Sections in This Document

1. Purpose

This Field Management Directive (FMD) provides criteria and instructions to investigators when conducting an investigation requested by a Center, of a facility engaged in the manufacturing, packaging, labeling or testing of certain medical products that may be granted an Emergency Use Authorization (EUA).

2. Scope

This FMD applies to investigations related to issuance or potential issuance of an EUA for medical products. These investigations can take place prior to or after the submission of an EUA request. Investigations conducted under this FMD will facilitate access to certain medical products that may be urgently needed for use in declared public health or other national emergencies by gathering information about the facility, the manufacturing processes and the ability to maintain the quality and consistency of the subject product.

This FMD is not intended to replace or supersede any existing FDA regulatory authority or oversight related to inspections, other types of investigations under Chapter 8 of the Investigations Operations Manual (IOM), or other review activities, including but not limited to: pre-operational reviews under FMD-135, *Pre-operational Reviews of Manufacturing Facilities*; New Drug Application (NDA) and Abbreviated New Drug Application (ANDA) pre-approval or Biologic

License Application (BLA) pre-license or pre-approval inspections for the Center for Drug Evaluation and Research (CDER); BLA pre-license inspections for the Center for Biologics Evaluation and Research (CBER); Premarket Approval inspections for the Center for Devices and Radiological Health (CDRH), or an inspection of a facility engaged in the manufacturing, packaging, labeling, or testing of a medical product(s) that may be subject to an EUA.

3. Responsibility

A. Center

1. Issue a written memorandum to the appropriate Office of Regulatory Affairs (ORA) Office of Medical Products and Tobacco Operations (OMPTO) program per established procedures requesting an investigation or, if there are exigent circumstances, an email providing all relevant background information and directions for the investigation.
2. Provide support to FDA investigators, as needed, during the investigation.
3. Direct any firms requesting a copy of the investigation memorandum to file a Freedom of Information Act (FOIA) request through (https://www.accessdata.fda.gov/scripts/foi/FOIRequest/index.cfm).

B. ORA Office of Medical Products and Tobacco Operations (OMPTO)

1. Assign an investigator(s) to conduct the EUA investigation as requested by the Center.
2. Provide direction to FDA investigators, as needed, during the investigation.
3. Coordinate and confer with the Center, as necessary, to optimize the efficiency and outcome of the investigation.

C. ORA Investigator(s)

1. Conduct the investigation in accordance with the request memorandum or email from the Center with direction from OMPTO and the ORA Program.
2. Engage with the facility's management during the investigation regarding any concerns FDA has with the operational status of the facility or the medical product(s) that may be subject to an EUA.

3. Hold a closeout meeting with facility management to convey any significant, unresolved concerns regarding the facility or the medical product(s) that may be subject to an EUA.
4. Complete an investigation memorandum.
5. Direct any firms requesting a copy of the investigation memorandum to file a FOIA request: (https://www.accessdata.fda.gov/scripts/foi/FOIRequest/index.cfm).

D. ORA's Division of Information Disclosure Policy in the Office of Strategic Planning and Operational Policy (DIDP)

Release, the EUA investigation memorandum as appropriate, when requested under FOIA procedures, and appropriately redacted, under FOIA and 21 C.F.R. Chapter 1, part 20.

4. Background

Section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) provides authority for FDA to grant an EUA during the effective period of a declaration issued pursuant to section 564(b) of the FD&C Act by the Secretary of the Department of Health and Human Services (HHS), for a medical product intended for use in an actual or potential emergency (emergency use). An EUA allows unapproved medical products and approved products with unapproved uses to be introduced into interstate commerce if they may be effective as medical countermeasures during declared public health and other national emergencies and there is no available, approved alternative.

FDA's authority to issue an EUA is separate and distinct from the use of a medical product under an investigational application (i.e., Investigational New Drug Application (IND) or Investigational Device Exemption (IDE)), section 561 expanded access authorities, and section 564A emergency use authorities.

Interactions between a sponsor and FDA prior to or after submission of an EUA request may include investigations by an FDA investigator(s) of a facility that will manufacture, package, label or test a medical product subject to an EUA, in order to gather information requested by the Center to inform their decision-making process on an EUA.

An investigation is an information gathering activity conducted by FDA under Chapter 8 of the Investigations Operations Manual (IOM). The purpose of an investigation is to determine and document facts concerning a particular issue

so that FDA can make informed and sound decisions[1]. The EUA investigation described in this FMD allows FDA to assess the current operational status of a facility, to provide feedback which may assist the facility in manufacturing, packaging, labeling or testing a product intended for use in a public health emergency, and help achieve the overall public health goal of providing emergency use access to safe, effective, and quality novel critical therapies or diagnostics.

EUA investigations can take place in any establishment, foreign or domestic, that may be associated with an EUA submission, including the drug substance, medical device, and finished dosage product manufacturing, and control testing laboratories. Section 351 of the Public Health Service Act and sections 702 and 704 of the Federal Food, Drug and Cosmetic Act provide regulatory authority for FDA to conduct investigations and to collect records at establishments where medical products, including those that may be subject to an EUA, are manufactured, packaged, labeled, or tested.

5. References/Supporting Documents

A. FDA Emergency Use Authorization website, including a list of current EUAs with authorization information.

B. FDA Guidance for Industry and Other Stakeholders, *Emergency Use Authorization for Medical Products and Related Authorities*, issued January 2017.

C. Investigations Operations Manual (IOM); Chapter 8

D. 21 CFR Chapter 1, part 20 – Public Information

6. Procedure

A. If a Center decides to request an investigation of a facility that is engaged or may become engaged in the manufacturing, packaging, labeling or testing of a medical product(s) that may be subject to an EUA, the Center will issue a written memorandum to the appropriate ORA OMPTO program, per the usual assignment procedures, to perform an investigation of that facility.

[1] Subchapter 8.1 of the IOM.

B. The Center memorandum will contain all relevant background information in the Center's possession, that is pertinent to an investigation of the facility and the medical products(s) that may be subject to an EUA. Background information will identify, as appropriate, those areas that the Center believes are important when considering the issuance of an EUA. When the Center believes that an immediate investigation is necessary, it may issue an abbreviated memorandum, or the relevant background and directions for the investigation may be communicated through an email.

C. ORA will assign an investigator(s) to perform an investigation of the facilities and manufacturing operations related to the medical product(s) that may be subject to an EUA. A Center staff member(s) will be invited to join the investigation on-site. Alternatively, a Center staff member(s) may be consulted to provide input to the investigator(s) during the investigation.

D. An ORA subject matter expert(s) will be assigned to serve in a consultative role in the development of the investigational plan, including liaising with Center and ORA management if needed, and will be the point of contact for the investigator(s) during the investigation for any on-site issues. The subject matter expert will work in close collaboration with the investigator(s)' supervisor(s).

E. Once assigned, the investigator(s) will contact the firm to schedule an EUA investigation. Upon arrival at the facility, the FDA investigator(s) will show their credentials and issue a Form FDA 482 to the most responsible individual at the facility.[2] A Form FDA 482 is not issued to foreign firms. The investigator(s) will collect information and records regarding the firm's operational activities including those that are in various stages of development.

F. After initiation of the EUA investigation, OMPTO will coordinate with the relevant Center, as necessary, to optimize the efficiency of the investigation. The investigator(s) should discuss FDA concerns regarding the facility, its operations, and/or the medical product(s) that may be subject to an EUA, with the facility's management during the course of the investigation.

G. The investigator(s) will hold a closeout meeting with the facility, during which they will orally convey any such concerns. In certain circumstances, with the appropriate OMPTO program concurrence, the investigator(s) may conduct the

[2] Subchapter 8.1 of the Investigations Operations Manual (IOM).

close-out meeting with the facility remotely. During the close-out meeting, the investigator(s) will advise the firm that they should promptly respond to any unresolved concerns in writing to the applicable program office according to established procedures. At this point, if requested under a Freedom of Information Act request, the EUA memo will be considered releasable with appropriate redactions of non-public information. As stated in the FDA's Guidance for Industry and Other Stakeholders, *Emergency Use Authorization for Medical Products and Related Authorities*, issued January 2017, "FDA will periodically review the circumstances and appropriateness of an EUA, including circumstances that might warrant revocation of the EUA. The review will include regular assessment based on additional information provided by the sponsor of the progress made with respect to the approval, licensure, or clearance of the unapproved product, or of the unapproved use of an approved product, for which an EUA was issued."[3]

H. In accordance with Chapter 8 of the IOM, investigations will be documented in an investigation memorandum. The investigation memorandum will be available to the facility subject to the inspection when DIDP determines that the document is releasable under FOIA and has been appropriately redacted under FOIA and 21 C.F.R. Chapter 1, part 20.

7. Glossary/Definitions

N/A

8. Records

N/A

9. Document History

Revision #	Status* (D, I, R)	Date	Author Name and Title	Approving Official Name and Title

[3] FDA Guidance for Industry and Other Stakeholders, Emergency Use Authorization for Medical Products and Related Authorities, issued January 2017, p. 29.

00	I	01/25/2021	Ann M. Metayer, Regulatory Counsel, Office of Strategic Planning and Operational Policy, Division of Operational Policy	Judy McMeekin, Pharm.D. Associate Commissioner for Regulatory Affairs

* - D: Draft, I: Initial, R: Revision

10. Change History

Revision #	Change
00	Initial Document

11. Attachments

N/A