Qualified Infectious Disease Product Designation Questions and Answers Guidance for Industry

DRAFT GUIDANCE

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

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic.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

I. INTRODUCTION

This guidance provides information on the implementation of Title VIII of the Food and Drug Administration Safety and Innovation Act (FDASIA),[2] titled *Generating Antibiotic Incentives Now* (GAIN). GAIN creates incentives for the development of antibacterial and antifungal drug products that treat serious or life-threatening infections. The purpose of this guidance is to provide a resource for information on FDA's policies and procedures related to the designation of a qualified infectious disease product (QIDP) under GAIN.

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

Title VIII, section 801 of FDASIA created the GAIN provisions under section 505E of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355f). GAIN offers incentives for the development of antibacterial and antifungal drugs for human use to treat serious or life-threatening infections. The primary incentive is a 5-year exclusivity extension for certain applications of drug products that have been designated as a QIDP and approved under section 505 of the FD&C Act. This 5-year exclusivity extension is added to any exclusivity for which the application qualifies upon approval. Additionally, section 524A of the FD&C Act (21 U.S.C. 360n-1) requires FDA to give priority review to the first application submitted for approval for a QIDP. A QIDP will also receive fast track designation at the sponsor's request (21 U.S.C.

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

[2] Pub. L. 112-144, 126 Stat. 993 (2012).

356(b)(1)). This guidance provides responses to common questions that might arise regarding QIDP designation and review of QIDP new drug applications (NDAs).

III. QIDP DESIGNATION DEFINED

Section 505E(g) of the FD&C Act provides for the designation by FDA of certain antimicrobial products as QIDPs. A QIDP is defined in section 505E(g) as: "an antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections, including those caused by –

> (1) an antibacterial or antifungal resistant pathogen, including novel or emerging infectious pathogens; or
>
> (2) qualifying pathogens listed by the Secretary under" section 505E(f) of the FD&C Act.

The Agency has codified the list of *qualifying pathogens* at 21 CFR 317.2.

For a drug product to be designated a QIDP, the sponsor is required to demonstrate that the drug is an "antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections."[3] A sponsor requesting a QIDP designation may also include documentation that the product is intended to treat an "antibacterial or antifungal resistant pathogen, including novel or emerging infectious pathogens"[4] or a *qualifying pathogen* as part of the designation request; however, such documentation is not required.

Q1. What does a QIDP designation cover (i.e., does the designation apply to any product containing the drug substance, or does it apply to a specific sponsor's drug product in the context of its specific proposed use)?

The QIDP designation applies to a specific drug product[5] from a specific sponsor for a specific use for which it is being studied. The designation is granted only to the sponsor making the request, and it does not apply to a drug substance in general or beyond the specified indications.

Q2. When can a sponsor make a request for QIDP designation?

A sponsor may request a QIDP designation at any time prior to that sponsor's submission of a marketing application under section 505(b) for that sponsor's drug product, as described in Q1, above (see section 505E(d)(1) of the FD&C Act).

[3] See section 505E(g) of the FD&C Act.
[4] Ibid.
[5] As defined in 21 CFR 314.3, "*Drug product* is a finished dosage form, e.g., tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients."

If a sponsor requests QIDP designation for a new indication for the sponsor's approved drug product, that request should be submitted to the investigational new drug (IND) application for that drug product. The marketing application for the new indication would then be submitted as an efficacy supplement.

Q3. How does a sponsor make a request for QIDP designation?

A request for QIDP designation should be submitted either to an IND or as pre-IND correspondence.[6] The cover letter should include the following text in bold font at the top of the page: **Request for Qualified Infectious Disease Product Designation**. Requests for multiple indications can be combined in a single submission or made separately. The sponsor should clearly identify each indication for which it is requesting QIDP designation.

Q4. What information should a QIDP designation request contain?

- A discussion of the information that supports the activity of the drug as an antibacterial or antifungal drug. For example:
  - In vitro data, including any available data on mechanism of action
  - Data from animal models of infection
  - Any available human data from phase 1, phase 2, or phase 3 studies

- The specific serious or life-threatening indication(s) for which the sponsor intends (or has begun) to develop the drug and the rationale or suitability for developing the drug for the proposed serious or life-threatening infection(s). Sponsors may wish to refer to the definition of *serious* that the Agency has used in the context of other programs intended to encourage the development of drugs to treat serious and life-threatening diseases or conditions: "Whether a disease is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one."[7]

- In addition, this request may (but is not required to) include information to demonstrate that the product is an antibacterial or antifungal drug that has the capacity to treat a serious or life-threatening infection caused by either of the following:
  - Resistant pathogen(s), including novel or emerging infectious pathogens
  - Qualifying pathogens listed in 21 CFR 317.2 (see Q12)

[6] Information regarding the CDER pre-IND consultation program for the Office of Antimicrobial products is available at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/Overview/default.htm.

[7] See guidance for industry *Expedited Programs for Serious Conditions—Drugs and Biologics*, citing the definition used in the preamble to the proposed rule, "New Drug, Antibiotic, and Biological Drug Product Regulations; Accelerated Approval," 57 FR 13234 at 13235 (April 15, 1992) and 21 CFR 312, subpart I. We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA Drugs guidance Web page at https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

Q5. When should a sponsor expect to hear from FDA regarding its QIDP designation request?

FDA will respond to a QIDP designation request within 60 calendar days of submission (see section 505E(d)(1) of the FD&C Act). For the purposes of QIDP designation, FDA considers the date of submission to be the date FDA receives the request.

Q6. Is fast track designation granted automatically with the QIDP designation or must a sponsor specifically request fast track designation?

Although a product designated as a QIDP is eligible for fast track designation,[8] the sponsor must specifically request fast track designation. If fast track has not previously been granted for the indication that is being considered for QIDP designation, fast track designation can be requested in the same letter with the QIDP designation request submitted to the sponsor's IND. If fast track designation has already been granted for this indication of the sponsor's proposed drug, there is no need to make an additional request. Fast track designation may also be requested at any time after the QIDP designation. Although QIDP designation may be requested prior to submission of an IND, a request for fast track designation may only be made concurrently with, or any time after, submission of an IND (see section 506(a)(2) of the FD&C Act).

Q7. GAIN defines *QIDP* as "an antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections…" Could an antibacterial or antifungal drug intended to prevent or diagnose a serious or life-threatening infection be eligible for QIDP designation?

In the context of other programs under the FD&C Act intended to expedite the development of drugs and biologics to address unmet medical needs, FDA has determined that a product is intended to treat a serious or life-threatening disease or condition if it is intended to have "an effect on a serious condition or a serious aspect of the [serious or life-threatening] condition," including diagnosing, preventing, and treating a serious aspect of the condition.[9] At the time of GAIN's enactment, Congress was aware of FDA's long-standing interpretation of the term "serious and life-threatening." Thus, FDA interprets the phrase "intended to treat a serious or life-threatening infection" in the context of QIDPs in a similar manner to these other programs. Accordingly, FDA will consider a drug to be "intended to treat a serious or life-threatening infection" if it is intended to diagnose, prevent, or treat such an infection.

Q8. Are biologic products or devices eligible for QIDP designation?

No. The provisions of GAIN refer only to human drugs that are the subject of applications under section 505 of the FD&C Act, and therefore, QIDPs must be human drugs whose applications are submitted pursuant to section 505(b) of the FD&C Act.[10] Accordingly, biologic products that are approved for marketing pursuant to section 351 of the Public Health Service Act (42 U.S.C.

[8] See section 524A of the FD&C Act.

[9] See guidance for industry *Expedited Programs for Serious Conditions—Drugs and Biologics*.

[10] Applications for combination products submitted under section 505(b) of the FD&C Act may qualify for QIDP designation.

262) or devices that are cleared pursuant to section 510 of the FD&C Act (21 U.S.C. 360) or approved pursuant to section 515 of the FD&C Act (21 U.S.C. 360e) are not eligible for QIDP designation.

Q9. Is priority review designation automatically given to any application or efficacy supplement submitted for a QIDP?

No. FDA automatically gives priority review designation to ***the first*** application or efficacy supplement submitted for a specific drug product and indication for which QIDP designation was granted (see section 524A of the FD&C Act, as amended by section 3101(a)(2)(N) of the 21st Century Cures Act).[11] A subsequent original application or efficacy supplement from the same sponsor for the same product and indication will receive priority review designation only if it otherwise meets the criteria for priority review.

IV. GAIN EXCLUSIVITY

Subject to the specified statutory limitations, a drug that is designated as a QIDP and is approved for the use for which the QIDP designation was granted will receive a 5-year extension to any exclusivity for which the application qualifies upon approval. Section 505E of the FD&C Act lists the following limitations under which the 5-year GAIN exclusivity extension is not available:

> (c) LIMITATIONS—Subsection (a) does not apply to the approval of—
> (1) a supplement to an application under section 505(b) for any qualified infectious disease product for which an extension described in subsection (a) is in effect or has expired;
> (2) a subsequent application filed with respect to a product approved under section 505 for a change that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength; or
> (3) a product that does not meet the definition of a qualified infectious disease product under subsection (g) based upon its approved uses.

Q10. When is an efficacy supplement to an approved NDA eligible for the 5-year GAIN exclusivity extension?

[11] Certain applications for QIDPs may qualify to receive a tropical disease priority review voucher (PRV) under section 524 of the FD&C Act, a rare pediatric disease PRV under section 529, or a material threat medical countermeasure PRV under section 565A. In order to receive a PRV, the application must be deemed (under section 524 or section 529) or determined (under section 565A) by the Agency to be eligible for priority review. In determining whether an application for a QIDP that receives priority review pursuant to section 524A is also eligible for priority review within the meaning of these provisions, if a PRV is requested, the Agency will determine whether the application satisfies the criteria for eligibility for a priority review designation, i.e., whether the drug treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. For more information on the priority review designation, see guidance for industry *Expedited Programs for Serious Conditions—Drugs and Biologics* (May 2014); see also Manual of Policies and Procedures 6020.3 Rev. 2, 6/25/13.

An efficacy supplement[12] to an approved NDA may be eligible for the 5-year GAIN exclusivity extension if the following conditions apply:

(1) The application that is being supplemented has not previously received the 5-year GAIN exclusivity extension,

(2) The supplement is for an indication for which the product has received a QIDP designation prior to submission of the supplement, and

(3) The supplement qualifies for 3-year exclusivity[13] and/or orphan drug exclusivity,[14] as applicable.

Q11. Can a subsequent application for a previously approved product be eligible for the 5-year GAIN exclusivity extension?

Under section 505E(c)(2) of the FD&C Act, a subsequent application for a previously approved product is not eligible for the 5-year GAIN exclusivity extension if the applicant (or its predecessor in interest) previously received approval and received the 5-year exclusivity extension pursuant to section 505E(a), and the subsequent application is seeking approval for a change that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength.

V. QUALIFYING PATHOGENS

Section 505E(f) of the FD&C Act instructs the Secretary (and thus FDA, by delegation) to establish and maintain a list of "qualifying pathogens," and make public the methodology for developing the list. A *qualifying pathogen* is defined as:

> . . . a pathogen identified and listed by the Secretary . . . that has the potential to pose a serious threat to public health, such as —
> (A) resistant gram positive pathogens, including methicillin-resistant Staphylococcus aureus, vancomycin-resistant enterococcus;
> (B) multi-drug resistant gram negative bacteria, including Acinetobacter, Klebsiella, Pseudomonas, and E. coli species;
> (C) multi-drug resistant tuberculosis; and
> (D) clostridium difficile.

Q12. Where can I find the list of "qualifying pathogens" mentioned in GAIN?

The list of "qualifying pathogens" can be found in 21 CFR 317.2. The final rule, "Establishing a List of Qualifying Pathogens Under the Food and Drug Administration Safety and Innovation

[12] See 21 CFR 314.3(b) for definition of an efficacy supplement.
[13] Section 505(c)(3)(E)(iv) and 505(j)(5)(F)(iv) of the FD&C Act.
[14] Section 527 of the FD&C Act.

Act," was published on June 5, 2014.[15] The final rule describes the factors FDA considered and the methodology used for developing the list.

Q13. Must a product be intended for the treatment of an infection caused by a qualifying pathogen to be eligible for QIDP designation?

No. The statutory standard for inclusion on FDA's list of qualifying pathogens is different from the statutory standard for QIDP designation. QIDP designation, by definition, requires that the drug in question be "an antibacterial or antifungal drug intended to treat a serious or life-threatening infection" (section 505E(g) of the FD&C Act). *Qualifying pathogen* is defined according to a different statutory standard; the term means "a pathogen identified and listed by the Secretary…that has the potential to pose a serious threat to public health" (section 505E(f) of the FD&C Act) (emphasis added). That is, a drug intended to treat a serious or life-threatening bacterial or fungal infection caused by a pathogen that is not included on the list of qualifying pathogens may be eligible for designation as a QIDP; however, a drug that is intended to treat an infection caused by a pathogen on the list may not always be eligible for QIDP designation if it is not intended to treat a serious or life-threatening infection.

[15] 79 FR 32464.