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Division of Dockets Management (HFA-305)
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2009-D-0008 – Draft Guidance on Citizen Petitions and Petitions for Stay of Action Subject to Section 505(q) of the Federal Food, Drug, and Cosmetic Act

Dear Sir or Madam:

Allergan submits the following comments with respect to the Food and Drug Administration's ("FDA" or "Agency") Draft Guidance on Citizen Petitions and Petitions for Stay of Action Subject to Section 505(q) of the Federal Food, Drug, and Cosmetic Act ("Draft Guidance").[1] The Draft Guidance describes FDA's current thinking about citizen petitions that relate to abbreviated new drug applications ("ANDA") subject to 21 U.S.C. § 355(j) or biosimilar biological product license applications subject to 42 U.S.C. § 262(k) (collectively referred to for brevity as "generic drug applications").

Allergan appreciates that FDA has sought public comment on this important Draft Guidance. Citizen petitions support an informed and accountable drug regulatory system, and can help FDA address its diverse obligations, which include:

1. the efficient evaluation and approval of applications, including those for generic drug products;

[1] 83 Fed. Reg. 49935 (Oct. 3, 2018).

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2. the establishment and application of evidence-based, lawful, transparent standards for the evaluation and approval of generic drug products; and

3. effective implementation of the rights of all stakeholders to provide input and to obtain the Agency's timely and substantive responses on important public health questions, concerns, and requests.

SPECIFIC COMMENTS

1. Section 505(q) Petitions Have "Rarely" Delayed Generic Drug Approvals

Section 505(q) of the Federal Food, Drug, and Cosmetic Act obligates FDA not to delay the approval of a pending generic drug application because of a citizen petition unless "delay is necessary to protect the public health."[2] Allergan appreciates FDA's acknowledgement that Section 505(q) petitions have "rarely" delayed the approval of generic drug applications.[3]

2. ANDAs Validly May Be Delayed Due To Questions Around Bioequivalence Standards Or Methods

Allergan also appreciates FDA's acknowledgement that ANDAs or other abbreviated applications may validly be delayed if there is an open question concerning the standards or methods for determining bioequivalence.[4] The bioequivalence requirement is the statutory cornerstone of the ANDA approval process; it provides the fundamental guarantee that a generic drug will be safe and effective for use by patients and may be freely interchanged with the innovator drug. Hence, any credible concerns about bioequivalence standards or methods *should* delay action on a generic drug application because their resolution implicates the public health and integrity of the generic drug approval process.[5]

[2] 21 U.S.C. § 355(q)(1)(A).

[3] Statement from FDA Commissioner Scott Gottlieb, M.D., on new agency actions to further deter "gaming" of the generic drug approval process by the use of citizen petitions (Oct. 2, 2018) ("Commissioner's Statement"), available at https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm622252.htm (also noting that FDA has approved or tentatively approved record numbers of generic drug applications during 2017 and 2018).

[4] Draft Guidance at 9.

[5] Id.

3. The Draft Guidance Should Expressly Acknowledge The Status Of Citizen Petitions

As FDA is well-aware, petitioning the government is a right rooted in and protected by the Constitution. The Administrative Procedure Act ("APA") builds on this right and directs federal agencies to provide all "interested persons" the right to petition and to give "prompt notice" if the agency denies a petition.[6] Furthermore, with limited exceptions, FDA must provide a "brief statement of the grounds for [any] denial" of a petition.[7] We appreciate that FDA has previously acknowledged that a robust citizen petition process is essential to further the core principles of open government – access, transparency, and accountability.[8]

We encourage the Agency to revise the Draft Guidance to acknowledge Congress' support of the citizen petition process in Section 505(q) itself, and its expectation that FDA will timely review and respond to credible issues raised.

4. FDA Should Commit To Provide Substantive Responses (And Not "Non-Substantive" Denials) To Citizen Petitions That Are Deemed Subject To Section 505(q)

The Draft Guidance would limit the number of petitions deemed subject to Section 505(q), by covering only petitions that may affect generic drug applications for which a regulatory action is expected to be taken within the 150 days following petition submission.[9] In at least one very important regard, this change should reduce a problem related to Section 505(q) and its 150-day response deadline. Specifically, to comply with the Section 505(q) deadline, while at the same time avoiding premature determinations about certain issues (e.g., because a generic drug application is not otherwise ready for approval), FDA has adopted the practice of denying certain citizen petitions on "non-substantive" grounds.[10] In reality, this means that FDA

[6] 5 U.S.C. § 555(e).

[7] Id. The requirements that any petition denials be promptly made and explained reflect the vital role that third-party petitioning plays in "provid[ing] a critical check on the influence of political vicissitude on an agency's divergence from its statutory mandate." Diana R.H. Winters, Intractable Delay and the Need to Amend the Petition Provisions of the FDCA, 90 Indiana Law Journal 1047, 1048 (2015).

[8] As the then-FDA Commissioner explained when the Agency's first regulations regarding petitions were promulgated, FDA had "come to recognize the benefits of opening up [its] decisionmaking to public scrutiny…." In addition, a robust process – including timely consideration of and responses to issues raised – would "strengthen the agency, and increase public confidence in the integrity of [its] decisions." Congressional Oversight of Administrative Agencies (Food and Drug Administration and Environmental Protection Agency, Hearings before the Subcomm. on Separation of Powers of the Comm. On the Judiciary, United States Senate, 94th. Cong., 1st Sess., at 5 and 9 (July 21 & 23, 1975)) (statement of Alexander M. Schmidt, Commissioner of Food and Drugs).

[9] Draft Guidance at 7.

[10] We are aware of at least 17 "non-substantive" denials of citizen petitions that concerned generic drug products.

procedurally deems a petition to be denied without actually substantively deciding whether the petition has merit and thus should be granted. And yet, the procedural nature of the denial notwithstanding, FDA makes no promise to provide substantive explication at a later date.

Unfortunately, under Section 505(q) and FDA's practice, the only means by which petitioners can currently preserve any expectation to receive a substantive response after a "non-substantive" denial is to file a new petition in order to open a new petition docket and renew FDA's obligation to respond under the citizen petition regulations.[11] Such petitions are sometimes referred to pejoratively as "serial petitions," but that is unfair and reflects a misunderstanding of Section 505(q) and FDA's practice of issuing non-substantive denials. After all, a petitioner should be entitled to receive a meaningful response to its petition at some point. If its initial petition results in a non-substantive denial because FDA is not yet ready to decide the issues raised by the petition, the petitioner has no way of knowing when or if FDA will become ready to decide those issues. Nor does the petitioner have any way of obtaining a reasoned, substantive explanation from FDA of its decision on those issues other than by filing a new petition. Allergan agrees that the current 505(q) process is highly inefficient, and this process has raised misperceptions about the nature of submissions. We support a regulatory approach that more accurately links the timing of a petition response to the timing for regulatory action on a pending generic drug application.

If FDA finalizes the Draft Guidance as proposed, the document should make clear that circumstances causing the denial of petitions subject to Section 505(q) *without addressing the merits* will be very rare, and that maximum efforts will be made to avoid this scenario. If the basis for deeming a petition to be subject to Section 505(q) is that FDA believes at the time the petition is submitted that it will be ready to decide the issues raised by the petition within 150 days in the context of a pending generic drug application, then it follows that most, if not all, petitions subject to Section 505(q) will warrant a substantive response by the 150-day deadline. Perhaps in unusual circumstances, unforeseen developments may cause a delay in FDA's timeframe for deciding the issues raised by a petition such that FDA's prediction that it will be ready to decide the issues within 150 days turns out not to be accurate and FDA thus needs to issue a non-substantive response to the petition while it continues to consider the issues it raises. In that event, FDA should make provision to ultimately inform the petitioner of the Agency's views on the merits of its petition, once the Agency has determined those merits. As discussed, the Agency carries an important responsibility to answer petitioners' concerns.

[11] 21 C.F.R. § 10.30.

5. FDA Omitted An Important Phrase In One Section Of The Draft Guidance, And That Phrase Should Be Added

Section F of the Draft Guidance omits an important statement of the issues that FDA must address when considering whether to refer a matter to the Federal Trade Commission ("FTC"). Specifically, lines 646-648 (p. 16) state: "[I]f we determine that a petition has been submitted with the primary purpose of delaying an application, we intend to refer the matter to the [FTC]." That sentence omits the phrase: "and fails to raise valid issues on its face." Both the "primary purpose" and facial invalidity criteria must be met for a referral to be appropriate under First Amendment law.

6. The Draft Guidance Should Clarify How Certain Petitions Will Be Addressed

We respectfully request that FDA discuss how it will process and respond to citizen petitions that are deemed *not* to be subject to Section 505(q), or may be of unclear status. At least two likely scenarios include:

(1) A citizen petition includes a Section 505(q) certification; however, FDA deems the petition not to be subject to Section 505(q) because there is not a pending generic drug application with a near-term user fee goal date. Allergan assumes, and asks FDA to confirm, that the Agency will process and respond to such a petition in accordance with 21 C.F.R. § 10.30(e)(2).[12]

(2) A citizen petition includes a Section 505(q) certification; however, FDA deems the certification to be deficient. The Draft Guidance states: "FDA will not review a petition that is subject to section 505(q) but is missing the required certification. … Although we may contact a petitioner to notify him or her of a missing or deficient certification, we note that it is the responsibility of the petitioner to ensure that its petition complies with the applicable requirements of section 505(q), as well as other applicable statutory and regulatory requirements."[13] Allergan asks FDA to agree that, if the Agency notes certification defects, FDA will affirmatively identify that fact to a petitioner and advise that the petition cannot be reviewed with deficient language (regardless whether FDA concludes that the petition is subject to Section 505(q)). If FDA were to simply ignore

[12] This should be true even if the citizen petition includes a Section 505(q) certification. As FDA has acknowledged, petitioners often have no means to determine whether a generic drug application is pending at the time a citizen petition is filed (let alone whether one is likely to be approved within 150 days). Indeed, the Agency amended its regulations in 2016 to require in relevant part that, for any citizen petition that "could … delay approval of an abbreviated new drug application [or other generic drug application]" (whether actually subject to 505(q) or not), petitioners submit the Section 505(q) certification. 21 C.F.R. § 10.31(c).

[13] Draft Guidance at 12-13 (lines 485-492).

and not process a petition under either Section 505(q) or the provisions of 21 C.F.R. § 10.30 applicable to non-Section 505(q) petitions, and provide no notice of this fact, it would cause uncertainty and inefficiency, and raise the potential for unnecessary administrative procedure challenges.

7. FDA Should Seek Continuing Enhancements For Its Non-505(q) Citizen Petition Processes

Allergan recognizes that the Draft Guidance is focused on Section 505(q) of the Federal Food, Drug, and Cosmetic Act and on citizen petitions directly subject thereto. More broadly, we request that FDA consider how to enhance its processes for addressing issues raised in non-Section 505(q) petitions in an efficient and timely manner. This is important because the Draft Guidance will enlarge the number of citizen petitions to be handled under the non-505(q) regulations. FDA often fails to respond substantively to non-505(q) petitions within the 180-day regulatory deadline.[14]

When promulgating its initial regulations on citizen petitions, the Agency supported goals of access, transparency, and accountability:

> The Commissioner has determined that the agency should obligate itself to respond to a petitioner, at least preliminarily, within a specified time period. He has determined that such a requirement will … enhance agency efficiency in conducting its business. Moreover … the obligation to respond to a citizen petition … *must be regarded as a priority matter* … if the agency is to maintain the public confidence in its ability to deal with the issues within its jurisdiction.[15]

In the context of citizen petitions implicating ANDAs, the Agency more recently reaffirmed: "It is incumbent upon FDA to consider and address the merits of petitions." In this regard, at times "petitions [lead] to a change in Agency policy" and, even if "petitions [do not] present new issues that CDER has not fully considered, … the Agency must nevertheless assure itself of that fact by reviewing the citizen petitions."[16]

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[14] In effect, FDA has been issuing "non-substantive" responses in the form of interim response letters in the non-505(q) petition context for many years. One key distinction of interim responses, compared to non-substantive denials issued to Section 505(q) petitioners, is that non-505(q) interim responses do not terminate the petition review process (and thus do not necessitate the filing of a new petition). The issue with non-505(q) petitions is the very long and unpredictable period for substantive response.

[15] See FDA, Administrative Functions, Practices, and Procedures, 42 Fed. Reg. 4680, 4685 (Jan. 25, 1977) (italics added).

[16] Statement of Gary Buehler, R.Ph., Director of the Office of Generic Drugs, Center for Drug Evaluation and Research, FDA, Before the Special Committee on Aging, United States Senate, Hearings on Improving Access to Generic Drugs (July 20, 2006) ("Buehler"), https://www.aging.senate.gov/imo/media/doc/hr161gb.pdf, at 7 and 8.

Allergan supports the implementation of efficiencies to promptly address the merits of citizen petitions. Indeed, we recognize that the Agency over time has made "considerable efforts … to improve the process for responding to citizen petitions."[17] For example, in the face of backlogs in its citizen petition responses, FDA previously underscored the importance of "mak[ing] the formal citizen petition process more efficient and more responsive."[18]

At all times, however, the government has recognized: "When FDA does not answer petitions in a timely manner, the public may lose confidence in the regulatory process."[19] We thus disagree with FDA's characterization of Section 505(q) petitions as "add[ing] to resource burdens on the generic drug review process and the FDA's regulatory decision making" and "tak[ing] resources away from the daily work of application review."[20] While we agree that the Agency's work in reviewing ANDAs is critical, this statement disregards the equally critical purposes and benefits of robust petitioning as envisioned by Congress when it instituted and then amended the citizen petition process. The statement fails to acknowledge any of these beneficial outcomes, and makes no attempt to facilitate their achievement.

FDA should also consider making available other means by which stakeholders can seek the Agency's views. When the Agency proposed circumscribing the scope of its citizen petition regulations in 1999 (as part of an effort to improve its ability to respond in a timely fashion to petitions received), FDA was, appropriately, careful to reassure stakeholders that other means would be available through which stakeholders could engage in discussions with it about topics of concern, including private correspondence and meetings, as provided for by 21 C.F.R. § 10.65.[21]

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[17] Buehler at 8.

[18] FDA, Citizen Petitions; Actions That Can be Requested by Petition; Denials, Withdrawals, and Referrals for Other Administrative Action; Proposed Rule, 64 Fed. Reg. 66822, 88626 (Nov. 30, 1999). This proposal followed a 1998 review by the Department of Health and Human Services' Office of Inspector General (OIG) that concluded that FDA did "not have an effective process for handling citizen petitions in a timely manner" and that improvements were needed in this regard. OIG, Review of the Food and Drug Administration's Citizen Petition Process (CIN: A-15-97-50002) (July 17, 1998) ("OIG Review").

[19] OIG Review. Although the Agency ultimately withdrew its 1999 proposed rulemaking to increase the promptness of its responses to citizen petitions, it did so by noting that it had achieved improvements in its ability to respond to citizen petitions through other mechanisms, thus again emphasizing the importance of issuing timely responses. 68 Fed. Reg. 16461 (April 4, 2003).

[20] Commissioner's Statement.

[21] In its 1999 proposal, "FDA emphasize[d] that the proposed rule is not intended to and does not reduce or curtail access to or discussions with the agency. For example, FDA's regulations provide for meetings and correspondence (see, e.g., Sec. 10.65)…. Informal avenues of communication, such as telephone calls, faxes, and electronic mail, also exist. These avenues of communication can be faster and more efficient methods for

Some of the Draft Guidance's provisions move away from the Agency's previous recognitions and regulations. For example, the § 10.65 regulation FDA previously emphasized as an important alternative to the citizen petition process provides, in relevant part, that "meetings may be held and correspondence may be exchanged between representatives of FDA and an interested person outside FDA on a matter within the jurisdiction of the laws administered by the Commissioner" (21 C.F.R. § 10.65(a)); that "[e]very person outside the Federal Government may request a private meeting with a representative of FDA in agency offices to discuss a matter … [and] FDA will make reasonable efforts to accommodate such requests" (21 C.F.R. § 10.65(c)); and that "FDA employees have a responsibility to meet with all segments of the public to promote the objectives of the laws administered by the agency" (21 C.F.R. § 10.65(d)). However, the Draft Guidance states that "communications with the Agency regarding any issues with the potential to delay the approval of an ANDA, 505(b)(2) application, or 351(k) application (regardless of whether the communications are considered to be petitions subject to section 505(q)) are appropriately submitted through the petition process pursuant to § 10.30 or 10.35 rather than as correspondence to the new drug application (NDA), ANDA, 505(b)(2) application, 351(k) application, or another process."[22] In a similar vein, in its recent report regarding FDA's processes for establishing bioequivalence standards for non-biological complex drugs, the Government Accountability Office ("GAO") wrote, "FDA officials stated that the agency will not engage in closed-door meetings [regarding bioequivalence standards] with individual drug sponsors unless it is in relation to the sponsor's own application."[23]

Delay of resolution of issues raised in citizen petitions, often with little to no transparency, can undermine confidence in the process overall. We request that FDA focus on increasing early opportunities for stakeholder understanding and interchange concerning generic drug regulatory issues of interest (e.g., explaining regulatory proposals, publishing underpinning data

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discussing issues or addressing concerns than citizen petitions." 64 Fed. Reg. 66822, 66823 (Nov. 30, 1999). See also id. at 66826 ("[T]he proposed rule does not restrict access to or contact with the agency; it simply redefines the types of actions that may be the subject of "citizen petitions" under Sec. 10.30 in order to make that formal administrative mechanism more responsive and efficient. Indeed, given that other FDA's [sic] regulations provide other means for contacting the agency (see, e.g., Sec. 10.65(a) (regarding correspondence)), the citizen petition regulation at Sec. 10.30 cannot and should not be viewed as being the sole or exclusive mechanism for "petitioning" FDA or as an exclusive mechanism for exercising a right to petition FDA. …Persons who wish to contact or "petition" FDA on issues that are outside the scope of proposed Sec. 10.30 would still be able to contact the agency, through letters, calls, or other means of communication. FDA emphasizes, again, that the proposed rule would not reduce public access to FDA; instead, it is intended to make the formal citizen petition process more efficient and responsive.").

[22] Draft Guidance at 6 (lines 225-230).

[23] GAO, Generic Drugs; FDA Should Make Public Its Plans to Issue and Revise Guidance on Nonbiological Complex Drugs (Dec. 2017) at 33.

(including FDA-sponsored research), and enabling robust debate about standards being proposed) – thereby supporting regulatory certainty and improved approval processes.[24]

In all of its efforts, FDA should avoid discouraging the submission of citizen petitions. For example, the Draft Guidance recommends (in a footnote) that "interested persons can express their views on issues related to bioequivalence for a drug product by submitting comments in response to a Federal Register notice regarding draft product-specific bioequivalence recommendations, instead of by submitting a petition concerning bioequivalence standards for a drug product."[25] However, the comment process does not enable stakeholders to receive a response from the Agency, much less in any time frame.

8. Further Considerations

In addition to the foregoing considerations, FDA's Draft Guidance can be improved by addressing the following limitations:

- **Provide A Petitioner With Reasonable Evidence That Its Concerns Have Been, or Will Be, Addressed**. FDA's current "non-substantive" denial approach to Section 505(q) leaves entirely unclear whether the Agency has actually made any decisions about issues raised in a petition (or whether the issues are still under evaluation) and provides no assurance that specific issues will be addressed at or before the time that a generic drug product is approved. This leaves a petitioner with no way to know whether or when consideration of important issues may occur, or what the outcome of FDA's deliberation might eventually be. As noted earlier, after a non-substantive denial, the only way for a petitioner to obtain a meaningful response is to file a subsequent petition. FDA regulations also require an Agency decision on a citizen petition before judicial review can be invoked in a court, 21 C.F.R. § 10.45(b), which further encourages stakeholders to submit additional petitions following non-substantive denials.

- **Allow Reasonable Cross-Referencing.** The inability to cross-reference material across citizen petitions causes an obligation to refile materials. Particularly with electronic technology, there may be opportunities to streamline citizen petition processes.

[24] We acknowledge that FDA has created some newer opportunities for interchange with the agency (e.g., hosting some public workshops of issues of current interest). These can be enhanced by more effective opportunities for two-way engagement. Unlike a response to a petition, however, whether and how to hold such workshops, and what information to provide in connection with them, is within FDA's discretion.

[25] Draft Guidance at 6 n. 15.

CONCLUSION

Allergan appreciates the many factors that FDA must balance as part of its mission. Thank you for your consideration of these comments about important stakeholder communication tools.

Sincerely,

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