently complete to support a substantive GRASE review (section 586B(b)(2) of the FD&C Act (21 U.S.C. 360fff-2(b)(2))).

regulation. The SIA process also establishes strict timelines for the necessary administrative actions.

B. Section 586D(a) Guidance on Withdrawal Process

Section 586D(a)(1)(A)(iii) of the FD&C Act requires the Agency to issue guidance on "the process by which a request under section 586A or a pending request is withdrawn."[13] The statute does not address the process by which a sponsor or FDA could withdraw a 586A request or pending request under the SIA. In addition, FDA's current regulations governing TEA requests do not include a withdrawal process (§ 330.14).[14] As directed by the SIA, FDA is issuing this guidance to explain how, at different stages of the SIA process, a 586A request or pending request may be withdrawn.

Although neither the SIA nor the current TEA regulation otherwise discuss the process of withdrawal, we note that in the preamble of the final rule promulgating the TEA regulation, FDA discussed the effect of a withdrawal of a TEA request when a non-GRASE determination for that condition is expected. We explained in the preamble to the 2002 TEA Final Rule that although a sponsor can withdraw its request after receiving a feedback letter indicating that a condition has been determined not to be GRASE, we would still consider the submission, including the data and information submitted, to be a part of the public docket and FDA would still have the discretion to publish the Agency's non-GRASE decision, notwithstanding the withdrawal.[15] As indicated in the preamble to the 2002 TEA Final Rule, it is the Agency's view that the OTC Drug Review is a public process, and thus, if a condition is determined to be eligible for review, all information provided to FDA should remain part of the public record, even if a sponsor withdraws its request.[16] The SIA process, like the OTC Drug Review, is also a public process. Thus, consistent with the 2002 TEA Final Rule and as explained in Section III of this guidance, the Agency may continue to rely on the data and information that have been submitted in the SIA process after a request is withdrawn.

Based on the requirements of the SIA and the Agency's prior consideration of a similar issue in implementing the TEA regulation,[17] this guidance describes our recommendations for addressing

[13] Section 586C(a)(1)(A)(iii) of the FD&C Act (21 U.S.C. 360fff-3(a)(1)(A)(iii)).

[14] We note that on April 4, 2016, the Agency issued a proposed rulemaking that proposes to revise section 330.14 of the Agency's regulations to include provisions regarding the withdrawal of TEAs and safety and effectiveness data submissions (81 FR 19069, April 4, 2016).

[15] See "Additional Criteria and Procedures for Classifying Over-the Counter Drugs as Generally Recognized as Safe and Effective and Not Misbranded" (2002 TEA Final Rule), 67 FR 3060 at 3066 and 3067 (January 23, 2002).

[16] There may be limited situations in which certain information submitted may be considered confidential. See 2002 TEA Final Rule, 67 FR 3060 at 3067 and 3066; see also section 586B(a)(3) of the FD&C Act (21 U.S.C. 360fff-2(a)(3)).

[17] See 2002 TEA Final Rule, 67 FR 3060 at 3067.

the process for withdrawal of a 586A request or pending request and the effect of a withdrawal on the GRASE review process.

C. Related Guidance

In addition to this guidance, the SIA directs FDA to issue draft and final guidance documents on three other topics.[18] These topics include:

- The format and content of information submitted by a sponsor in support of a 586A request or a pending request;
- The data required to meet the safety and efficacy standard for determining whether a nonprescription sunscreen active ingredient or combination of nonprescription sunscreen active ingredients is GRASE and not misbranded; and
- The process by which FDA will carry out section 586C(c) of the FD&C Act as amended by the SIA, including the process for requesting an advisory committee meeting, the circumstances that limit the number and frequency of advisory committee meetings FDA is required to convene, and the number of requests to be considered per advisory committee meeting.

In November 2015, FDA issued draft guidance on all four topics. As they become available draft or final guidances are posted on the FDA Drugs guidance Web page at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.[19]

III. GENERAL WITHDRAWAL PROCEDURES

A. Request for Withdrawal

A sponsor seeking to withdraw its 586A request or pending request should submit its written or electronic request for withdrawal to the docket with a copy to the Division of Nonprescription Drug Products in the Office of Drug Evaluation IV.[20] Written requests should be submitted to:

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061

[18] Section 586D(a)(1)(A) of the FD&C Act (21 U.S.C. 360fff-4(a)(1)(A)).

[19] When available, FDA will post each final guidance on the FDA Drugs guidance Web page at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

[20] If the Agency has not opened a docket for the proceeding, the sponsor should submit its written request for withdrawal to the Division of Nonprescription Drug Products in the Office of Drug Evaluation IV as described in this guidance.

Rockville, MD 20852

and

Food and Drug Administration
Division of Nonprescription Drug Products
Bldg. 22, Mail Stop 5411
10903 New Hampshire Avenue
Silver Spring, MD 20993

Electronic requests, and electronic copies of written requests, should be submitted to http://www.regulations.gov in the applicable docket. The withdrawal request should include the following information:

- submitter
- submission date
- active ingredient or other condition that is the subject of the submission
- applicable docket number

A request to withdraw informs FDA of the sponsor's intent to discontinue its request for a determination from the Agency of whether the sunscreen active ingredient, or combination of active ingredients, is GRASE and should be included in the sunscreen OTC monograph. FDA intends to respond to a request for withdrawal from the sponsor by sending a letter to the sponsor acknowledging the withdrawal of the request. If the withdrawal is made after a docket has been opened for that proceeding, FDA intends to place a copy of the acknowledgement letter in that docket.

As explained in more detail below, generally, if a sponsor submits a request to withdraw its 586A or pending request at any time prior to FDA's issuance of a final sunscreen order, FDA intends to consider the request withdrawn. If a proposed sunscreen order has not been issued, FDA intends to stop its review of that request. However, similar to FDA's approach under the TEA regulation, if a proposed sunscreen order has already been issued prior to the withdrawal, FDA may proceed with issuing a final sunscreen order consistent with the SIA and as priorities and resources permit. In addition, FDA intends that the original submission and the data and information submitted in support of the 586A request will remain a part of the public docket for that proceeding, and FDA may continue to rely on such data and information.[21]

B. Withdrawal Due to Sponsor's Failure to Take Action

We note that there are several stages in the review process for 586A requests and pending requests at which the Agency will be waiting for the sponsor or other interested parties to submit necessary information or data. With the exception of designated comment periods, the SIA does not require the sponsor or others to submit such information or data within an established

[21] See 2002 TEA Final Rule, 67 FR 3060 at 3067. Generally, the Agency will open a docket when the notice of eligibility (NOE) is issued.

deadline. Based on our past experience with the OTC monograph process, this may create a situation in which the necessary information or data are never submitted.

Accordingly, we recommend that sponsors keep us apprised of the anticipated timing of their data submissions if those submissions are expected to occur more than 1 year from the date of the notice of eligibility (NOE) or the sponsor's most recent submission. To facilitate the review process and better utilize the Agency's time and resources, FDA may also request periodic updates from the sponsor on the status of the information or data to be submitted if nothing has been submitted by the sponsor for more than 1 year. If an update is not provided or no information or data are submitted to FDA within 90 days of FDA's request for an update, the Agency intends to consider the sponsor's failure to respond to be a request by the sponsor to withdraw the 586A or pending request. By failing to take action, the sponsor will have indicated that it is no longer interested in pursuing a GRASE determination for a particular request. FDA intends to send a letter notifying the sponsor that the request is withdrawn, and FDA intends to place a copy of the letter in the public docket for that proceeding. It is the Agency's view that this withdrawal process will provide notice to the public of the status of the proceeding and of our intent to stop review of the request due to the sponsor's failure to take action. As discussed in section IV.C, if a 586A request or pending request is withdrawn, a sponsor can submit a new request for the same sunscreen active ingredient or combination of sunscreen active ingredients.

IV. EFFECT OF WITHDRAWAL OF 586A REQUESTS AND PENDING REQUESTS

As explained above, the SIA process calls for an initial eligibility determination phase followed by the submission of safety and efficacy data, a filing determination by FDA, and a GRASE determination phase, which includes a proposed sunscreen order and final sunscreen order.

If a 586A request is determined to be eligible for review, the Agency opens a docket for the proceeding, publicly posts the NOE and the 586A request,[22] and provides interested parties 45 days to submit comments relating to a GRASE determination on the request, including data and other information related to the safety and efficacy of the request.[23]

A key step in the SIA process requires FDA to determine whether the information and data submitted to support a GRASE determination are appropriately formatted and sufficiently complete to support a substantive GRASE review (filing determination).[24] Based on that determination, FDA will either file or refuse to file the request (thus triggering various action timelines).[25]

[22] For information on the treatment of confidential data in 586A requests, see section 586B(a)(3) of the FD&C Act(21 U.S.C. 360fff-2(a)(3)).

[23] Section 586B(b)(1) of the FD&C Act (21 U.S.C. 360fff-2(b)(1)).

[24] Section 586B(b)(2) of the FD&C Act (21 U.S.C. 360fff-2(b)(2)).

[25] Section 586B(b)(3) of the FD&C Act (21 U.S.C. 360fff-2(b)(3)).

The following sections address the effect that a withdrawal of a 586A request or pending request may have on these and other key phases of the SIA process.

A. 586A Request — Withdrawal

1. Withdrawal Prior to an Eligibility Determination or After a Determination That a Request Is Ineligible

If a sponsor withdraws its 586A request before FDA issues a determination that the request is eligible for review, we intend to stop our review of the request because we no longer have a 586A request upon which to make a determination of eligibility. Similarly, if FDA has made a determination that the 586A request is not eligible for review under the SIA process, the matter may be considered closed without the need for a withdrawal because there is no longer an open matter from which to withdraw. For requests withdrawn prior to an eligibility determination, FDA does not intend to publicly post the withdrawal notification.

2. Withdrawal After an Eligibility Determination but Prior to a Filing Determination

a. Presubmission of Data Package

If a sponsor withdraws its 586A request after FDA has determined that the request is eligible for review and has issued an NOE, but before the data package described in section 586B(b)(1) of the FD&C Act has been submitted, FDA intends to stop its review of the withdrawn request. Upon the sponsor's withdrawal, there will be no 586A request which may be filed. If a new 586A request is submitted for the same sunscreen active ingredient or combination of sunscreen active ingredients after the withdrawal of the original request, we intend to follow the process for the new request as explained in section IV.C of this guidance.

b. Postsubmission of Data Package

If a sponsor withdraws its 586A request after FDA has determined that the request is eligible for review and has issued an NOE determination, and after the data package described in section 586B(b)(1) of the FD&C Act has been submitted, but prior to FDA's filing determination, the Agency intends to stop its review of the 586A request. Upon the sponsor's withdrawal, there will be no 586A request. If a new 586A request is submitted for the same sunscreen active ingredient or combination of sunscreen active ingredients after the withdrawal of the original request, we intend to follow the process for the new request as explained in section IV.C of this guidance.

3. Withdrawal After Filing Determination

a. Filed 586A Request

If FDA determines that the data and information are sufficiently complete to conduct a GRASE review, the Agency will file the 586A request. If a sponsor withdraws its 586A request after the Agency has filed the request and before the Agency has issued the proposed sunscreen order, the Agency intends to stop its review of the withdrawn request. If a new 586A request is submitted for the same sunscreen active ingredient or combination of sunscreen active ingredients after the withdrawal of the original request, we intend to follow the process for the new request as explained in section IV.C of this guidance.

b. Refuse to File

If a sponsor withdraws its 586A request after FDA refuses to file the request, the Agency intends to stop its review of the withdrawn request. A sponsor can submit additional data or other information in response to a refuse to file. If a sponsor withdraws its 586A request after it has submitted additional data or information, but before FDA has made a new filing determination, the Agency intends to stop its review of the withdrawn request.[26] If a new 586A request is submitted for the same sunscreen active ingredient or combination of sunscreen active ingredients after FDA refuses to file the original 586A request, we intend to follow the process for the new request as explained in section IV.C of this guidance.

4. Withdrawal After a Proposed Sunscreen Order Under Section 586(7)(C)

If a sponsor withdraws the 586A request after the Agency has issued a proposed sunscreen order and has made a tentative determination on whether or not an active ingredient is GRASE under certain conditions of use, [27] FDA intends to deem the 586A request withdrawn, but may continue to rely on the information submitted to the docket and may proceed to issuing a final sunscreen order. As explained in section II.B, we consider all data and information submitted (e.g., in response to the NOE, a feedback letter, or tentative GRASE determination) to be part of the public record. Upon submission of such information, the Agency has the data upon which to base its final sunscreen order notwithstanding the withdrawal. If a new 586A request is submitted for the same sunscreen active ingredient or combination of sunscreen active ingredients after the withdrawal of the original request, we intend to follow the process for the new request as explained in section IV.C of this guidance.

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[26] Section 586B(b)(3) of the FD&C Act provides sponsors with a process to submit additional information and request meetings if FDA refuses to file the request. If FDA makes a new filing determination based on the additional information and accepts the request for filing, then any withdrawal of the request sought thereafter will fall under the approach described in section IV.A.3.a of this guidance.

[27] Section 586C(a)(5)(A) of the FD&C Act (21 U.S.C. 360fff-3(a)(5)(A)). Under the SIA, FDA has 300 days to evaluate the information and data submitted to the docket and to issue a proposed sunscreen order on its GRASE determination (section 586C(a)(1) of the FD&C Act (21 U.S.C. 360fff-3(a)(1))). In the proposed sunscreen order, FDA can find that the active ingredient under consideration is GRASE, not GRASE, or not GRASE and more information and data are necessary to allow FDA to determine otherwise (section 586(7) of the FD&C Act (21 U.S.C. 360fff(7))). The sponsor and interested parties will have 45 days to submit comments on the proposed order (section 586C(a)(3) of the FD&C Act (21 U.S.C. 360fff-3(a)(3))).

B. Pending Requests — Withdrawal

As explained above, a pending request under the SIA is defined to mean a request for a nonprescription sunscreen active ingredient submitted under § 330.14 for consideration for inclusion in the OTC monograph that was determined to be eligible for review and for which safety and effectiveness data were submitted prior to the enactment of the SIA (section 586(6) of the FD&C Act). There are eight pending requests as defined under section 586(6) of the FD&C Act. FDA has issued proposed sunscreen orders for all eight pending requests,[28] and the proposed orders tentatively determined that the active ingredients are not GRASE and more data are necessary to allow FDA to determine otherwise.[29]

Accordingly, FDA intends for the same withdrawal process described in section IV.A.4 to apply if a sponsor of a pending request withdraws the pending request prior to the issuance of the final sunscreen order. If a new 586A request is submitted for the same sunscreen active ingredient after the withdrawal of the pending request, we intend to follow the process for the new request as explained in section IV.C of this guidance.

C. New Requests

The same or a different sponsor can submit a new 586A request for the same sunscreen active ingredient or combination of sunscreen active ingredients after the original request has been withdrawn. If FDA has already made a determination that the active ingredient is eligible for further review under the SIA process, FDA intends for the existing NOE to remain in effect and the sunscreen active ingredient or combination of active ingredients to remain eligible for consideration under the SIA. The sponsor of the new 586A request may rely on the existing NOE for that active ingredient; but, thereafter, we intend to treat the new submission as a new 586A request under the SIA process, and the sponsor should submit a new and complete data submission package for its request. The data package may include data and other information that were submitted as part of a prior 586A or pending request for that ingredient under the SIA. If there is no existing NOE or the active ingredient has been found ineligible, then we intend to treat the submission of another 586A request for this ingredient as a new 586A request subject to the full SIA process, including an eligibility determination.

[28] Section 586C(b)(3) of the FD&C Act (21 U.S.C. 360fff-3(b)(3)).

[29] See http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingOver-the-CounterMedicines/ucm239463.htm.