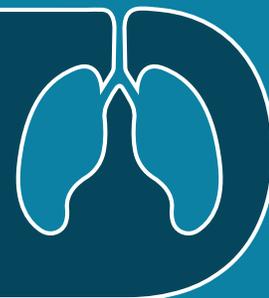


SPECIMEN SUBMISSION GUIDANCE FOR PATHOLOGIC EVALUATION OF AUTOPSY TISSUE SPECIMENS FROM DEATHS WITH SUSPECTED E-CIGARETTE, OR VAPING, PRODUCT USE-ASSOCIATED LUNG INJURY (EVALI)



Pathologic findings in lung tissue from cases of e-cigarette, or vaping, product-use associated lung injury (EVALI) have included patterns of acute lung injury, such as diffuse alveolar damage, organizing pneumonia, and acute fibrinous and organizing pneumonia. Acute lung injury can have many different causes, including EVALI, but also infectious etiologies. In the setting of deaths in individuals with a history of e-cigarette, or vaping, product use, who had antecedent respiratory, gastrointestinal, or constitutional symptoms, or for whom EVALI is otherwise suspected, autopsies should be considered. CDC's Infectious Diseases Pathology Branch can provide assistance in the evaluation of fixed autopsy tissue specimens from deaths with suspected EVALI.

AUTOPSY TISSUE SPECIMENS

CDC can receive formalin-fixed, paraffin-embedded (FFPE) tissue blocks or formalin-fixed (wet) tissues from autopsy for evaluation. Preferred specimens for submission to CDC include:

1. Lung parenchyma, trachea and bronchi.
2. Liver
3. Kidney
4. Heart
5. Other organs showing significant gross or microscopic pathology.

Respiratory tissues should be thoroughly sampled. Since influenza and other respiratory viral infections may be in the differential diagnosis, submission of tissues from the trachea and central lung with segmental and primary bronchi in addition to the lung parenchyma is encouraged. Viral antigens and nucleic acid may be focal or sparsely distributed in patients with influenza, and are most frequently detected in respiratory epithelium of these larger airways.

Because the pathology of acute lung injury and related death is often systemic, preferred specimens for submission to CDC also include tissues from other major organs.

LUNG BIOPSY TISSUE SPECIMENS

Fixed lung biopsy tissue specimens may also be submitted on a limited case-by-case basis if there is a specific suspicion for a possible infectious disease etiology.

EVALUATION AT CDC

CDC's Infectious Diseases Pathology Branch will review tissue histopathology and perform additional testing, including testing for possible infectious etiologies by special stains, immunohistochemistry (IHC) and molecular testing, as indicated. Note that if infectious disease testing is desired, FFPE tissue blocks are preferred if formalin-fixation of the wet tissues has exceeded 2 weeks. Prolonged formalin-fixation can lead to degradation of antigens and nucleic acids, reducing the sensitivity of infectious disease assays.

SUBMISSION OF SPECIMENS

Pre-approval is required prior to submission of any tissue specimens. For pre-approval, please contact Pathology@cdc.gov (see below for additional guidance).

FORMALIN-FIXED (WET) TISSUE

Place tissue in 10% buffered formalin for three days (72 hours) for biopsies, and a week for thinly-sliced autopsy tissues. The volume of formalin used to fix tissues should be 10x the volume of tissue.

FORMALIN-FIXED, PARAFFIN-EMBEDDED (FFPE) TISSUE BLOCKS

In general, this is the preferred specimen for infectious disease testing, and is especially important to submit in cases where tissues have been in formalin for a significant time. Prolonged fixation (>2 weeks) may interfere with some immunohistochemical and molecular diagnostic assays.

INFECTIOUS DISEASES PATHOLOGY BRANCH SPECIMEN SUBMISSION REQUIREMENTS

- A. **Healthcare providers, pathologists, medical examiners, and coroners—please first report any suspected cases of lung injury associated with e-cigarette product use to your state, tribal, local, or territorial health department**
- B. **Health departments—contact Pathology@cdc.gov with**
 1. A brief clinical history
 2. A listing of available formalin-fixed specimen types including tissue source and if formalin-fixed (wet) tissue, FFPE tissue blocks, or slides are available
 3. Description of histopathologic findings in tissues to be submitted
 4. CDC Case ID (used by state epidemiologists for submitting case data to CDC) and State Case ID numbers. Email correspondence **should not** include patient identifiers such as name, date of birth, or medical record number. All applicable federal, state, and local regulations must be followed to adhere to patient confidentiality and privacy protections.
- C. **After you receive approval by email to submit the case to CDC's Infectious Diseases Pathology Branch (IDPB)**
 1. Electronically fill, save, and print both pages of the Specimen Submission Form CDC 50.34.
 - a. The form must be filled electronically to generate three bar-codes required for accessioning
 - b. E-mail addresses of the Original and Intermediate submitters (if any) are mandatory fields
 2. Select Test Order Code CDC-10365 (Pathologic Evaluation of Tissues for Possible Infectious Etiologies).
 3. Enter "E-cigarette, or Vaping, Product Use Associated Lung Injury" and provide CDC and State Case ID numbers in the Comments section on Page 2 of the CDC 50.34 form.
 4. In addition to the CDC 50.34 form, enclose the following in the specimen submission package:
 - a. Surgical pathology, autopsy report (preliminary is acceptable), or both
 - b. Relevant clinical notes, including admission History and Physical (H&P), discharge summary, if applicable

D. Packaging and container guidance

1. If formalin-fixed (wet) tissues are being submitted, there are restrictions on the amount of formalin that can be shipped. Small quantities (inner container less than 30 ml, with a maximum net quantity of 1 L for the entire package) are allowable.
2. For shipping purposes, you may:
 - a. Drain off almost all the formalin, leaving enough to keep the tissue moist
 - b. Place leakproof jar(s) in double Ziploc bags prior to shipping, and add absorbent material to the outer bag (alternatively, heat-sealable bags can be used)
 - c. Ship for overnight delivery if possible

E. Guidance for specimen labeling

1. Please ensure that the formalin-fixed (wet) tissue specimen containers/bags and formalin-fixed paraffin-embedded tissue blocks are labeled with two primary patient identifiers (i.e., first and last name, date of birth, unique patient identifier from time of collection, such as surgical pathology number, autopsy number, or medical record number).
2. The patient identifiers on the specimen containers/bags or specimens should match the patient identifiers listed on the CDC 50.34 Form, Surgical Pathology Report, Autopsy Report, and/or other medical records submitted with the specimen(s).
3. Specimens without adequate labeling are subject to delay in accessioning and testing.

F. Mailing contact information

1. Ship to Dr. Sherif Zaki, CDC, IDPB, 1600 Clifton Rd NE, MS: H18-SB, Atlanta, GA 30329-4027
2. Mail in suitable packaging for delivery Monday to Friday, excluding Federal holidays
3. Send tracking number to Pathology@cdc.gov
4. Tel: 404-639-3132, Fax: 404-639-3043, Email: Pathology@cdc.gov

For more information on shipping instructions and specimen handling, see:

<https://www.cdc.gov/laboratory/specimen-submission/detail.html?CDCTestCode=CDC-10365>

Digital slides or microscopic images can also be submitted for an informal, image-only consultation (i.e., no patient report will be issued). Contact epathology@cdc.gov and see <https://www.cdc.gov/ncezid/dhcpp/idpb/epathology/index.html> for more information.

For more information on CDC's Infectious Diseases Pathology Branch, see: www.cdc.gov/pathology

