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# OUT OF EUA – FDA'S GUIDANCE & RECOMMENDATIONS

# LAST WEBINAR – WHAT IS AN EUA:

- EUA is a temporary and expedited pathway, under section 564 of the FD&C Act, that FDA employs in times of public health emergency to introduce certain medical products into interstate commerce:
    - By approving an unapproved medical product; or
    - By approving an unapproved (off-label) use of an approved medical product
- EUA Declaration: HHS Secretary must declare that circumstances exist justifying the authorization (section 564(b)(1))
- Over 900 EUAs have been issued to date.
- New EUAs continue to be reviewed and issued.

# LAST WEBINAR – TERMINATION OF EUA

- Termination of an EUA Declaration
  - The HHS Secretary's EUA declaration will terminate on the earlier of:
    - A determination by the HHS Secretary that the circumstances that precipitated the EUA issuance have ceased;
    - A change in the approval status (e.g., received FDA approval).
- Before an EUA terminates, the Secretary of HHS must provide an Advance Notice that is sufficient to allow for the disposition of an unapproved product and of any labeling or other information provided related to an unapproved use of an approved product (section 564(b)(3))
  - A few days of advance notice under normal operation;
  - 180 days for COVID-19 EUAs provided in the FDA's guidance documents.

# FDA'S GUIDANCE DOCUMENTS:

- **Transition Plan for Medical Devices Issued Emergency Use Authorization (EUAs) During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency**
  - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/transition-plan-medical-devices-issued-emergency-use-authorizations-euas-during-coronavirus-disease
- **Transition Plan for Medical Devices That Fall Within Enforcement Policies Issued During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency**
  - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/transition-plan-medical-devices-fall-within-enforcement-policies-issued-during-coronavirus-disease

***This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic.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

# I. Introduction

- **“Manufacturer”: any person who designs, manufactures, fabricates, assembles, or processes a finished device. See 21 CFR 820.3(o). Importers and distributors should follow the guidance where it is applicable.**

- **“Normal operations”: circumstances when the COVID-19 PHE (public health emergency) under section 319 of the Public Health Service Act has expired and/or the relevant device COVID-19 EUA declaration is terminated.**

# II. Background

- "This guidance contemplates that the advance notice of termination of each EUA declaration pertaining to devices will be published in the Federal Register 180 days before the day on which the EUA declaration is terminated (the EUA termination date)."

# E.g. Advance Notice of Termination of EUA Declaration

## Advance Notice Date: June 21, 2010; EUA Termination Date: June 25, 2010

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NATIONAL ARCHIVES

FEDERAL REGISTER

The Daily Journal of the United States Government

Notice

### Termination of Declarations Justifying Emergency Use Authorizations of Certain In Vitro Diagnostic Devices, Antiviral Drugs, and Personal Respiratory Protection Devices

A Notice by the Food and Drug Administration on 06/25/2010

PUBLISHED DOCUMENT

**AGENCY:**

Food and Drug Administration, HHS.

**ACTION:**

Notice.

**SUMMARY:**

The Food and Drug Administration (FDA) is issuing this notice, under the Federal Food, Drug, and Cosmetic Act (the act), of the termination of the declarations of emergency justifying Emergency Use Authorizations (EUAs) of certain in vitro diagnostic devices, personal respiratory protection devices, and antiviral products that were issued in response to the public health emergency involving 2009 H1N1 Influenza. Advance notice of the termination of the declarations was provided under the act.

**DATES:**

The Authorizations are terminated as of June 23, 2010.

**FOR FURTHER INFORMATION CONTACT:**

RADM Boris Lushniak, Office of Counterterrorism and Emerging Threats, Food

DOCUMENT DETAILS

Printed version:
PDF

Publication Date:
06/25/2010

Agencies:
Food and Drug Administration

Dates:
The Authorizations are terminated as of June 23, 2010.

Document Type:
Notice

Document Citation:
75 FR 36432

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Agency/Docket Number:
Docket Nos. FDA-2009-N-0276, FDA-2009-N-0277, FDA-2009-N-0278, and FDA-2009-N-0521

Document Number:
2010-15448

DOCUMENT DETAILS

## II. Advance Notice of Termination

FDA is issuing this notice, under section 564(b)(4) of the act, of the termination of the declarations of emergency justifying EUAs of certain in vitro diagnostic devices, personal respiratory protection devices, and antiviral products that were issued in response to the public health emergency involving 2009 H1N1 Influenza. Under section 564(b)(3) of the act, the Commissioner of Food and Drugs provided advance notice of the termination of the declaration of emergency to the EUA requestor for each product authorized for emergency use in response to the public health emergency involving 2009 H1N1 Influenza. The June 21, 2010, letters notifying the EUA requestors of the termination of the declaration of emergency follow:

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Expand Table

Thomas R. Frieden, MD, MPH

Director

Centers for Disease Control and Prevention

1600 Clifton Rd., MS D-14

Atlanta, GA 30333

Re: Termination of Declarations of Emergency Justifying Emergency Use Authorization (EUA) of Certain Antiviral Drugs—Zanamivir, Oseltamivir Phosph and Peramivir

Dear Dr. Frieden:

This letter is to provide advance notice of the termination of:

(1) the declaration of emergency that was issued by the then Acting Secr of the Department of Health and Human Services (HHS) Charles E. Johnson on April 26, 2009, pursuant to section 564(b)(1) of the Fede Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. § 360bbb-3, justif the authorization of the emergency use of certain products from the neuraminidase class of antivirals Oseltamivir Phosphate and Zanami and

(2) the declaration of emergency that was issued by the Secretary of HH October 20, 2009, pursuant to section 564(b)(1) of the Act, 21 U.S.C. 360bbb-3, justifying the authorization of the emergency use of the antiviral peramivir.

Both of the declarations described above will terminate when the Public Healt Emergency determination for 2009 H1N1 influenza expires on June 23, 2010. Therefore, after June 23, 2010, the EUA authorizing the unapproved uses of zanamivir and oseltamivir phosphate and the use of the unapproved drug peram will no longer be in effect. For any patient who began a treatment course of pera prior to June 23, 2010, the authorization shall continue to be effective after June 2010, to allow completion of that treatment course, to the extent the patient's

# III. Scope

- Devices have been issued an EUA under section 564 of the FD&C Act ( 21 U.S.C. 360bbb-3) on the basis of a device-related COVID-19 EUA declaration:
- Does not apply to devices for which FDA has revoked the EUA under section 564(g)(2)(B)-(C) of the FD&C Act because the criteria under section 564(c) of the FD&C Act were no longer met or because other circumstances made such revocation appropriate to protect the public health or safety.

# IV. Guiding Principles

- Help facilitate continued access;
- Orderly and transparent transition;
- Follow a risk-based approach with consideration of differences of devices;
- FDA may take actions regarding a specific device or device type, including revocation or revision of an EUA, withdrawal or revision of an enforcement policy, or enforcement action.

# V. Transition Plan for Devices Authorized Under EUA

- **Discussion with FDA:**
  - **Q-Submission Program;**
    - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program
  - **Pre-Submission – very helpful tool.**
    - **Pre-submission for EUA;**
    - **Pre-submission for section 510(k) clearance;**

# V. A. “Notifications of Intent” for Certain Reusable Life-Supporting or Life-Sustaining Devices

**Table 1**

| Product Code | Device Type | Classification Regulation |
|---|---|---|
| BSZ | Gas-machine, anesthesia | 21 CFR 868.5160 |
| CAW | Generator, oxygen, portable | 21 CFR 868.5440 |

# V. A. “Notifications of Intent” for Certain Reusable Life-Supporting or Life-Sustaining Devices

| | | |
|---|---|---|
| BTT | Humidifier, Respiratory Gas, (Direct Patient Interface) | 21 CFR 868.5450 |
| QAV | High flow/high velocity humidified oxygen delivery device | 21 CFR 868.5454 |
| CBK | Ventilator, Continuous, Facility Use | 21 CFR 868.5895 |
| MNT | Ventilator, Continuous, Minimal Ventilatory Support, Facility Use | |
| NOU | Continuous, ventilator, home use | |
| MNS | Ventilator, continuous, non-life-supporting | |
| ONZ | Mechanical Ventilator | |
| BTL | Ventilator, Emergency, Powered (Resuscitator) | 21 CFR 868.5925 |
| QOO | Tubing Connector for Co-venting | No corresponding CFR section |

# V. A. "Notifications of Intent" for Certain Reusable Life-Supporting or Life-Sustaining Devices (cont'd)

- Notification of Intent: whether intend to submit marketing submission
- Should submit ASAP after the Guidance is finalized:
  - Early submission is encouraged – submit now;
  - After publication of Advance Notice, submit within 90 days after such publication.
- Submit as "EUA Report"
  - Note on cover letter: "Attention: Notification of Intent"

# V. A. "Notifications of Intent" for Certain Reusable Life-Supporting or Life-Sustaining Devices

- **Information requested (submit to CDRH Document Control Center asap after this guidance is finalized):**
  - General information (e.g., contact information);
  - EUA request number
  - List of all model numbers or other device identifying information;
  - Whether the manufacturer plans to submit a marketing submission;
  - If not planning to submit a marketing submission, the manufacturer should discuss, as applicable, its plan to discontinue distribution of the device, or to restore the device to a previously FDA-cleared or approved version, to provide a physical copy or electronic updated labeling, and any other efforts to address or mitigate potential risks of devices that remain distributed after EUA termination date. (Risk Mitigation Plan)

# V. B. Marketing submissions for devices distributed after the EUA termination date

- **Marketing submissions:**
  - PMA, 510(k) clearance, humanitarian device exemption (HDE), Do Novo classification request, etc.
- **Submit with sufficient time for the submission to be accepted by FDA (not necessarily approved/cleared) before EUA termination date (the key to ensure continued distribution);**
- **After EUA termination date, while an accepted marketing submission is under consideration by FDA, manufacturers are expected to comply with all applicable regulatory requirements:**
  - applicable marketing submission requirements (not the EUA terms),
  - Quality System (QS) Regulation under 21 CFR Part 820,
  - Adverse event reporting requirements under 21 CFR Part 803,
  - Registration and listing under 21 CFR Part 807 Subparts B-D,
  - Unique Device Identification under 21 CFR Part 801 Subpart B and 21 CFR Part 830.

# V.B.(1) Recommendation for Transition Implementation Plan

- **When: to be included in the marketing submission;**
- **Purpose: to address the already-distributed devices if the marketing submissions include changes/updates to devices, or if FDA makes negative decisions on marketing submissions;**
- **Information to be included, as applicable:**
  - Estimated number of devices distributed under EUA in US;
  - An explanation of plan (benefit-risk based plan) for disposition if receives a negative decision on marketing submission;
  - An explanation of plan if receives a positive decision on marketing submission

# V.B.(1) Recommendation for Transition Implementation Plan (Cont'd)

- An explanation of benefit-risk based plan for disposition of already-distributed product in the event of a negative decision on the marketing submission.
  - If plan to leave the product in market, the plan should address the rationale for doing so and considerations as follows, where relevant:
    - » Process of notifying end users and distributors;
    - » Process and timeline for restoring distributed devices to previously cleared or approved version; publicly available labeling;
    - » Description of maintenance plan for distributed devices.
- An explanation of plan for addressing already-distributed product in the event of a positive decision on the market submission decision:
  - Process of notifying distributors and end users;
  - Process and timeline for providing updated labeling or components reflecting changes made to the cleared or approved device.

# V.B.(2) Enforcement policy for devices with a marketing submission under review by FDA

- FDA does not intend to object to the continued distribution of devices within scope of this guidance after EUA termination where:
  - Manufacturer has submitted a marketing submission to FDA and had it accepted by FDA before EUA termination; and
  - FDA has not taken a final action on the marketing submission.
  - **Marketing submission is key**
- Labeling should be updated to accurately state device's regulatory status:
  - "Product was authorized under an EUA issued during the COVID-19 PHE and remains under FDA review for clearance or approval."

# V.C. If a manufacturer does not intend to continue to distribute its device after the EUA termination date

- **FDA does not intend to object to the disposition of already-distributed devices (i.e., FDA does not intend to request market removal):**
  1. Single use, non-life-supporting/non-life-sustaining devices (e.g., face masks) that were distribute before EUA termination date remain distributed and are consumed by the end user;
  2. Reusable, non-life-supporting/non-life-sustaining devices (e.g., remote patient monitoring devices), remain distributed and consumed provided:
     - Be restored to previously cleared or approved version (early software version, component replacement); **or**
     - Have publically available labeling that accurately describes the product features and regulatory status (i.e., the product lacks FDA clearance or approval).
  3. Reusable life-supporting/life-sustaining devices (e.g., ventilators, extracorporeal membrane oxygenation systems, continuous renal replacement therapy systems) remain distributed provided:
     - Restore to cleared or approved version; **or**
     - Publically available labeling

# V.C. If a manufacturer does not intend to continue to distribute its device after the EUA termination date (cont'd)

- 4. In vitro diagnostic devices: used for no more than 2 years after EUA termination date or until expiration date, whichever is lesser.

# V. D. Discontinuing distribution of a device

- **FDA expects manufacturers to discontinue distribution of a device within the scope of this guidance:**
  - On the EUA termination date, if has not submitted a marketing submission and has a marketing submission accepted by FDA before EUA termination date;
  - On the date the manufacturer receives a negative decision on its marketing submission as FDA'a final action, or on the date the manufacturer withdraws its submission or fails to provide a complete response to an FDA request for additional information within the time identified in the FDA's letter.
- **Certain FD&C Act requirements may extend beyond cessation of distribution:**
  - Adverse event reporting under 21 CFR Part 803.

# V. E. Additional consideration

- **Before EUA termination, manufacturers are expected to have completed any steps necessary to transition into compliance with all FD&C Act requirements once EUA terminates:**
- **FDA does not intend to object to continued distribution of certain products under Section V.B(2):**
  - Marketing submission made and accepted before EUA termination date;
  - No FDA final decision yet;
- **Under section 704(a)(1) of the FD&C Act, FDA may enter and inspect any factory, warehouse, or establishment in which devices are manufactured, processed, packed, or held for introduction into interstate commerce … at reasonable times and within reasonable limits and in a reasonable manner.**

# E. Additional consideration (cont'd)

- **Non-traditional manufacturers (who previously operated under different quality standards or requirements)**
  - Will allow more time to address transitioning;
  - Case-by-case compliance and enforcement decisions.
  - Manufacturers may request an exemption or variance from a device QS requirement as outlined in 21 CFR 820.1(e) and section 520(f)(2) of the FD&C Act. Must be requested within 90 days of publication of Advance Notice of termination of EUA declaration.

# SUMMARY – What Do Manufacturers Need To Do In The 180 Days Of Transition Period

- **If intends to continue distribution after EUA termination:**
  - Submit Notification of Intent (certain reusable life-sustaining/life-supporting devices);
  - Submit marketing submission and have it accepted by FDA before termination of EUA;
    - Include in marketing submission a transition implementation plan;
      - If receives a negative FDA decision on marketing submission;
      - If receives a positive FDA decision on marketing submission.
  - Risk mitigation plan addressing already-distributed devices;
  - Update labeling to accurately reflecting device's current regulatory status;
  - Comply with EUA terms before EUA termination; with applicable marketing submission requirements after EUA termination even before FDA final decision.

# SUMMARY – What Do Manufacturers Need To Do In The 180 Days Of Transition Period (cont'd)

- **If intends NOT to continue distribution of device after EUA termination:**
  - Submit Notification of Intent (certain reusable life-sustaining/life-supporting devices);
  - Risk mitigation plan addressing already-distributed devices;
    - Restoring already-distributed devices to its previous FDA approved/cleared version;
    - Update labeling to accurately reflect current regulatory status;
  - Report of corrections or removal for certain Class I devices (masks, tools, etc.);
  - Continue comply with EUA terms before EUA termination; restore device to the FDA approved/cleared version after EUA termination;
  - Comply with adverse event requirements.

# VI. Examples

- **Example 1 – a single-use surgical mask marked under EUA; manufacturer does not intend to continue distribution beyond EUA.**
  - July 1, advance notice of termination published, with termination date of January 1;
  - January 1, manufacturer ceases distribution
  - "Report of corrections or removals" submitted per 21 CFR Part 806:
    - https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=806.10
    - Should submit within 10 working days of correction or removal
  - Already distributed masks remain distributed and are consumed by end user.

# VI. Examples (cont'd)

- **Example 2: A continuous ventilator:**
  - July 1, advance notice of termination published; January 1, EUA termination date;
  - Before August 1, manufacturer submitted Notification of Intent, informing FDA of not intending to pursue marketing submission (outlined in Section V. A);
  - On termination date of January 1, manufacturer ceases distribution;
  - FDA does not intend to object the already-distributed products remaining in market, if manufacturer develops a plan (the risk mitigation plan) and provides a physical copy of updated labeling to hospitals that have expressed interest in keeping the ventilators;
  - For healthcare facilities wishing to retain the ventilator for use in the future, the future use would be subject to regulatory requirements of future authorization, including marketing authorization or EUA (What does it mean? Expect clarification in final guidance.).

# VI. Examples (cont'd)

- **Example 3: a non-traditional device manufacturer (contract manufacturer) worked with a traditional device manufacturer (i.e. original equipment manufacturer or OEM) to produce ventilators designed by the OEM; authorized under EUA for ventilators;**
  - July 1, advance notice of termination; January 1, EUA termination date
  - Before August 1, OEM submitted EUA Report, Attention: Notification of Intent, informing FDA of intent to file marketing submission;
  - October 1, OEM submits marketing submission to FDA, including a "transition implementation plan" for already-distributed ventilators;
  - On EUA termination date (January 1), OEM and contract manufacturer must both comply with all applicable regulatory requirements (the marketing submission requirements);
  - OEM's marketing submission has been accepted by FDA, has provided updated labeling;
  - Therefore, FDA does not intend to object to the continued distribution of the ventilators before FDA issues a final decision on the marketing submission;

# VI. Examples (cont'd)

- FDA issued a negative decision (withdrawal) because OEM fails to respond to FDA request for additional information; (distribution needs to stop immediately)
- FDA and OEM engage on benefit-risk plan to address already distributed devices;
- FDA may request that the firm initiate a recall of devices in certain circumstances if a recall has not been initiated (21 CFR 7.45).

# VI. Examples (cont'd)

- **Example 4: a molecular diagnostic test kit manufactured by a commercial manufacturer, under an umbrella EUA;**
  - July 1, advance notice of termination published; January 1, EUA termination date;
  - October 1, manufacturer submits a marketing submission to FDA, including a "transition implementation plan" for already distributed products; (no need to submit Notice of Intention)
  - On EUA termination date (January 1), manufacturer must comply with all applicable regulatory requirements;
  - If manufacturer's marketing submission is accepted by FDA (prior to EUA termination) and manufacturer has provided updated device labeling, then the FDA does not intend to object to continued distribution until FDA final decision on marketing submission.
  - Manufacturer receives a positive decision from FDA on February 20. No outstanding issues were identified during FDA review that would result in a correction or removal of already distributed products.

# COMPANION GUIDANCE - TRANSITION OF DEVICES UNDER ENFORCEMENT POLICIES

- Applies to devices subject to 17 enforcement policies during the PHE.
- 180 days transition period beginning on “implementation date” of the Guidance and ending on the date that the enforcement policies are withdrawn.
- Same requirements as provided in the EUA transition guidance.

# III. SCOPE

- **Applies to 17 enforcement policies:**

**List 1**

- Enforcement Policy for Remote Digital Pathology Devices During the COVID-19 Public Health Emergency[10]
- Enforcement Policy for Imaging Systems During the COVID-19 Public Health Emergency[11]
- Enforcement Policy for Non-Invasive Fetal and Maternal Monitoring Devices Used to Support Patient Monitoring During the COVID-19 Public Health Emergency[12]
- Enforcement Policy for Telethermographic Systems During the COVID-19 Public Health Emergency[13]

- Enforcement Policy for Digital Health Devices for Treating Psychiatric Disorders During the COVID-19 Public Health Emergency[14]
- Enforcement Policy for Extracorporeal Membrane Oxygenation and Cardiopulmonary Bypass Devices During the COVID-19 Public Health Emergency[15]
- Enforcement Policy for Remote Ophthalmic Assessment and Monitoring Devices During the COVID-19 Public Health Emergency[16]
- Enforcement Policy for Infusion Pumps and Accessories During the COVID-19 Public Health Emergency[17]
- Enforcement Policy for Clinical Electronic Thermometers During the COVID-19 Public Health Emergency[18]
- Enforcement Policy for Face Masks, Barrier Face Coverings, Face Shields, Surgical Masks, and Respirators During the COVID-19 Public Health Emergency (Revised)[19]
- Enforcement Policy for Gowns, Other Apparel, and Gloves During the COVID-19 Public Health Emergency[20]
- Enforcement Policy for Sterilizers, Disinfectant Devices, and Air Purifiers During the COVID-19 Public Health Emergency[21]
- Enforcement Policy for Ventilators and Accessories and Other Respiratory Devices During the COVID-19 Public Health Emergency[22]
- Enforcement Policy for Non-Invasive Remote Monitoring Devices Used to Support Patient Monitoring During the COVID-19 Public Health Emergency (Revised)[23]
- Enforcement Policy for Modifications to FDA Cleared Molecular Influenza and RSV Tests During the COVID-19 Public Health Emergency[24]

- Enforcement Policy for the Quality Standards of the Mammography Quality Standards Act During the COVID-19 Public Health Emergency[25]
- Coagulation Systems for Measurement of Viscoelastic Properties: Enforcement Policy During the COVID-19 Public Health Emergency (Revised)[26]

# When is the Implementation Date – it may vary

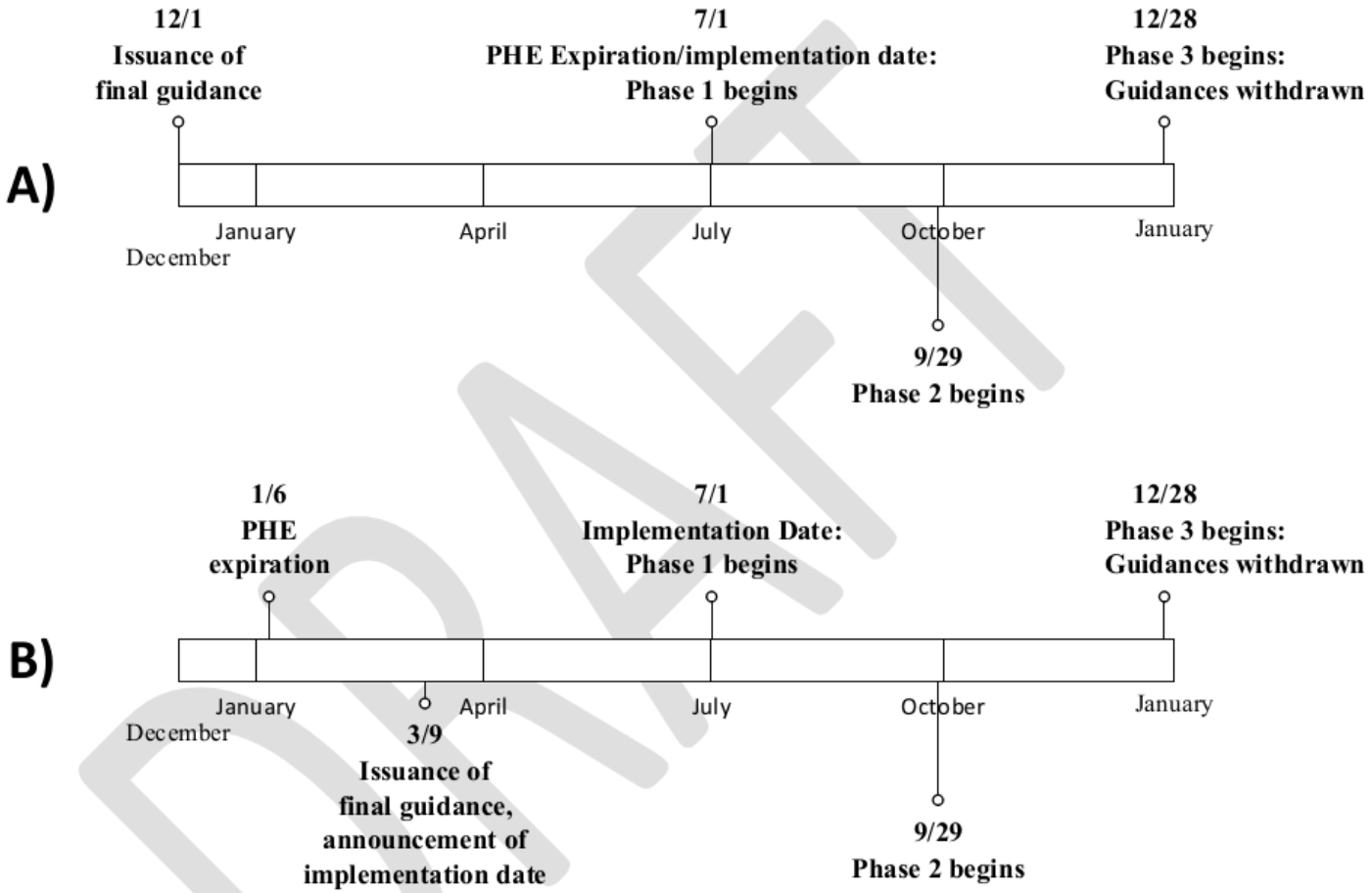


**Figure 1. Hypothetical Transition Timelines. A) Implementation date occurring on the expiration date of the COVID-19 section 319 PHE declaration. B) Implementation date occurring after the expiration of the COVID-19 section 319 PHE declaration.**

# V. Phased Transition Plan for Devices That Fall Within COVID-19 Enforcement Policies

- **Phase 1: begins on the implementation date**
  - Manufacturers should start following adverse event reporting requirements under 21 CFR Part 803;
  - Begin preparing for marketing submission to help avoid supply chain disruption;
  - Submit reports for corrections and removals;
- **Phase 2: begins 90 days after the implementation date**
  - If intends to continue distribution, should also begin to follow 21 CFR Part 807 Subparts B-D for registration and listing requirements;
  - Submit Notification of Intent for certain reusable life-sustaining/life-supporting devices;
  - Submit marketing submission and have it accepted by FDA;
    - Include transition implementation plan.
  - Full FDA registration
- **Phase 3: begins 180 days after the implementation date**
  - FDA intends to withdraw all 17 enforcement policy guidances listed in the transition plan;
  - Manufacturers to comply with all applicable statutory and regulatory requirements;
  - Distribution should be discontinued unless marketing submission made and accepted and no final decision received from FDA.

# FDA ENCOURAGED COMMENTS:

- **Whether the 180-day period is sufficient;**
- **Whether the Guidances are helpful.**

Department of Health and Human Services, Food and Drug Administration, Docket No. FDA-2021-D01149, Supplemental Information

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