Responding to FDA Form 483 Observations at the Conclusion of a Drug CGMP Inspection

Guidance for Industry

DRAFT GUIDANCE

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For questions regarding this draft document, contact (CDER) Tara Gooen Bizjak, 301-796-3257; (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010; (CVM) AskCVM@fda.hhs.gov; or (OII) OIIPolicyStaffs@fda.hhs.gov.

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Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Veterinary Medicine (CVM)
Office of Inspections and Investigations (OII)

March 2026
Current Good Manufacturing Practice (CGMP)

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Responding to FDA Form 483 Observations at the Conclusion of a Drug CGMP Inspection Guidance for Industry[1]

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic.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 is intended for foreign and domestic human and animal drug manufacturing establishments inspected by FDA[2] whose drugs are regulated by the Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), and the Center for Veterinary Medicine (CVM).[3,4] This guidance is also intended for combination product manufacturers where CDER or CBER is the lead Center.[5] The purpose of this guidance is to assist drug manufacturers who choose to respond to FDA when they receive an FDA Form

[1] This guidance has been prepared by the Office of Compliance in the Center for Drug Evaluation and Research in cooperation with the Center for Biologics Evaluation and Research, the Center for Veterinary Medicine, and the Office of Inspections and Investigations (OII) at the Food and Drug Administration. In preparing this guidance, CDER has also consulted with the Office of Combination Products.

[2] See section 704(a)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 374(a)(1)).

[3] This guidance is specific to CDER, CBER, and CVM product manufacturers because of the expectation to thoroughly investigate unexplained discrepancies per current good manufacturing practice (CGMP) requirements (21 CFR 211.192). Although device manufacturers have a similar expectation, the Center for Devices and Radiological Health already has a corollary guidance for industry and FDA staff *Nonbinding Feedback After Certain FDA Inspections of Device Establishments* (April 2020). 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.

[4] This includes outsourcing facilities registered under section 503B of the FD&C Act (21 U.S.C. 353b).

[5] A *combination product* is a product comprised of two or more regulated medical products (i.e., a combination of a drug, device, and/or biological product with one another) that are physically, chemically, or otherwise combined or mixed and produced as a single entity. 21 CFR 3.2(e)(1). The drugs, devices, and biological products included in combination products are referred to as *constituent parts* of the combination product.

483 Inspectional Observations (FDA 483) at the conclusion of an inspection to assess conformity with current good manufacturing practice (CGMP).[6,7]

Among other requirements, establishments must ensure compliance with applicable CGMP[8] requirements under the Federal Food, Drug, and Cosmetic Act (FD&C Act), such as through implementing needed corrective actions to address observations, regardless of whether the establishment responds to FDA's observations in writing or whether FDA provides feedback on such written response. Although FDA generally considers corrective actions and other factors in determining whether to pursue regulatory action, partially implemented or promised corrective actions do not preclude FDA from taking regulatory action at any time.

Recommendations regarding the structure and content of a response to an FDA 483 are intended to support clear communication.

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

Typically, when FDA identifies objectionable conditions or practices with respect to an FDA-regulated product that in the investigator's judgment may constitute violations of the FD&C Act, it issues an FDA 483 to an inspected establishment's owner, operator, or agent in charge on completion of the inspection. An FDA 483 contains inspectional observations made by FDA representative(s) during the inspection but does not represent the Agency's final findings or conclusions regarding an establishment's compliance with CGMP requirements under the FD&C Act or other applicable requirements.

[6] This applies to all CGMP inspections, including routine surveillance, for-cause, and preapproval, and prelicense inspections.

[7] FDA recommends that a response is submitted within 15 business days of the issuance of an FDA 483. See section III.D, Response Submission Timeframe, for additional information.

[8] Under section 501(a)(2)(B) of the FD&C Act (21 USC 351(a)(2)(B)), a drug, including an active pharmaceutical ingredient, is deemed adulterated if the methods used in, or the facilities or controls used for its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with CGMP requirements. For CGMP requirements, see 21 CFR part 210, 21 CFR part 211, and 21 CFR part 212, as well as 21 CFR part 4 for combination products, and 21 CFR part 226 for Type A medicated articles. For biological products, also see additional applicable requirements under 21 CFR parts 600-680.

Responding to an FDA 483 gives an establishment an opportunity to provide, among other things:

- An assessment on whether a distributed drug's quality is of concern based on the observations
- Details regarding how an establishment has addressed the observations and/or plans to address the observations, including short-term and long-term actions
- Information concerning conditions or systemic issues that led to the observations
- Additional information relevant to observations, such as information on the scope of the issue, effect on other drugs, and whether the observation is an isolated incident or is systemic in nature

The FDA 483 response can also address observations of a verbal nature (including non-reportable observations and discussion items) that are not listed on the FDA 483, but which FDA representatives discussed during the inspection.[9]

III. SUBMITTING A RESPONSE TO FDA

If a written FDA 483 response is submitted, it may be the primary or a key component in FDA's review when evaluating whether subsequent Agency action is warranted. FDA 483 responses should be as accurate, clear, concise, and well-organized as necessary to convey an establishment's position. FDA recommends that establishments take advantage of this voluntary opportunity to respond to inspectional observations.

A. Response Format and Content

The FDA 483 response should show that an establishment has addressed or is actively addressing observations identified in the FDA 483 and underlying issue(s).[10] The establishment should take a comprehensive approach to ensure that it has considered all relevant information (e.g., derived from investigations, corrective action and preventative actions (CAPAs),[11] or any other actions) when drafting the FDA 483 response.

The FDA 483 response should include a table of contents and at least the following elements:

[9] See FDA Investigations Operations Manual (2024) section 5.5.11 and 5.7.3.7.12.

[10] Establishments may also provide additional information in their FDA 483 response (e.g., responding to verbal discussion items).

[11] The term *CAPA* is defined in International Council for Harmonisation (ICH) guidance for industry *Q10 Pharmaceutical Quality System* (April 2009). ICH guidances are available on the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents. See the Glossary at the end of this guidance for additional information.

(1) The identity of the establishment submitting the response, including the establishment's name, full address of the inspected site, and the inspected site's FDA Establishment Identifier (FEI). The FEI number is at the top of the FDA 483.

(2) A copy of the FDA 483 issued at the close of the inspection.

(3) The identity of the response preparer, and if not prepared by the establishment, the preparer's relationship to the establishment (e.g., the establishment's consultant, U.S. agent, or outside counsel).

(4) The identity of the signatory of the written response.

- The written response should be signed by a person in the establishment's executive management who allocates resources and has the authority to implement commitments. Other key personnel may also opt to sign the written response such as a site head or the head of the quality unit.[12]

(5) Any letters of authorization, if the establishment has retained a consultant[13] or outside counsel.

(6) Any associated global investigation plans (see section IV.B) and reports, either prepared by the establishment or others (e.g., consultants).[14]

(7) An executive summary of all remediation activities with key details, as well as a more detailed description of each observation or grouped observations and associated remediation activities, including each of the following:

- A patient- and product-focused risk assessment of the observations, with an assessment of inventory and distributed drugs still within expiry and any possible effects on safety, identity, strength, quality, and purity of potentially affected drugs.

- A detailed investigation report with scope; summary; list of associated drug(s) and lot number(s); identified root cause(s) of the observation and any related systemic issues; the CAPA plan; a summary of completed actions, including interim actions; and a planned effectiveness evaluation, with results if available.

[12] See ICH Q10 and the Glossary at the end of this guidance for reference to executive management responsibilities.

[13] The term *consultant* includes someone who is a third party and proficient in the remediation of CGMP deviations. See 21 CFR 211.34.

[14] See Question 18 in the guidance for industry *Data Integrity and Compliance with Drug CGMP Questions and Answers* (December 2018).

- Attachments related to the associated observation. Attachments can include documents, pictures, video, diagrams, or data. All attachments should be signed, indicating support for the contents contained therein. All documents provided by a consultant, including attachments, should be signed by the consultant.

Tables could be used to organize this information in the executive summary, for example:

Example of Executive Summary Format

FDA 483 Observation Number or Other Item Related to Inspection (e.g., discussion item)	General Category/System	Summary	CAPA Number	Target Date	Current Progress of Remediations
1., 1a., etc. (include brief descriptive name)	Facility, equipment, etc.	Brief summary of issue and CAPA	CAPA number, if applicable	Target date, including any interim actions taken	Substantive summary of status, including (1) to be initiated; (2) in-progress; or (3) completed. Describe any issues that may influence timing of completion

(8) Discussion of each FDA 483 observation and other items as appropriate.
Note: Observations can be grouped by topic. Each observation or group of observations should have its own section and be individually noted and numbered in the table of contents.

For FDA to fully evaluate any FDA 483 response, establishments should submit all correspondence in English. If an English translation of a document is provided, a copy of the original document in the foreign language should be submitted to FDA, and verified as complete and accurate, with the name, address, and a brief statement of the translator's qualifications. If an English translation of a document in a foreign language is not provided, FDA generally does not intend to include these documents in the Agency's review of the response or supporting evidence.

B. Interim Reporting

For any remediation activities that are not complete, establishments should consider submitting, as part of the response and follow-up responses, preliminary results with a timeline for completion, along with interim measures they have put in place until the CAPA is completed.

FDA encourages establishments to develop a communication plan for all ongoing remediation activities. A communication plan should incorporate milestone deliverables and written follow-up reports to FDA, including when an establishment intends to submit follow-up reports regarding commitments it made in the initial response or responses, as well as what information would be included in these reports.

FDA can review these reports to periodically assess the risk associated with the status of the corrective actions and will take additional actions, in accordance with our applicable authorities, as necessary to protect patient and public health.

C. Where to Send Responses

In general, establishments should electronically submit responses to the email address provided on the FDA 483. Files greater than 100 megabytes may be submitted as smaller files in separate emails or can be submitted through an alternative electronic gateway. If there are any attachments that cannot be submitted electronically (e.g., large video files), please contact FDA at the email address listed on the FDA 483 for additional options.

D. Response Submission Timeframe

Although establishments are not required to respond to FDA's observations listed in an FDA 483, FDA recommends that those establishments that choose to respond submit their responses within 15 business days[15] after the FDA 483[16] was issued. Generally, if FDA receives a response to an FDA 483 within 15 business days after the FDA 483 was issued, FDA plans to conduct a detailed review of the response before determining whether to pursue subsequent action.[17] FDA recommends establishments address all observations[18] within this 15-day time period by submitting a single response to an FDA 483, rather than multiple responses to individual observations. In the case of complex observations that are not fully addressed within 15 business days, FDA recommends establishments submit a CAPA plan and a proposed time frame for substantive responses to the observations within 15 business days. FDA will not ordinarily delay regulatory action, such as issuing a warning letter, to review a response to an FDA 483 that is received more than 15 business days after the FDA 483 was issued.

[15] *Business day* is defined as Monday through Friday, excluding Federal holidays as defined in 5 U.S.C. section 6103.

[16] If FDA amends an FDA 483, establishments may submit their responses 15 business days from the amendment.

[17] See the *Investigations Operations Manual* (2025) Chapter 5 subsections 5.5.12.3 "Reportable Observations" and 5.7.3.7.14 "General Discussion with Management." See generally "Review of Post-Inspection Responses" (74 FR 40211, August 11, 2009).

[18] Where this guidance discusses investigations, root cause analysis, and CAPA plans related to an observation, it assumes the observation describes a CGMP deficiency or deviation for a drug product that must be investigated under 21 CFR 211.192 (i.e., to determine root cause) with appropriate follow-up (i.e., implement appropriate corrective action and preventive actions) in accordance with CGMP requirements, notwithstanding contested observations addressed in section V, Resolving Scientific or Technical Disagreements with FDA 483 Observations. For active pharmaceutical ingredient manufacturing, these deficiencies or deviations should also be investigated as described in ICH guidance for industry *Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients* (September 2016).

IV. RECOMMENDATIONS FOR ADDRESSING FDA 483 OBSERVATIONS

Establishments should consider the severity of each observation and prioritize corrective actions accordingly, which might include grouping issues or taking a systemic approach to corrective actions. Some observations may be clustered, such as in general categories (e.g., investigations, cleanrooms, staff competencies) or systems (quality, production, facilities and equipment, packaging and labeling, materials, and laboratory control). Establishments should also examine past inspections and internal audits for repeat observations or similar observation trends. Identifying categories and trends may highlight a systemic issue at a facility or within an organization. There are quality risk management[19] tools which may be useful to assist in clustering and prioritizing observations (e.g., cause-and-effect analysis).

Establishments should determine if deficiencies described in an observation affect other drugs, processes, or associated facilities and contract organizations and expand their investigations accordingly. As investigations proceed, additional gathered or obtained information may indicate that changes should be made to the initial risk assessment and the investigation plan. (see section IV.C, Develop an Investigation Plan and Conduct an Investigation).

FDA 483 observations are not an exhaustive list of all deficiencies that could be present at an establishment. If an establishment identifies an issue for additional follow-up that is outside the initial scope of the establishment's investigation of an observation from an issued FDA 483, the establishment should take appropriate corrective action within its quality management system to address any non-cited objectionable conditions that might exist.

There may be situations where a consultant is useful for additional insight to understand and assess inspectional observations and to develop an appropriate CAPA plan. For example, FDA recommends establishments engage a CGMP consultant when observations involve data integrity findings.[20]

Establishments must thoroughly document actions, findings, and any resulting changes to their investigations or CAPA plans.[21] The proposed CAPA plan and commitments should be realistic, measurable, and achievable. FDA may evaluate these activities during the next inspection of an establishment to verify that they have been implemented and are effective.

A. Understanding and Assessing the Observations

Understanding the observations on the FDA 483 is important to correcting issues and preventing their recurrence. Throughout the FDA inspection process, including at the closing meeting, an establishment should engage with the FDA representative(s) to elicit any necessary clarification

[19] See the ICH guidance for industry *Q9(R1) Quality Risk Management* (May 2023).

[20] See Question 18 in the guidance for industry *Data Integrity and Compliance with Drug CGMP Questions and Answers* (December 2018).

[21] 21 CFR 211.192.

on findings. During and immediately after the close of an inspection, an establishment's management should fully understand all observations and assess any related risks to product quality and patient safety. Establishments should take timely and appropriate actions based on this risk assessment. Actions may include, but are not limited to, notifying customers, recalling drugs, conducting additional testing, adding lots to stability programs, design improvements (e.g., process, equipment, or facility), amending or supplementing drug application or master files, enhanced complaint monitoring, and labeling revisions. If applicable, establishments that manufacture animal drugs should perform a risk assessment of the animals receiving the drug as well as any person handling the drug or humans consuming the products of food-producing animals.[22]

The following elements are helpful to fully understand the observation and assess the scope and risks to product quality and patient safety:

(1) Any related complaints about the drugs, whether confirmed or unconfirmed, and associated health hazard evaluations, as appropriate

(2) Any information verbally communicated by an FDA representative(s) during the inspection, or notes taken by establishment employees during the inspection to help understand the investigator's observation(s)

(3) Interviews of employees in roles connected with the observation

(4) Review of related documentation, such as standard operating procedures, batch records, lab records, logbooks, or other internal documents

(5) Applicable statutes, regulations, and related FDA guidance for industry on the topic, and consideration of appropriate recognized standards

B. Management Responsibility

If the responsible officials are not present for discussion when the observations are first communicated, FDA recommends that the responsible officials are notified of potential inspectional observations during the inspection and that they are notified in writing of reports of inspectional observations issued by FDA.[23] FDA expects that an establishment's management reviews the FDA 483 at the facility level and, if applicable, at the corporate level. This review should ensure that everyone is aware of and understands the issues raised during the inspection.

In addition to understanding inspection observation(s), an establishment's management should consider if adequate resources have been committed (e.g., use of a dedicated team or consultants

[22] See sections 501, 512, 571, and 572 of the FD&C Act (21 U.S.C. 351, 360b, 360ccc, and 360ccc-1) and 21 CFR 211.192.

[23] For finished drug products, responsible officials must be notified in writing of reports of inspectional observations issued by FDA (21 CFR 211.180(f)).

for complex activities, facility upgrades, and regulatory filings as appropriate) and if interim CAPAs are needed to address risks to patient safety and product quality.

An establishment's management should form a multidisciplinary investigation team with clear roles and responsibilities to understand an observation and set the foundation for a robust investigation. The team should have full support, including regular communication, from executive management to conduct an objective and effective investigation into root causes. Also, an establishment's management should consider an observation in the context of their entire manufacturing and quality governance at all relevant levels of the company.

Establishment management should provide the leadership needed for the successful functioning of a quality system. The Agency recommends that managers ensure that the quality system facilitates systematic evaluation of issues. Ultimately, the establishment is responsible for meeting CGMP requirements (e.g., ensuring all observations are appropriately remediated).[24]

C. Develop an Investigation Plan and Conduct an Investigation

FDA recommends establishments prepare an investigation plan and include a detailed protocol and methodology. A comprehensive investigation using the prepared investigation plan demonstrates to FDA that an establishment is addressing the observations and the underlying issue(s). This plan should include a scientifically justified and risk-based scope, including justification for any part of an establishment's operations that is excluded from the investigation.

For finished drugs, 21 CFR 211.192 requires a thorough investigation of issues such as an unexplained discrepancy or the failure of a batch or any of its components to meet any of its specifications (and investigation of other batches of the same drug product and other drug products that may have been associated with the specific failure or discrepancy). A written record of the investigation is also required, including its conclusions and follow-up.[25] Toward this end, a comprehensive investigation plan addressing FDA 483 observations also generally includes identifying any related trends, linking any connected FDA 483 observations, assessing

[24] See section 501(a)(2)(B) of the FD&C Act (21 U.S.C. 351(a)(2)(B)) and paragraph following section 501(j) of the FD&C Act ("*For purposes of paragraph (a)(2)(B), the term 'current good manufacturing practice' includes the implementation of oversight and controls over the manufacture of drugs to ensure quality, including managing the risk of and establishing the safety of raw materials, materials used in the manufacturing of drugs, and finished drug products*"); also see generally 21 CFR parts 210 and 211 and FDA guidance for industry *Quality Systems Approach to Pharmaceutical CGMP Regulations* (September 2006).

[25] 21 CFR 211.192.

risks, and analyzing root causes.[26,27] FDA recommends that the same approach should be used for other drugs.[28]

A risk assessment helps establishments identify and understand the potential effect an observation has on patient safety, manufactured drugs (whether or not they have been distributed), and future drug quality.[29]

For example, an inspectional observation cited that a particular piece of equipment was cleaned improperly. Interviews with employees revealed that the same deficient cleaning procedures are used for multiple pieces of equipment. In this hypothetical situation, it would be important to expand the scope of the investigation to include all equipment using the deficient cleaning procedures, all drugs manufactured using that equipment, as well as the adequacy of all of their cleaning procedures.

Preventing recurrence of an observation is based on determining the root cause(s); addressing the most obvious causal factor is often not sufficient. A methodical approach to identifying the root cause(s) is important, including identifying potential causes (there may be more than one), investigating each potential cause individually, and testing product or systems using scientifically supported approaches for verification. An establishment should be aware of and minimize bias in risk evaluation and decision-making when determining root cause. For example, testing that only supports the first hypothesized root cause may exclude the real (or complete) root cause and may bias the interpretation of data. The real (or complete) root cause may not be investigated, which could lead to additional CGMP failures.[30]

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[26] See ICH Q9(R1) *Quality Risk Management* (May 2023); *Investigating Out-of-Specification (OOS) Test Results for Pharmaceutical Production* (May 2022).

[27] Additional examples of elements that are often included in a comprehensive investigation are: review of the variables that can compromise state of control or lead to failure, either on their own or in combination (see Ishikawa, Kaoru (Translator: J H Loftus), 1990; Introduction to Quality Control, Chapman and Hall); determining the appropriate scope; complaints; out-of-specification and out-of-trend test results and investigations (see the guidance for industry *Investigating Out-of-Specification (OOS) Test Results for Pharmaceutical Production* (May 2022)); any related analytical tests, including dates of testing; and initial and retest results. General considerations include materials; people, including management oversight; production; environment; facility; equipment; laboratory; and historical experience with the product and process.

[28] See ICH Q7 at section 2.16.

[29] Additionally, submission of drug quality issues in an FDA 483 response does not negate the need to file a Field Alert Report required under 21 CFR 314.81(b)(1) or Biological Product Deviation Report required under 21 CFR 600.14, 606.171, or 1271.350(b), when appropriate. Under these regulatory requirements, applicants have a responsibility to report information to FDA concerning quality defects or certain deviations and unexpected events in manufacturing. See also the guidance for industry *Field Alert Report Submission: Questions and Answers* (July 2021) and *Biological Product Deviation Reporting for Licensed Manufacturers of Biological Products Other than Blood and Blood Components* (October 2006).

[30] See ICH Q9(R1).

During an investigation, it may also be valuable for an establishment to determine why the issues leading to the observation were not previously identified by the quality unit or corrected by the establishment's management before the FDA inspection. Further, the establishment should consider how improvements to the quality system, personnel management, and overall quality culture[31] may improve organizational performance.

D. Develop and Implement a CAPA Plan

FDA encourages establishments to begin developing a CAPA plan during, or immediately after, the close of an inspection to address issues underlying the observations and correct and prevent the issue(s) from recurring. The CAPA plan should be updated once an establishment has thoroughly investigated the scope of the issue(s).

A thorough CAPA plan should address the root cause or causes identified during the investigation and be commensurate with the level of the risks identified through a risk assessment (e.g., consider the potential effect on patient health, safety, and product quality), as well as ensure that operational design, procedures, and systems are adequate and modified as necessary.

A CAPA plan should include a communication plan with clear steps toward completion, timelines, and deliverables. Corrective actions should be implemented in all affected areas and verified to ensure effectiveness and that there are no unintended consequences.

E. Evaluate CAPA Effectiveness

Determining the effectiveness of CAPA is a fundamental part of evaluating whether the actions establishments take successfully address the associated issues and associated root cause or causes.[32] An adequate effectiveness check should consist of more than routine sampling and testing.

If the effectiveness evaluation indicates that CAPA measures do not adequately address the issue, the establishment should revisit the investigation and CAPA plan. The root cause may have been incorrectly identified, or more than one root cause exists, and additional investigations may be warranted to identify modifications to the CAPA plan.

FDA recommends that establishments use a monitoring system to track overall CAPA effectiveness and periodically evaluate their investigation and CAPA systems to identify the need for changes and improvements.

[31] An example of quality culture appears in the guidance for industry *Data Integrity and Compliance with Drug CGMP Questions and Answers*.

[32] ICH Q10; Quality Management Systems, ISO 9001:2015 (International Organization for Standardization, September 2015) is a useful standard that describes the plan-do-check-act (PDCA) cycle of a quality system.

V. RESOLVING SCIENTIFIC OR TECHNICAL DISAGREEMENTS WITH FDA 483 OBSERVATIONS

Disagreements related to scientific or technical issues may arise during an FDA inspection. Establishments are encouraged to seek clarification of these disagreements with the FDA representative(s) during the inspection.

In the event that a significant scientific or technical disagreement is not resolved with the FDA representative(s) before issuance of an FDA 483 that includes the contested observations, establishments should further communicate those concerns in the FDA 483 response. The response should describe the contested facts and provide scientific data and supporting information to allow FDA to evaluate the issue. FDA also recommends that establishments reference any applicable FDA statutes, regulations, or guidance as part of their response.[33]

With any additional concerns, establishments may contact the FDA Ombudsman[34] or the appropriate office directing the inspection.

[33] See guidance for industry *Formal Dispute Resolution: Scientific and Technical Issues Related to Pharmaceutical CGMP* (January 2006) for more information on resolving disagreements.

[34] Contact information for FDA's Office of the Ombudsman is available at https://www.fda.gov/about-fda/office-chief-scientist/office-ombudsman.

GLOSSARY

For purposes of this guidance, we use certain terms with the following specific meanings:

Consultant: Someone who is a third party and proficient in the remediation of current good manufacturing practice deviations.

Corrective action: An action to eliminate the cause of a detected nonconformity or other undesirable situation and to prevent recurrence (see International Council for Harmonisation (ICH) guidance for industry *Q10 Pharmaceutical Quality System* (April 2009)).[1]

Corrective action and preventive action (CAPA): Systemic implementation of corrective actions and preventive actions resulting from the investigation of complaints, product rejections, nonconformances, recalls, deviations, audits, regulatory inspections and findings, trends and data from process performance, and product quality monitoring (see ICH Q10).[2]

Executive management: A senior person(s) who directs and controls an establishment or site at the highest levels, with the authority and responsibility to mobilize resources within the establishment (see ICH Q10 for definition of senior management).

FDA Form 483 Inspectional Observations (FDA 483): A written report (list) that informs the most responsible person at an inspected establishment of significant, objectionable conditions relating to products and/or processes, or other violations of the Federal Food, Drug, and Cosmetic Act (FD&C Act) or related Acts and regulations which were observed by Food and Drug Administration (FDA) representative(s) during an inspection. Some types of observations that do not pertain to current good manufacturing practice/manufacturing are not eligible for inclusion on an FDA 483, and the FDA 483 is not intended to be a comprehensive list of an establishment's potential issues. The FDA 483 consists of observations an FDA representative(s) made during an inspection and does not represent FDA's final findings or an Agency determination regarding compliance. See FDA's reference web page, FDA Form 483 Frequently Asked Questions at https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-references/fda-form-483-frequently-asked-questions.

Observation: A condition or practice deemed objectionable and listed on an FDA 483 when, in the investigator's judgment, the observed conditions or practices are significant and indicate that an FDA-regulated product may be in violation of FDA requirements (see section 704 of the FD&C Act (21 U.S.C. 374) and Chapter 5 of the Investigations Operations Manual).[3]

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[1] We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

[2] Consistent with 21 CFR part 4, the CAPA process for combination products should consider implications of corrective and preventive actions for all constituent parts and for the combination product as a whole. See the guidance for industry and FDA staff *Current Good Manufacturing Practice Requirements for Combination Products* (January 2017).

[3] Investigations Operations Manual is available at https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-references/investigations-operations-manual.

Preventive action: An action to eliminate the cause of a potential nonconformity or other potential undesirable situation and prevent occurrence (see ICH Q10).

Quality: The suitability of either a drug substance or drug product for its intended use. The term includes such attributes as the identity, strength, and purity (see ICH guidance for industry *Q6A Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances* (December 2000) and ICH guidance for industry *Q9(R1) Quality Risk Management* (May 2023), which incorporates a manufacturing system and process mindset).

Quality risk management: A systematic process for the assessment, control, communication, and review of risks to the quality of the drug product across the product lifecycle (see ICH Q9(R1)).

Risk assessment: A systematic process of organizing information to support a decision made within a risk management process. The process consists of the identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards (see ICH Q9(R1)).

Root cause: A factor that caused a nonconformance (e.g., product design, material or component deficiency, design flaw that led to human error, manufacturing deviations). Root causes are generally documented in the conclusion of an investigation under 21 CFR 211.192.

State of control: A condition in which the set of controls consistently provides assurance of continued process performance and product quality (see ICH Q10).