# Advancement of Emerging Technology Applications for Pharmaceutical Innovation and Modernization

## Guidance for Industry

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

**September 2017**
**Pharmaceutical Quality/CMC**

*Contains Nonbinding Recommendations*

# Advancement of Emerging Technology Applications for Pharmaceutical Innovation and Modernization

## 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*
*http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm*

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

**September 2017**
**Pharmaceutical Quality/CMC**

## TABLE OF CONTENTS

*Contains Nonbinding Recommendations*

# Advancement of Emerging Technology Applications for Pharmaceutical Innovation and Modernization 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 provides recommendations to pharmaceutical companies interested in participating in a program involving the submission of chemistry, manufacturing, and controls (CMC) information containing emerging technology[2] to FDA. The program is open to companies that intend to include the technology as part of a regulatory submission including investigational new drug applications (IND), original or supplemental new drug applications (NDA), abbreviated new drug applications (ANDA) or biologic license applications (BLA), or application-associated Drug Master Files (DMF)[3] reviewed by the Center for Drug Evaluation and Research (CDER), and where that technology meets other criteria described in this guidance. This program does not cover products reviewed by the Center for Biologics Evaluation and Research.

Issues in pharmaceutical manufacturing have the potential to significantly impact patient care as failures in quality may result in product recalls and harm to patients. Additionally, product failures or facility, equipment, or manufacturing problems are a major factor leading to disruptions in drug supply. Modernizing manufacturing[4] technology may lead to a more robust manufacturing process with fewer interruptions in production, fewer product failures (before or after distribution), and greater assurance that the drug products manufactured in any given period of time will provide the expected clinical performance. For example, contemporary aseptic

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

[2] For the purpose of this document, emerging technology should be novel in the context of the pharmaceutical and related industries and it should have the potential to modernize the pharmaceutical manufacturing body of knowledge related to product quality. Emerging technology will be new to FDA in the context of pharmaceutical quality, with limited prior experience and knowledge.

[3] This program is also open to companies or manufacturers that intend to include emerging technology in a drug master file (DMF) that will be referenced by the planned application(s). The steps to request participation in the program are described in section III.B Process.

[4] For the purpose of this guidance, the definition of manufacturing includes testing, packaging and labeling operations, and quality control across the product lifecycle (e.g., design, qualification, and commercial manufacturing). Refer to 21 CFR 210.3(b)(12).

manufacturing facilities that are highly automated and use isolators and other modern separation technologies have the potential to decrease the risk of contamination from the processing line. Encouraging development of emerging technology may lead to pharmaceutical innovation and modernization, such as a more robust drug product design and improved manufacturing with better process control, thereby leading to improved product quality and availability throughout a product's lifecycle.

In this program, pharmaceutical companies can, prior to the regulatory submission, submit questions and proposals about the use of specific emerging technology to a group within FDA (Emerging Technology Team – ETT), which includes relevant representation from all FDA pharmaceutical quality functions. The ETT works in partnership with relevant pharmaceutical quality offices and assumes a leadership or co-leadership role for the cross-functional quality assessment team (including review and on-site facility evaluation or inspection) for submissions involving emerging technology. The ETT serves as the primary point of contact for companies that are interested in implementing emerging technology in the manufacture of their drug products and for the relevant quality assessment team to:

(a) Answer sponsor/applicant questions about the information FDA expects to see in their submission;

(b) Identify and help facilitate regulatory assessment of an emerging technology in accordance with existing legal and regulatory standards, guidance, and Agency policy related to quality assessment;

(c) Serve as the lead or co-lead on the quality assessment team (i.e., staff involved in the review of the CMC sections of the application and evaluation of the manufacturing facilities), in partnership with relevant pharmaceutical quality offices, including the Office of Compliance and Office of Regulatory Affairs, as appropriate, to conduct review, on-site evaluation, and make the final quality recommendation regarding the potential approval of submissions in the program; and

(d) Identify and resolve policy issues to inform FDA approaches and recommendations regarding future submissions that involve the same technology.

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 is committed to supporting and enabling pharmaceutical innovation and modernization as part of the Agency's mission to protect and promote the public health. The Agency hopes that

these efforts may also help reduce the number of drug shortages, as noted in FDA's drug shortage strategic plan.[5] In 2002, FDA launched an initiative entitled "Pharmaceutical cGMPs for the 21st Century: A Risk-Based Approach," to encourage the implementation of a modern, risk-based pharmaceutical quality assessment system.[6] One of the goals of this initiative was to encourage the early adoption of new technological advances by the pharmaceutical industry and ensure that regulatory review, compliance, and inspection policies are based on state-of-the-art pharmaceutical science. In 2004, this was further described in the FDA guidance for industry entitled *PAT—A Framework for Innovative Pharmaceutical Development, Manufacturing, and Quality Assurance*.[7] This guidance describes a scientific, risk-based framework intended to support innovation and efficiency in pharmaceutical development, manufacturing, and quality assurance. The guidance also describes the concept that quality cannot be tested into products; in other words, it should be built in or should be present by design. Quality is built into pharmaceutical products through a comprehensive understanding of the intended use of the product, the characteristics of the product, and the design of the product and manufacturing process using principles of engineering, material science, and quality assurance to ensure acceptable and reproducible product quality and performance throughout a product's lifecycle.

FDA continues to support flexible approaches in the manufacturing of quality pharmaceutical products. While the implementation of emerging technology is critical to advancing product design, modernizing pharmaceutical manufacturing, and improving quality, FDA also recognizes that the adoption of innovative approaches may represent challenges to industry and the Agency. By the very nature of an approach being innovative, a limited knowledge and experiential base about the technology may exist. Pharmaceutical companies may have concerns that using such technologies could result in delays while FDA reviewers familiarize themselves with the new technologies and determine how they fit within existing regulatory framework. Through the Emerging Technology Program, FDA intends to encourage the adoption of innovative approaches to product design and pharmaceutical manufacturing by leveraging existing resources within the Agency to facilitate the regulatory assessment of submissions to the Agency involving novel technologies likely to improve product quality and availability throughout a product's lifecycle.

## III. DISCUSSION

As part of this program, FDA intends to provide early engagement and additional meeting opportunities, which enable the participants and FDA to discuss: (1) product or manufacturing design and development issues, and (2) submission content related to the emerging technology. The process will include appropriate coordination with the FDA quality assessment team. Based on experience gained during the program, FDA intends to develop guidance and standards, as

[5] See *FDA's Strategic Plan for Preventing and Mitigating Drug Shortages* at: https://www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM372566.pdf.

[6] See *Pharmaceutical cGMP's for the 21st Century: A Risk-Based Approach* at: https://www.fda.gov/downloads/drugs/developmentapprovalprocess/manufacturing/questionsandanswersoncurrentgoodmanufacturingpracticescgmpfordrugs/ucm176374.pdf.

[7] 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.

necessary, on emerging technologies and approaches to encourage and facilitate the innovation and modernization in pharmaceutical industry.

### A. Scope

Acceptance of a request to participate in this program will depend on the applicant's proposed plan for submission of an IND, original or supplemental ANDA, BLA, or NDA, or application-associated DMF based on the criteria described below.

- The planned submission should include one or more elements which will be subject to quality assessment for which the Agency has limited review or inspection experience. Examples of such elements include an innovative or novel: (1) product technology (e.g., dosage form or container-closure system); (2) manufacturing process (e.g., design, scale-up, or lifecycle approaches); and/or (3) control strategy (e.g., testing technology or process controls).

- The proposed technology in the planned submission has the potential to improve product safety, identity, strength, quality, or purity (e.g., an innovative process design that can lead to a more robust and predictable production of quality pharmaceutical products).

In the request to the Agency, the applicant should provide sufficient justification that the proposed emerging technology in the planned submission meets the above criteria (see section III.B Process for details regarding steps to request participation in the program). Such an approach, rather than providing a prescriptive set of acceptance criteria, enables the program to be open to a wide variety of novel manufacturing technologies. As a reminder, this program only affects the quality section of the submission (CMC and facility-related information). Existing requirements related to the review and determination of adequacy or approval of a submission will not be waived, suspended, or modified for purposes of this program. Applicants must make the submission in accordance with 21 CFR parts 312, 314, 601, and other applicable standards.

### B. Process

Parties planning to submit an IND, original or supplemental BLA or NDA, or application-associated DMF, and who have an interest in participating in this FDA program should submit a written request for a Type C meeting as described in the FDA guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicant*. The request should specify the meeting request as a "Type C meeting – request to participate in the Emerging Technology Program." Interested parties planning to submit an ANDA should submit a pre-ANDA meeting request and specify the meeting request as a "Pre-ANDA meeting – request to participate in the Emerging Technology Program." Either type of request should be submitted at least three months prior to the planned application submission date. The meeting request and related questions should be submitted electronically to CDER-ETT@fda.hhs.gov.[8] In addition to the items outlined in the

[8] If the request includes commercial confidential information, it is the responsibility of the company to ensure it is one of FDA's secure messaging partners. Companies may request to be added to the list of FDA's secure messaging partners by sending a request to: SecureEmail@fda.hhs.gov.

referenced guidance, the request should also include the following items and should not exceed five pages including figures and tables:

(1) A brief description of the proposed emerging technology;

(2) A brief explanation why the proposed emerging technology is substantially novel and unique and should be considered under this program;

(3) A description of how the proposed emerging technology could potentially improve product safety, identity, strength, quality, or purity;

(4) A summary of the development plan and any perceived roadblocks to implementation (e.g., technical or regulatory); and

(5) A timeline for a submission of an IND, original or supplemental ANDA, BLA, or NDA, or DMF and its associated application.

Based on the availability of Agency resources, we expect to limit acceptance into the program to technologies that are likely to advance product design or modernize pharmaceutical manufacturing, and with which the Agency has limited prior experience and knowledge. FDA expects to notify companies of its decision regarding acceptance into the program in writing within 60 days of receipt of the request. Although incomplete and/or unclear requests will generally be denied, FDA may contact the applicant to request additional information. Once accepted into the program, the participant can engage with the ETT and quality assessment team in accordance with existing meeting procedures and guidance(s).[9]

[9] See the FDA guidances for industry on *Formal Meetings Between the FDA and Sponsors or Applicants* (see information on "Type C" meetings) and *Controlled Correspondence Related to Generic Drug Development*.