Advanced Manufacturing Technologies Designation Program

Guidance for Industry

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

December 2024
Pharmaceutical Quality/CMC

Advanced Manufacturing Technologies Designation Program

Guidance for Industry

Additional copies are available from:
Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353
Email: druginfo@fda.hhs.gov
https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs
and/or
Office of Communication, Outreach and Development
Center for Biologics Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 71, Room 3128
Silver Spring, MD 20993-0002
Phone: 800-835-4709 or 240-402-8010
Email: ocod@fda.hhs.gov
https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances

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

December 2024
Pharmaceutical Quality/CMC

TABLE OF CONTENTS

Contains Nonbinding Recommendations

Advanced Manufacturing Technologies Designation Program 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

Advanced manufacturing is a general term for an innovative pharmaceutical manufacturing approach or technology that has the potential to improve the reliability and robustness of the manufacturing process and supply chain and increase timely access to quality medicines. Advanced manufacturing can integrate novel technological approaches, use established techniques in an innovative way, or apply production methods in a new domain where there are no defined best practices or experience.[2]

FDA encourages the early adoption of specific advanced manufacturing technologies (AMTs) that have the potential to benefit patients by improving manufacturing and supply dependability and optimizing development time of drugs.[3] These technologies can be integral to ensuring quality and supporting a robust supply of drugs that are life-supporting, life-sustaining, of critical importance to providing health care, or in shortage. AMTs can directly improve product quality (e.g., through better manufacturing controls and fewer human interventions).

This guidance provides recommendations to persons and organizations interested in participating in FDA's Advanced Manufacturing Technologies Designation Program, which facilitates the development of drugs manufactured using an AMT that has been designated as such under the program (hereinafter *designated AMT*). The guidance outlines the eligibility criteria for AMT designation, the submission and assessment process for requests, and the benefits of receiving an AMT designation and includes a questions and answers section to cover additional details about key concepts important for program utilization. Specifically, the guidance describes:

---

[1] This guidance has been prepared by the Office of Pharmaceutical Quality in the Center for Drug Evaluation and Research in cooperation with the Center for Biologics Evaluation and Research at the Food and Drug Administration.

[2] For additional information about advanced manufacturing in general, see FDA's web page "Advanced Manufacturing" at https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/advanced-manufacturing.

[3] In this guidance, the term *drug* refers to human drug products and biological products, other than biological products that meet the definition of a device under section 201(h)(1) of the FD&C Act (21 U.S.C. 321(h)(1)).

- The process for submitting an AMT designation request, including a description of eligibility criteria and the data and other information to be included.

- When and how FDA will assess AMT designation requests.

- The process by which FDA will engage with requestors, holders of designated AMTs, and applicants for drugs manufactured using, referencing, or relying upon a designated AMT.

- Benefits related to drug development and application assessment.[4]

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

FDA's Advanced Manufacturing Technologies Designation Program, which is required under section 506L of the Federal Food, Drug, and Cosmetic Act (FD&C Act),[5] offers a framework for persons or organizations (e.g., applicants, contract manufacturers, technology developers) to request designation of a method or combination of methods of manufacturing[6] a drug as an AMT. The program facilitates the development of drugs as described in section 506L(b) of the FD&C Act that are manufactured using a designated AMT, submitted in an application under section 505 of the FD&C Act (21 U.S.C. 355) or section 351 of the Public Health Service Act (PHS Act, 42 U.S.C. 262), and regulated by the Center for Drug Evaluation and Research (CDER) or the Center for Biologics Evaluation and Research (CBER). The holder of the AMT designation or another authorized party may reference or rely upon data or information about the designated AMT in an application in the same context of use for which the designation was granted.[7] FDA will facilitate development and expedite assessment of an application, including

[4] In this guidance, the term *assessment* also means *review*. *Assessment* is the term that the Center for Drug Evaluation and Research's Office of Pharmaceutical Quality and Office of Generic Drugs will generally use in place of *review*. *Assessment* means the process of both evaluating and analyzing submitted data and information to determine whether the application meets the requirements for approval and documenting that determination.

[5] Section 3213 of the Food and Drug Omnibus Reform Act of 2022 (FDORA) amended the FD&C Act, in part, to add section 506L (21 U.S.C. 356l).

[6] In this guidance, the term *manufacturing* includes the steps outlined in the definition of *manufacture* in 21 CFR 207.1.

[7] See sections 506L(c)(1) and 506L(d)(2) of the FD&C Act. In this guidance, *context of use* refers to the specified purpose and manner of use for a designated AMT that will be used in developing and manufacturing a particular drug type (e.g., dosage form or class). For more information about how FDA interprets the term *context of use* as it relates to AMT designation, see the questions and answers section of this guidance (section V, Q1).

supplements, for drugs that are manufactured using a designated AMT as described in section 506L(d)(1) of the FD&C Act.[8]

Use of designated AMTs can provide greater assurance of quality, shorten drug development time, assist industry in more efficiently meeting regulatory requirements for commercial manufacturing, and strengthen regulatory predictability for products that use a designated AMT. To encourage the adoption of designated AMTs, the Advanced Manufacturing Technologies Designation Program offers early interaction opportunities, before application submission, with designated AMT holders and applicants to advise on designated AMTs and their implementation in drug manufacturing.[9]

III. AMT DESIGNATION REQUESTS

AMT designation requests are made independently of application submissions. Therefore, there is no predetermined stage during which AMT designation requests should be submitted to FDA. Before submitting an AMT designation request, persons or organizations seeking designation of a method of manufacturing as an AMT (hereinafter *requestors*) should familiarize themselves with the data requirements described in section 506L of the FD&C Act, the recommendations outlined in this guidance, and other publicly available sources of product development information.[10]

Any technology can be considered for AMT designation provided that the technology meets the eligibility criteria described in section 506L(b) of the FD&C Act, the requestor has sufficient data and information to demonstrate eligibility, and the technology is mature enough to consistently and reliably manufacture product in the context of use for which AMT designation is sought.

For developers of technologies that do not yet meet the data requirements to support eligibility for AMT designation, FDA recommends early engagement with CDER's Emerging Technology Team (ETT), which manages CDER's Emerging Technology Program, or CBER's Advanced Technologies Team (CATT), which is part of CBER's Advanced Technologies Program, if a technology meets the criteria for these programs.[11] ETT and CATT assist companies interested in implementing emerging or advanced technologies in drug development, and their programs are suitable for technologies in various stages of maturity.

This section covers eligibility criteria, the data and information needed to demonstrate eligibility, the submission process, AMT designation determination, and lifecycle considerations.

---

[8] In this guidance, an expedited assessment does not refer to an expedited user fee review goal.

[9] For a description of the differences between *requestor*, *designated AMT holder*, and *applicant*, see section V, Q2.

[10] See, e.g., International Council for Harmonisation guidance for industry *Q8(R2) Pharmaceutical Development* (November 2009). We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[11] For information about these two programs, how they differ from the Advanced Manufacturing Technologies Designation Program, and the benefits of early engagement with ETT or CATT, see section V, Q7 and Q8.

A. Criteria

Per the criteria described in section 506L(b) of the FD&C Act, a method of manufacturing or combination of methods is eligible for AMT designation if it incorporates a novel technology or uses an established technique or technology in a novel way[12] that will substantially improve the manufacturing process for a drug while maintaining equivalent, or providing superior, drug quality, including by:

- Reducing development time for a drug using the designated manufacturing method;[13] or
- Increasing or maintaining the supply of a drug that is life-supporting, life-sustaining, or of critical importance to providing health care, or a drug that is on the drug shortage list under section 506E of the FD&C Act (21 U.S.C. 356e).

B. Content of the Request

An AMT designation request must include data or information demonstrating that the method of manufacturing for which a requestor is seeking designation (hereinafter *proposed AMT*) meets the statutory criteria in a particular context of use.[14] The types of supportive data and information to include in a request depend on the specific method of manufacturing and its proposed context of use and should be determined by the requestor in preparing its request. In addition, the request must demonstrate the ability of the proposed AMT to substantially improve the manufacturing process for a drug while maintaining or improving upon its quality, including by reducing drug development time or increasing or maintaining the supply of a drug that is life-supporting, life-sustaining, of critical importance to providing health care, or in shortage.[15] The robustness of the data and information should be commensurate with the level of risk inherent to the process and proposed context of use.

Specifically, an AMT designation request should include the following information:

- A brief description of the method of manufacturing or combination of methods and why it should be considered for AMT designation, including a brief explanation of how the method, in part or in whole, incorporates a novel technology or uses an established technique or technology in a novel way.
- The context of use under which the proposed AMT will be used, including information (e.g., dosage form, class of drug) about the model (i.e., representative) drug used to generate manufacturing or development data submitted in the request.

[12] For an explanation of how FDA interprets the term *novel* in the context of AMT designation, see section V, Q3.

[13] In this guidance, *reducing development time* means decreasing the time it takes for a product to get to market, such as through more efficient manufacturing or faster generation of higher quality data to support application approval.

[14] Section 506L(c)(1) of the FD&C Act.

[15] Section 506L(b) of the FD&C Act.

- A detailed description of how the method of manufacturing or combination of methods meets the eligibility criteria described in section 506L(b) of the FD&C Act in a particular context of use. This description should include:
    - An outline of the steps of the proposed AMT, including information about where in the overall manufacturing process the proposed AMT is intended to be used.
    - Information about how the proposed AMT will ensure equivalent or superior drug quality, including the proposed control strategy.[16]
    - A description of how the proposed AMT will reduce drug development time or how it will address a critical drug supply need.
    - Developmental data, including quality-related data generated through process development studies that evaluate the proposed AMT, and information that describes and justifies the proposed AMT's context of use.
- Perceived regulatory, technical, or other challenges to implementation of the proposed AMT.
- For requestors who are also applicants or prospective applicants, and if known at the time of the AMT designation request, the anticipated timeline for drug development activities that incorporate the proposed AMT, including the planned submission of any applications that would use, reference, or rely upon data and information about the proposed AMT in the same context of use.
- If applicable, information about previous engagement with ETT or CATT.
- For a proposed AMT that is intended for use in manufacturing an existing drug (i.e., a drug that is the subject of a previously approved application) that meets the criteria in section 506L(b)(2)(A) or (B) of the FD&C Act:
    - A cross-reference to the existing application.[17]
    - Information demonstrating that the proposed AMT will increase or maintain the supply of the drug.
    - Evidence that the proposed AMT will maintain equivalent or provide superior drug quality (e.g., quality data from studies comparing drugs manufactured using the proposed AMT and those manufactured using an established technology in the same context of use).

[16] For more information on control strategies, see ICH Q8(R2).

[17] If the requestor plans to leverage confidential commercial information from a previously approved application in their request, but they are not also the applicant, they should obtain a right of reference to such information.

FDA acknowledges that requestors who are not also applicants may not have data about a specific drug to include in their AMT designation request. In these cases, FDA recommends that requestors include data generated using a model drug to provide the Agency with a clear understanding of the proposed AMT's parameters, limitations, and context of use.

C. Submission Process

Requestors should only submit a request once supporting data and information to demonstrate eligibility for AMT designation are available and ready for inclusion in the request. Requestors should submit their AMT designation request electronically to AMT_designation_requests@fda.hhs.gov.[18] The subject line should be REQUEST FOR AMT DESIGNATION in uppercase letters. In addition to the data and information described in section III.B of this guidance, the email should include the requestor's contact information—including the name, address, email address, and telephone number for their main point of contact in the United States—and indicate if the request is specific to CDER, CBER, or both.

Upon receipt of the AMT designation request, FDA intends to acknowledge receipt, confirm whether the request is complete, and begin an evaluation to determine whether to designate the proposed AMT.

D. Designation Determination

AMT designations will be limited to those methods of manufacturing that meet the criteria described in section 506L(b) of the FD&C Act and explained in section III.A of this guidance. To determine eligibility, a team of FDA experts from the center with jurisdiction over the type of drug that would incorporate the proposed AMT will review the request. This team, including members of ETT or CATT, where applicable, will evaluate the data and information submitted in the request, including information relating to the context of use, and will seek input from subject matter experts, as needed, to determine if the proposed AMT meets the designation criteria and should therefore be granted AMT designation. For proposed AMTs that have potential cross-center impact, a cross-disciplinary team, including members from CDER and CBER, will evaluate the requests.[19]

The team will include a designated lead with demonstrated expertise in the manufacturing process, product type, or other elements specific to the proposed AMT to serve as the primary subject matter expert for the request. The designated lead may facilitate contact with the requestor to obtain additional information about the AMT designation request or to coordinate discussions between FDA and the requestor regarding specific aspects of the proposed AMT during the designation determination process.[20] The format of such discussions will be determined by FDA on a case-by-case basis. As appropriate, the designated lead will facilitate

[18] If the request includes confidential commercial information, it is the responsibility of the company to ensure it is submitted using one of FDA's secure messaging partners. Requestors can ask to be added to the list of FDA's secure messaging partners by emailing SecureEmail@fda.hhs.gov. Confidential commercial or trade secret information should be clearly marked as such in accordance with 21 CFR 20.61(d).

[19] See section 506L(c)(1)(B) of the FD&C Act.

[20] See section 506L(c)(1)(A) of the FD&C Act.

the involvement of senior FDA managers and other experienced FDA staff in a collaborative, cross-disciplinary review of the proposed AMT.[21]

Section 506L(c)(2) of the FD&C Act requires FDA to complete AMT designation determinations regarding designation for a particular context of use and program acceptance or denial within 180 calendar days of FDA's receipt of the request. Submission of an AMT designation request does not guarantee designation or acceptance into the program. FDA expects to deny requests that are incomplete or are submitted for methods of manufacturing that do not meet the criteria described in section 506L(b) of the FD&C Act. Denial of an AMT designation request does not preclude a requestor from submitting a new request if additional data and information to support eligibility become available.

E. Lifecycle

Designated AMT holders should communicate updates or proposed changes that could affect the context of use or eligibility of their designated AMTs, such as when additional supportive data become available (e.g., additional batch analysis data), by emailing AMT_designation_requests@fda.hhs.gov. The subject line should be PROPOSED CHANGE FOR DESIGNATED AMT in uppercase letters. In addition to the requestor's contact information described in section III.C of this guidance, the email requesting a change should include the product center that reviewed the request (CDER, CBER, or both), a brief description of the proposed change, supporting data for the proposed change, and a list of persons or entities who have been given a right of reference to the designated AMT.[22] The email should also address the potential impact of the proposed change on the criteria for designation or the particular context of use for which the AMT was designated, as defined at the time of initial designation.

FDA intends to assess the proposed changes, including supporting data, to confirm that the designated AMT continues to meet criteria for designation and maintains the same context of use for which the AMT was designated. FDA will also determine whether additional data or a new designation request are necessary. Once assessment of the proposed change is complete, FDA will communicate results to the AMT holder. It is the responsibility of the AMT holder to inform applicants about any changes to their designated AMT, including changes to the context of use.

Once FDA has gained significant experience assessing a designated AMT and the designated AMT has been used in multiple approved applications, FDA may decide to graduate the technology and transfer the review of future applications that use, reference, or rely upon that AMT—including supplements to an original application that had previously been granted the designation—to the standard quality assessment process (rather than an expedited process). FDA intends to make such graduation decisions on a case-by-case basis. Graduation would keep AMT designation aligned with the statutory prerequisite of novelty[23] and facilitate further innovation

[21] See section 506L(c)(1)(B) of the FD&C Act.

[22] Entities that obtain a right of reference to reference or rely upon a designated AMT should ensure that the agreement (i.e., letter of authorization) includes mechanisms for communication regarding future changes.

[23] See section 506L(b) of the FD&C Act.

over the program's duration[24] by leveraging FDA's available AMT-related resources on new AMTs that continue to meet the program's goal of encouraging adoption of novel technologies to shorten drug development times for critical medicines while maintaining or improving product quality. As a designated AMT reaches graduation, the designated lead will facilitate communication with the AMT holder, relevant applicants, and FDA assessment teams about pending and final changes to an AMT's designation status, including a justification for such changes.

Similar to other established methods of manufacturing, a graduated AMT is not precluded from reentry into the Advanced Manufacturing Technologies Designation Program, provided that the technology is proposed for use in a novel way (i.e., different from its previously designated context of use or its role in a manufacturing process) such that it again meets the eligibility criteria described in section 506L(b) of the FD&C Act.

IV. BENEFITS OF AMT DESIGNATION

A key benefit of AMT designation is FDA's early interaction with applicants regarding the development and manufacture of drugs using a designated AMT.[25] As resources permit, FDA intends to provide timely advice and to engage in additional communication, in the form of written correspondence or meetings, with applicants for a drug manufactured using a designated AMT. Such communication may take place during both early drug development and subsequent application assessment and will be used to address designated AMT-related questions and issues, including submission content related to implementation of a designated AMT and other AMT-related topics. When appropriate, the designated lead for the AMT request will coordinate with the appropriate FDA quality assessment team.

FDA expects to prioritize applicant interactions involving the use of a designated AMT in drug development or commercial manufacturing, with higher priority being given to drug development activities and applications using a designated AMT with the potential to significantly improve product quality, address known quality issues for a drug or class of drugs, or increase or maintain the supply of drugs that are life-supporting, life-sustaining, of critical importance to providing health care, or in shortage. For new drug applications (NDAs), biologics license applications (BLAs), and abbreviated new drug applications (ANDAs) involving complex generic drugs, these interactions would typically occur under the appropriate

[24] Under section 506L(f) of the FD&C Act, FDA may not consider requests for AMT designation after October 1, 2032.

[25] See sections 506L(c) and (d) of the FD&C Act.

user fee meeting type.[26] For ANDAs not involving complex generic drugs, these interactions would typically take place through controlled correspondence.[27] However, applicants with a designated AMT—whether the ANDA involves a complex product or a non-complex product—can also request product development and presubmission meetings.[28] Any additional interaction deemed necessary by FDA will be facilitated by the designated lead for the AMT request.

The designated lead will facilitate communication with the applicant regarding advice and information relevant to product quality to support the successful adoption of a designated AMT. As needed, the designated lead will also connect applicants with other FDA disciplines outside the scope of product quality when an applicant requires expertise or advice from these other disciplines.

Although knowledge gained during the AMT designation process will be leveraged during FDA's assessment of an application that uses a designated AMT, it is the applicant's responsibility to demonstrate, through the required technical data submitted in the chemistry, manufacturing, and controls (CMC) section,[29] that a designated AMT is suitable for inclusion in their application.

A. Drug Development

Applicants are encouraged to take advantage of the benefits afforded under the program to engage with the team that designated the AMT to discuss, early in the development process, how the designated AMT can be used to shorten or otherwise optimize drug development time.[30] The designated lead will work to:

- Ensure that meetings with the applicant are collaborative and productive.
- Answer applicant questions about the information appropriate to be included in their application.
- Discuss the quality assessment of the applicant's future applications that plan to use, reference, or rely upon a designated AMT.

---

[26] See draft guidances for industry *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products,* Revision 1 (September 2023) and *Formal Meetings Between the FDA and Sponsors or Applicants of BsUFA Products,* Revision 1 (August 2023). When final, these guidances will represent FDA's current thinking on these topics. See also guidances for industry *Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA,* Revision 1 (October 2022) and *Expedited Programs for Regenerative Medicine Therapies for Serious Conditions* (February 2019).

[27] See guidance for industry *Controlled Correspondence Related to Generic Drug Development*, Revision 1 (March 2024).

[28] Applicants should submit requests for a product development meeting in an appropriate format, such as the format described in the guidance for industry *Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA,* Revision 1. In addition to the applicable information identified in sections V and VIII of the Formal Meetings guidance, applicants should provide documentation of the AMT designation.

[29] See 21 CFR 314.50(d)(1), 21 CFR 314.94(a)(9), and 21 CFR 601.2.

[30] See section V, Q10, in this guidance for information about requesting engagement.

B. Application Assessment

The designated lead will facilitate the quality assessment of an application for a drug manufactured using the designated AMT with the aim of making the assessment process more efficient than the process for applications using manufacturing methods not designated under the program. FDA intends to use this approach to support applicants while they are developing the CMC section of their applications such that the incorporation of a designated AMT will not increase the time or number of assessment cycles required to arrive at a quality-related decision and, as a result, will not increase the time required to arrive at a decision regarding overall application approval. The knowledge and familiarity gained by FDA though the assessment of applications that use a particular designated AMT should streamline the assessment of subsequent applications that use the same designated AMT.

When a designated AMT graduates from the program as described in section III.E of this guidance, FDA will take appropriate steps to transfer information about the previously designated AMT to the appropriate assessment team for applications that used, referenced, or relied upon the previously designated AMT. New applications received after the transfer will receive the standard level of FDA communication and interaction afforded to all applicants. Graduation of a designated AMT will not affect approved applications that reference the previously designated AMT or the ability of an applicant to continue to use that technology with an appropriate right of reference.

V. QUESTIONS AND ANSWERS

Q1. How is context of use considered when determining AMT designation and assessing applications for other products (i.e., not the model drug used for the AMT designation request)?

Consistent with section 506L(c) of the FD&C Act, AMT designation applies to a method of manufacturing within a particular context of use rather than to a specific application. For this reason, requestors can use model (i.e., representative) drugs instead of application-specific drugs to generate the supporting data for proposed AMTs to be included in their designation requests. The data and information generated using a model drug should, at a minimum, be specific to a particular class of drugs and, as described in section III of this guidance, should include development data, including batch analysis data generated using either a developmental candidate molecule or a model drug. Requestors should fully and clearly describe the context of use within which they are requesting the AMT be designated, including how it will be used to develop and manufacture a specific type or range of drugs.

Whether the use of a designated AMT for manufacturing a specific drug that is the subject of an application would be considered to be the same context of use for which the AMT was designated can be discussed in presubmission meetings and will be determined during the application assessment process.

Q2. What is the difference between a requestor, a designated AMT holder, and an applicant?

Multiple entities can be involved in the development or use of a designated AMT over its lifecycle. These entities include requestors, designated AMT holders, and applicants. An entity might meet the definition of all three terms described below.

In this guidance, the term *requestor* describes a person or organization that has developed a technology and has submitted an AMT designation request to FDA for that technology. As described in sections III.B and III.C of this guidance, requestors define the context of use for their proposed AMTs, determine the types of supporting data and information to include in AMT designation requests, and prepare and submit the requests to FDA. FDA may facilitate communication with requestors as described in section 506L(c)(1)(A) of the FD&C Act.

In this guidance, the term *designated AMT holder* describes a person or organization whose AMT designation request has been evaluated by FDA and granted designation under the program.[31] As described in section III.E of this guidance, designated AMT holders should communicate changes that could impact eligibility or the context of use for their designated AMTs to FDA. They can also authorize applicants to incorporate by reference data and information about the designated AMT in their application (see Q5 and Q6).

In this guidance, the term *applicant* describes an entity that has submitted or plans to submit to FDA an NDA, ANDA, BLA, or investigational new drug application (IND). An applicant can use, reference, or rely upon a designated AMT in the development or manufacturing of a drug that is the subject of their application if they are authorized to do so by the designated AMT holder or are themselves the AMT holder.[32] When doing so, applicants determine if the designated AMT is appropriate for their specific drug, incorporate the designated AMT into the drug's development and manufacture, and submit drug-specific data in the application.

Q3. What does FDA consider a novel technology or use of an established technique or technology in a novel way?

For purposes of evaluating eligibility for AMT designation, FDA generally considers a novel technology or an established technique or technology used in a novel way to be one for which FDA has limited assessment or inspectional experience. A novel technology can be a completely new technology that FDA has not previously seen in a submission or a technology with which FDA has experience but with a significantly different use than is now being proposed.

Although novelty is an essential element of AMT designation, it is not the only defining characteristic of a designated AMT. Certain technologies might be considered novel based on the above description, but their incorporation into the manufacturing process alone would not meet statutory eligibility criteria to qualify for AMT designation.

[31] See section 506L(c)(2) of the FD&C Act.

[32] See section 506L(d)(2) of the FD&C Act.

Q4. What happens if FDA independently receives more than one AMT designation request for a similar technology?

FDA may determine that multiple similar technologies, independently submitted by different requestors in separate AMT designation requests, are each eligible for designation. In this event, FDA will individually assess the data and information contained in each request and independently determine AMT designation, as described in section III.D of this guidance. Unless they are used in a novel way, technologies similar to AMTs that have graduated from the program or are close to graduation are likely not eligible for designation.

Q5. How can an NDA, ANDA, or IND applicant reference or rely upon a designated AMT in an application?

When an NDA, ANDA, or IND applicant and designated AMT holder are different entities, the designated AMT holder, who can also be the holder of a drug master file (DMF) that contains the designated AMT, can authorize the applicant to incorporate by reference data and information about the designated AMT in their application.[33] An application that references or relies upon a designated AMT can receive the benefits provided by the AMT designation with the appropriate authorization if the referenced AMT is used to manufacture a drug in the same context of use for which the designation was granted as described above.

Although multiple applications can reference the same designated AMT, each application referencing a particular designated AMT will be assessed on its own merits. When referencing or relying upon a designated AMT in an application, applicants should explain how the designated AMT will be used to manufacture the drug that is the subject of the application and why that context of use is consistent with the context of use for which the AMT received designation.

Q6. How can a BLA applicant reference or rely upon a designated AMT in an application?

A BLA applicant can use, reference, or rely upon a designated AMT in the development or manufacturing of a biological product that is the subject of their application if they are authorized to do so by the designated AMT holder or are themselves the AMT holder.[34]

However, because a BLA holder is expected to have knowledge of and control over the manufacturing process for the biological product for which it has a license, FDA expects that supporting data and information for the drug substance, drug substance intermediate, and drug product (DS/DSI/DP) be submitted directly to the BLA rather than be incorporated by reference

[33] For more information about DMFs, see 21 CFR 314.420 and draft guidance for industry *Drug Master Files,* Revision 1 (October 2019). When final, this guidance will represent FDA's current thinking on this topic.

[34] See section 506L(d)(2) of the FD&C Act.

to a DMF, consistent with 21 CFR 601.2(g).[35] For this reason, even when using a designated AMT, BLA applicants should have access to such supporting data and information, including the controls and validation of the manufacturing process and other information critical to evaluating the BLA holder's control over product quality, and should include this information in their BLA.[36]

The exclusion in 21 CFR 601.2(g) against cross-referencing a DMF in a BLA is limited to information about the DS, DSI, and DP. Some AMT-related data and information can be included in a DMF, such as certain equipment used in manufacturing the DS, DSI, and DP. FDA will evaluate whether it is permissible to include such data and information in a DMF on a case-by-case basis. For a drug-biologic combination product,[37] an applicant can incorporate by reference a DMF for nonbiological product constituent parts.[38]

Q7. How does the Advanced Manufacturing Technologies Designation Program differ from CDER's Emerging Technology Program and CBER's Advanced Technologies Program?

All three programs focus on engagement between FDA and prospective drug developers to discuss potential regulatory challenges and clarify related questions about using novel technologies for which CDER or CBER have limited assessment experience. Despite these similarities, there are also several differences between the three programs, including the maturity level of the technology accepted into the program and the timing, intended participants, and scope of each program.

In some cases, a technology that is not eligible for CDER's Emerging Technology Program or CBER's Advanced Technologies Program could nevertheless be eligible for AMT designation. The opposite could also be the case. For example, as noted in section III, the data and information necessary for AMT designation might not yet be available for a technology granted acceptance into either of the other two programs.

CDER's Emerging Technology Program allows potential applicants to submit to ETT questions and proposals about the use of a specific emerging technology (e.g., questions about regulatory

---

[35] In the preamble to codification of this final rule, FDA noted that "the inability to incorporate by reference DS/DSI/DP information contained in a master file does not remove BLA applicants' incentives or ability to proceed with product development. An applicant who does not intend to manufacture all aspects of the product for licensure may…consider other types of cooperative manufacturing arrangements, while still assuming responsibility for meeting the applicable product and establishment standards. These other arrangements would provide alternatives in cases where the incorporation by reference of a master file is not permitted" (89 FR 9743 at 9746, February 12, 2024).

[36] The preamble, in discussing the general complexity of biological products, noted "As a scientific matter, for biological products, the Agency considers it to be generally impractical for the applicant to confirm DS/DSI/DP quality characteristics without complete knowledge of, and control over, all aspects of the manufacturing process, including the manufacturing process for the DS/DSI/DP" (89 FR 9743 at 9746, February 12, 2024).

[37] For more information, see FDA's web page "Frequently Asked Questions About Combination Products" at https://www.fda.gov/combination-products/about-combination-products/frequently-asked-questions-about-combination-products#CP and 21 CFR 3.2(e).

[38] See 21 CFR 601.2(g)(3).

issues or submission of CMC information). ETT serves as the primary point of contact for companies interested in implementing an emerging technology into CDER-regulated products. CBER's Advanced Technologies Program promotes dialogue, education, and input between CBER and prospective developers of advanced manufacturing and testing technologies. CATT facilitates such communications to promote the implementation of these technologies in the development of CBER-regulated products.[39]

ETT and CATT discussions can begin earlier in the drug development process. In contrast, the Advanced Manufacturing Technologies Designation Program is intended for methods and technologies that, while still novel (or used in a novel way), are more mature, such as those for which model drug-specific data to support eligibility are available.

As discussed elsewhere in this guidance, the designated AMT holder may not necessarily be the same entity as the applicant who ultimately uses a designated AMT in their application. Although ETT engagement can occur before a specific product is in development, CDER's Emerging Technology Program is primarily designed for companies that intend to eventually incorporate an emerging technology into the CMC section of their application. For CBER's Advanced Technologies Program, CATT is limited to early engagement before regulatory submission. Therefore, any meetings regarding the use of a designated AMT that take place after application submission would generally occur through the Advanced Manufacturing Technologies Designation Program.

Finally, CDER's Emerging Technology Program and CBER's Advanced Technologies Program may involve activities outside the scope of AMT designation, including discussions with industry about other elements such as novel dosage forms or drug delivery systems. Of note, only the statutory Advanced Manufacturing Technologies Designation Program confers an official designation for technologies accepted into the program.

Q8. What are the benefits of engaging with ETT or CATT before requesting AMT designation?

Although AMT designation should not be requested at the same time as ETT or CATT engagement, early engagement with ETT or CATT can provide an avenue for potential requestors to elicit FDA feedback about the technical components of a technology before it has reached a maturity level appropriate for AMT designation. ETT and CATT are not suitable, however, to address whether a technology has reached a maturity level appropriate for AMT designation or provide decisions on AMT eligibility or designation.

[39] For more information about CDER's Emerging Technology Program, see guidance for industry *Advancement of Emerging Technology Applications for Pharmaceutical Innovation and Modernization* (September 2017) and https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/emerging-technology-program. For more information about CBER's Advanced Technologies Program, see https://www.fda.gov/vaccines-blood-biologics/industry-biologics/cber-advanced-technologies-program.

Q9. How does the Advanced Manufacturing Technologies Designation Program differ from the Platform Technology Designation Program?

Both the Advanced Manufacturing Technologies Designation Program and the Platform Technology Designation Program[40] aim to increase the efficiency of drug development and manufacturing. However, the two programs generally serve different purposes and apply to different types of technologies at different maturity levels.

Regarding program purpose, one of the distinguishing criteria for a method of manufacturing or combination of methods being proposed for AMT designation is that it must incorporate a novel technology or an established technique or technology used in a novel way.[41] In contrast, one of the distinguishing criteria of a designated platform technology is that it is a well-understood and reproducible technology that is incorporated in or used by an approved drug or licensed biological product.[42] For this reason, FDA expects to have previous assessment or inspectional experience with a designated platform technology at the time of designation.

Regarding eligible methods of manufacturing, a designated AMT is limited to a method or combination of methods of manufacturing a drug. In contrast, a broader range of technologies (e.g., nucleic acid sequences, molecular structures, mechanisms of action, delivery methods) is eligible for platform technology designation, and applicants must demonstrate, among other criteria,[43] that the platform technology is incorporated in or used by a drug and is essential to the structure or function of such drug to receive designation.[44]

Because of the differences between the two programs, FDA recommends requesting only the designation that is appropriate for the particular method or technology in question. There should be no expectation that requesting both designations simultaneously would offer additional benefits.

Q10. How should an applicant request engagement with FDA regarding the use of a designated AMT?

Applicants can request a meeting with FDA to have a preliminary discussion about using a designated AMT and request subsequent meetings throughout the drug development process. As described in section IV of this guidance, such meeting requests will typically occur under the appropriate user fee meeting type and should be made in accordance with the electronic submission guidance[45] and other guidances related to formal meetings between FDA and

---

[40] See section 506K of the FD&C Act (21 U.S.C. 356k) and draft guidance for industry *Platform Technology Designation Program for Drug Development* (May 2024). When final, this guidance will represent FDA's current thinking on this topic.

[41] See section 506L(b) of the FD&C Act.

[42] See sections 506K(b)(1) and 506K(h)(1) of the FD&C Act.

[43] See section 506K(h)(1) of the FD&C Act.

[44] See section 506K(h)(1)(A) of the FD&C Act.

[45] See guidance for industry *Providing Regulatory Submissions in Electronic Format—Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications,* Revision 7 (February 2020).

applicants.[46] Although applicants can request such a meeting at any milestone during the application assessment process, FDA encourages earlier engagement to enable prompt resolution of regulatory challenges and more efficient application assessment. Any such submissions should be clearly identified as a **REQUEST FOR A MEETING UNDER THE ADVANCED MANUFACTURING TECHNOLOGIES DESIGNATION PROGRAM** in bold, uppercase letters. In addition to the content recommended in relevant guidances,[47] the meeting background package should include the timing for application submission and a summary of how the designated AMT will be used to manufacture the drug.

[46] See footnotes 26 and 28.

[47] Ibid.