NEW YORK STATE OF OPPORTUNITY. Department of Health

ANDREW M. CUOMO
Governor

HOWARD A. ZUCKER, M.D., J.D.
Commissioner

SALLY DRESLIN, M.S., R.N.
Executive Deputy Commissioner

November 8, 2019

TO: Healthcare Providers, Hospitals, Off-Campus Emergency Departments, Substance Use Disorder/Mental Health Agencies, College and University Health Clinics, and Local Health Departments

FROM: New York State Department of Health (NYSDOH)

HEALTH ADVISORY:
Investigation Updates and Clinical Recommendations for E-cigarette, or Vaping, Product use Associated Lung Injury (EVALI)

For healthcare facilities/hospitals, please distribute to the Emergency Department, Director of Nursing, Medical Director, Director of Psychiatry, Director of Pharmacy, and Laboratory Service.

Summary

This message includes updated information about reported cases of e-cigarette, or vaping, product use associated lung injury (EVALI), formerly known as vaping-associated pulmonary illness (VAPI), in New York State (NYS).

Additionally, this message provides:

- Guidance for clinical evaluation and management of patients presenting with concerns for EVALI, including a clinical algorithm;
- Clarification of the differences between a clinical diagnosis of EVALI and the most recent Centers for Disease Control and Prevention (CDC) case definition;
- Important instructions for case reporting, collection, and shipment of clinical specimens and vape product samples to the New York State Department of Health (NYSDOH); and
- Recommendations for patients enrolled in the NYS Medical Marijuana Program.

Current Situation

Cases of EVALI continue to be reported in NYS. As of November 4, 2019, 165 patients have been reported from all regions of NYS, including one EVALI-related death. This includes 98 confirmed and probable cases, and 64 reports which remain under investigation. A weekly summary of reported cases in NYS is available on the NYSDOH website, including a map showing reported cases by county. Reported cases continue to be fully investigated by the NYSDOH through interviews and medical chart reviews. Nationally, 2,051 confirmed and

probable cases of lung injury have been reported from 49 states, the District of Columbia and one U.S. territory. Additionally, 39 deaths have been confirmed in 24 states and the District of Columbia.

In NYS, patients have ranged in age from 14 to 71 years old with 62% being under the age of 25 years old. Patients reported using a variety of vape products including:

- both nicotine- and cannabinoid-containing products (41%)
- cannabinoid-containing products only (43%)
- nicotine-containing products only (16%)

The Wadsworth Center is carrying out a range of analyses on the fluids found in the variety of pens, pods, and cartridges received from NYS patients suspected of having EVALI. These include assays specific for THC, CBD, and vitamin E acetate, and testing for a wide range of other organic compounds present in these products using untargeted analyses. These include screens for opioids, synthetic cannabinoids and other drugs of abuse, and pesticides.

To date, Wadsworth Center has received more than 200 product samples, representing different kinds of nicotine- or cannabinoid-containing products, from over 40 patients. Wadsworth scientists have found a range of diluents and thickeners in the cannabinoid-containing products. These include vitamin E acetate, medium chain triglycerides, polyethylene glycol and even castor oil. Most cannabinoid-containing products have been found to include vitamin E acetate. The majority (95%) of the patients who have submitted a cannabinoid-containing product have submitted one or more containing vitamin E acetate.

No single product or specific chemical has been linked to all cases. As stated, some patients report nicotine-containing vape product use exclusively and many patients report combined use of nicotine- and cannabinoid-containing products. Therefore nicotine-containing products have not been excluded as a possible cause or as playing a role in cases of EVALI. NYS will continue to investigate all reported cases to better understand the underlying cause(s) of EVALI. While the investigation continues, **NYSDOH strongly advises that all New Yorkers stop using e-cigarette and vape products**.

Clinical Presentation and Findings:

Patients with EVALI present with respiratory and other gastrointestinal and constitutional symptoms. Symptom onset ranges from days to weeks prior to presentation. Many patients report several days of constitutional symptoms progressing to respiratory symptoms which prompt them to seek care in outpatient and ED settings. The overwhelming majority of NYS confirmed and probable cases (93%) have ultimately required hospitalization. Nearly half of the patients have required admission into the intensive care unit (44%), and at least 16 patients have required intubation.

Chest radiographs have demonstrated bilateral opacities, typically in the lower lobes. Computed tomography (CT) imaging of the chest has shown diffuse bilateral ground-glass opacities, often with subpleural sparing. CT imaging findings may also be suggestive of acute eosinophilic pneumonia, diffuse alveolar damage, organizing pneumonia, lipoid pneumonia, or

reveal findings of diffuse nodules. Bronchoscopy findings have intermittently revealed lipid-laden macrophages but have also been unremarkable in other cases.

Interim Diagnostic and Therapeutic Guidance for EVALI:

On October 18, 2019, the CDC released interim guidance for healthcare providers evaluating and caring for patients with suspected vaping related lung injuries. In addition, through a partnership between the NYSDOH, the University of Rochester, Upstate Poison Control Center, and New York City Poison Control Center, an algorithm to provide interim diagnostic and therapeutic guidance has been developed and can be found in **Appendix A**.

History and Physical:
In addition to obtaining an appropriate history and physical exam for symptoms and signs consistent with EVALI, it is critical to conduct a thorough vaping-specific history, including asking about the timing and types of substances used. Clinicians should familiarize themselves with various terminology as it relates to vaping in order to take an appropriate history. The CDC Clinician Outreach and Communication Activity (COCA) recently provided a webinar which reviewed this information, and can be found in the "Resources for Healthcare Providers" section at:
https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease/healthcare-providers/index.html.

Radiographic Imaging:
If history and physical exam are concerning for EVALI, clinicians should obtain chest imaging, with chest x-ray or chest CT. The decision for appropriate imaging type should be guided by the patient's age and overall clinical status, including disease severity and progression. In addition, chest CT may be helpful if initial chest x-ray findings do not correlate with clinical findings. Initial negative chest imaging findings may not rule out EVALI as a clinical diagnosis, and repeat imaging and close follow-up (within 48 hours) should be considered.

Screen for Alternative Diagnosis:
As EVALI is a diagnosis of exclusion, positive findings on chest imaging should be followed by appropriate infectious testing as well as screening for other etiologies including cardiac, rheumatologic, and neoplastic testing at the clinician's discretion. A respiratory virus panel, including influenza testing, should be performed for all patients for whom EVALI is suspected, particularly during influenza season. Positive findings should prompt providers to consider alternative diagnoses or an EVALI-concomitant respiratory infection. Urine toxicology testing should also be performed, including testing for THC.

Bronchoscopy:
Decisions to perform bronchoscopy should be based on individual clinical circumstances at the discretion of the clinical team but should be considered in patients who are intubated and able to undergo the procedure. Testing of the bronchoalveolar lavage (BAL) fluid should include total cell count with differential, appropriate gram and fungal stains and cultures, and medical cytology. Lipid staining should also be obtained using oil-red O stain. Remaining BAL samples should be retained to facilitate submission to CDC for additional testing. Guidance for this process can be found below and in **Appendix B**.

Lung Biopsy:
Lung biopsies have been performed in some patients with EVALI, and the decision to perform a lung biopsy should be made at the discretion of the clinical team. If a lung biopsy is obtained, lipid staining may be considered during pathologic examination, and is best performed on fresh tissue. Routine pathology tissue processing (including formalin-fixation and paraffin-embedding) can remove lipids. Conducting routine tissue processing and histopathologic evaluation is still important. If available, formalin-fixed (wet) tissues or formalin-fixed, paraffin-embedded (FFPE) lung tissue blocks can be submitted to the CDC through coordination with NYSDOH for additional testing. Guidance for this process can be found below and in **Appendix B**.

Outpatient Management:
While most patients in NYS presenting with EVALI have been hospitalized, patients may also present in the outpatient setting. As some patients with initially mild symptoms have quickly experienced a worsening of symptoms within 48 hours, outpatient management of suspected EVALI may be considered on a case-by-case basis in patients who are clinically stable, will not be alone and where reliable follow up within 24-48 hours of initial evaluation can be assured. These patients should have normal oxygen saturation and, if indicated, empiric antimicrobial and antiviral therapy should be initiated. Patients should also be instructed to seek medical care promptly if respiratory symptoms worsen prior to their scheduled follow-up appointment. Any patient presenting with EVALI in the outpatient setting who has decreased oxygen saturation (<95% on room air), is in respiratory distress, or has comorbidities that may compromise pulmonary reserve, should be admitted for further management.

Treatment and Management Considerations:
At this time there is no specific treatment for patients presenting with EVALI. Treatment continues to be supportive, including oxygen and respiratory/ventilator support, as required. Empiric antibiotic coverage should be considered until infectious etiologies are excluded, when the patient has severe disease including severe hypoxemia despite supplemental oxygen or is intubated. During influenza season, antivirals should be considered until influenza is excluded. Systemic corticosteroids may result in clinical improvement, particularly if there is no improvement in patient status with antibiotics or respiratory support. Corticosteroid dosing and duration should be considered on a case by case basis. The appropriate length of a steroid taper when used in treatment of EVALI is unclear at this time and should be based on the patient's clinical course of recovery and close follow-up. Management of all cases of EVALI should include early pulmonary and toxicology consultation. Upon patient discharge, close outpatient follow-up should be arranged with the patient's primary care and/or pulmonary teams.

Substance Use Counseling and Treatment:
Substance use counseling and treatment services should also be arranged prior to discharge. As a definitive cause of EVALI continues to be investigated, **NYSDOH strongly advises that all New Yorkers stop using e-cigarette and vape products**. Patients being treated for EVALI should be strongly advised not to resume use of any vape products, including both cannabinoid- and nicotine-containing products. As many individuals with EVALI report using nicotine-containing products, providers should assist patients with cessation attempts and

provide FDA-approved cessation medications and counseling. Providers can also refer patients to the NYS Smokers' Quitline at 1-866-NYQUITS (1-866-697-8487) or to online help at http://www.nysmokefree.com. While NYSDOH understands that some individuals are substituting e-cigarettes for combustible cigarettes, **we strongly recommend that individuals DO NOT return to smoking cigarettes.**

ICD Coding:
For clinical management purposes, the CDC recently provided interim recommendations for possible ICD codes that may be applicable when diagnosing and treating a patient with EVALI. These recommendations will be updated as additional information is available and can currently be found at:
https://www.cdc.gov/nchs/data/icd/Vapingcodingguidance2019_10_17_2019.pdf.

Clinical Diagnosis:

The current CDC case definition (September 18, 2019) is used by both CDC and states for case surveillance purposes. However, this case definition is not intended to guide clinical diagnosis or clinical care. EVALI is a diagnosis of exclusion because, at present, no specific test or marker exists for its diagnosis. Health care providers should consider multiple etiologies per the interim guidance above, including the possibility of EVALI and concomitant infection.

Case Reporting and Surveillance

Providers should remain on high alert for potential cases among patients who report a history of vaping and present with progressive respiratory symptoms and/or gastrointestinal and constitutional symptoms, especially in younger, previously healthy, individuals. As EVALI is an emerging health condition, **it is critical that providers report suspected cases of EVALI to the NYSDOH through the local Poison Control Center**. Reporting assists State and federal efforts to fully understand the scope and variety of presentations involved in EVALI. The information learned through case reporting and investigation is vital for developing future recommendations.

All cases of suspected EVALI should be reported to the local Poison Control Centers (PCC) in New York State (1-800-222-1222). If a patient is re-admitted or transferred to another facility, the health care provider should make an additional report to the Poison Control Center in order to update case surveillance information. Providers should have the following information readily available when making a case report:

- Patient name
- Patient date of birth
- Patient contact information
- Patient medical record number
- Symptom onset date
- Date(s) of admission or visit
- Vaping usage history

    - Verify a patient history or suspected history of e-cigarette use (“vaping”) or dabbing* in the 90 days prior to symptom onset (*For this purpose, this means using an electronic device, such as an electronic nicotine delivery system, electronic cigarette, e-cigarette, vaporizer, vape(s), vape pen, dab pen, or other device, to inhale substances, such as nicotine, marijuana, THC, THC concentrate, CBD, synthetic cannabinoids, flavorings, or other substances)
- Chest imaging findings
    - Verify the patient had a pulmonary infiltrate on chest imaging, such as opacities on plain film chest radiograph or ground-glass opacities on chest CT
- Status of viral, bacteriological, and toxicology testing
    - Whether all other clinically indicated respiratory ID testing was negative (such as urine antigen for *Streptococcus* pneumoniae and *Legionella*, sputum or bronchoalveolar lavage culture, blood culture, testing for HIV-related opportunistic respiratory infections, respiratory viral panel AND negative influenza PCR/rapid test)
    - If an infection was identified via culture or PCR, or if the infectious work up was not fully completed, does the clinical team believe that an infectious process is not the sole cause of the underlying respiratory illness
    - Any toxicology results
- Status of performed or planned pulmonary procedures (i.e. bronchoscopy)
- Whether the clinical team has any indication of an alternative plausible diagnosis (for example a cardiac, rheumatologic, or neoplastic process).
- Availability of patient vape products for testing
- Availability of clinical specimens for submission

Be sure to obtain and record the Poison Control Center unique identifier number (PCC #) assigned to this case provided at the time of the case report. At the time of case reporting, the Poison Control Center will provide any necessary forms for submission of available clinical specimens or product samples for testing. The PCC # is required to complete these forms.

Collection of Samples:

Vape product samples:
Providers should determine the name(s) and types of recently used vape products and whether the actual product(s) used remain(s) available for testing. To assist in the public health investigation, all vape product samples (devices, fluid, and any other materials associated with vaping) should be obtained from EVALI patients for testing at Wadsworth Center. Note, even apparently empty devices may contain enough material for testing. When obtaining e-cigarette product information, ask about the source of the vape devices and fill material. If vape product samples for submission are identified after the initial case report, please contact the PCC again for further guidance. **Health care facilities should ensure vape product samples are NOT destroyed as this compromises the public health investigation.**

Clinical specimens:
Clinical specimens obtained from patients with EVALI are important to further our understanding of the cause(s) of this condition. If specimens are available, they should be submitted to Wadsworth Center for testing at CDC. Wadsworth Center will coordinate all specimen submissions to CDC unless otherwise indicated. Based on recent CDC guidance, the following clinical samples will be accepted: blood and urine proximal to admission, bronchoalveolar lavage (BAL) fluid, lung biopsy tissue, and autopsy tissues. Retention and storage of residual samples that were collected for other types of diagnostic screening and testing can also be considered. Healthcare providers should contact their hospital laboratories to identify and retain such samples before disposal. It is recommended that healthcare facilities develop internal protocols with on-site clinical laboratories for specimen processing and appropriate storage prior to shipment to Wadsworth Center. Further instructions for clinical sample collection and submission to Wadsworth Center can be found in **Appendix B**.

Recommendations for NYS Medical Marijuana Program (MMP):

At this time, products approved for use in the NYS MMP have not been associated with reported cases of EVALI in NYS. All patients enrolled in the NYS MMP should be counseled that products that are not MMP-approved should not be used. Rigorous testing continues on all vape products authorized in the State's highly regulated MMP. As the health risks associated with vape product use are still not adequately studied, health care providers should determine if potential alternatives to vape products should be used while the investigation into the cause(s) of EVALI continues. For additional information, providers and patients can also contact the state's MMP at 844-863-9312.

Additional Resources:

New York State Vaping Hotline: 1-888-364-3046

Poison Control contacts:

New York Regional Poison Control Centers: 1-800-222-1222
Upstate: http://www.upstate.edu/poison
New York City: https://www1.nyc.gov/site/doh/health/health-topics/poison-control.page

APPENDIX A:

E-Cigarette, or Vaping, Product Use Associated Lung Injury (EVALI): Interim Diagnostic and Therapeutic Guidance

E-Cigarette, or Vaping, Product Use Associated Lung Injury (EVALI)

Interim Diagnostic and Therapeutic Guidance

History and Physical

Symptoms:

- Cough, dyspnea, pleuritic chest pain
- Nausea, vomiting, diarrhea
- Headache, fatigue, weight loss

Physical Exam Findings:

- Hypoxemia, fever, tachypnea

AND

Positive Screen for Vaping-specific History:

- E-cigarette ("vaping") or "dabbing" (inhaling concentrated liquid) within 30 days
- Most cases involve use in days to weeks preceding presentation. CDC case definition includes vaping use in prior 90 days

(+) → Obtain Chest Imaging

(-) → If history, physical, and/or chest imaging not suggestive consider alternative diagnoses

If atypical presentation:

- Repeat imaging
- Close follow-up (within 48 hours)

Obtain Chest Imaging

Chest X-ray:

- Diffuse bilateral infiltrates/disease

Chest CT:

- Nonspecific bilateral ground glass opacities +/- sub-pleural sparing
- Acute eosinophilic pneumonia, diffuse alveolar damage, organizing pneumonia, or lipoid pneumonia
- Diffuse lung nodules

(+) → Obtain Lab Data to Screen for Alternate Diagnoses

(-) → Consider alternative diagnoses

Obtain Lab Data to Screen for Alternate Diagnoses

Cardiac, Rheumatologic, Neoplastic Testing (at clinical discretion):

- CBC with differential
- ESR, CRP, LDH
- CMP (i.e., BMP + LFTs)
- Urinalysis
- ECG

Infectious Testing:

- Blood cultures
- Extended viral panel including influenza testing
- Mycoplasma NAAT
- Strep. Pneumo urinary Ag
- Legionella Ag
- HIV testing

(+) Or → Consider an EVALI– concomitant respiratory infection

No alternative diagnoses (-)

EVALI Clinical Management:

If EVALI is suspected, clinical management should proceed immediately and be further guided by individual laboratory results:

- Early pulmonology and toxicology consultation, including screening for urine THC
- Oxygen and respiratory/ventilatory support as required
- Empiric antibiotic coverage for at least 48 hours if history is unclear, if patient is intubated, or patient has severe hypoxemia despite supplemental oxygen
- During influenza season, antivirals should be considered until influenza is excluded
- Systemic steroids if no improvement with antibiotics and/or respiratory support
- Corticosteroid dosing and duration should be considered on a case by case basis
- Length of steroid taper should be made based on patient's clinical course of recovery and close follow up
- Arrange for outpatient follow up with primary care team and/or pulmonary team
- Report to local Poison Control Center for case surveillance
- Collect vaping cartridges for state public health lab testing
- Advise patient against all vaping, refer for smoking cessation, as appropriate

If bronchoscopy performed: (consider in intubated patients or at the discretion of treatment team)

- Lipid staining of samples
- Oil-red O stain
- Total cell count with differential
- Bacterial and fungal cultures
- Gram stains and smears
- Medical cytology
- Fungal stains
- Additional testing as clinically indicated

New York State Department of Health | NYC Poison Control Center 212-POISONS | UR Medicine Strong Memorial Hospital — Medicine of the Highest Order | Upstate New York Poison Center 1-800-222-1222 www.upstatepoison.org

© 2019 New York State Department of Health, University of Rochester Medical Center, New York City Poison Center and Upstate New York Poison Center

APPENDIX B:

Clinical Specimen Collection Guidance

Clinical Specimen Shipping Instructions:

Information on CDC recommendations for collection and storage of specimens is provided below. Submission of all clinical tissue samples to the CDC must be coordinated by Wadsworth Center. To initiate specimen submission, providers must first report the suspected case of EVALI to PCC and then contact vaping.inquiries@health.ny.gov for additional shipping instructions. Shipping instructions will only be provided after the case has been reported.

CDC requests that patient identifiers such as name, date of birth, or medical record number not be used to label clinical specimens. When submitting specimens, please use the NYS PCC Case ID (PCC #) for identification, which will be provided at the time of the case report. Each sample should be uniquely labeled e.g. PCC# - 1, PCC# - 2…

When preparing specimen shipment, 2 forms must be included and fully completed: the Wadsworth Center IDR form and the CDC Specimen Submission Form. Forms that are not complete will delay specimen submission to CDC. In addition, CDC requests the following clinical information accompany specimens, if applicable:

- Histopathology report, including results of any special stains, including lipid stains
- Surgical pathology report
- Autopsy report (preliminary is acceptable)
- Relevant clinical notes, including admission History and Physical, discharge summary, if applicable

Clinical Specimen Collection and Storage Guidance for Providers and Laboratory Personnel:

The CDC has issued general specimen collection and storage guidance for healthcare providers involved in the care of patients who meet **probable** or **confirmed** case definitions. These recommendations are **not intended to direct laboratory guidance for patient care** because these decisions are best made by the clinical treatment team.

The following is summarized CDC guidance (issued 10/17/2019). The full version of this CDC guidance is available at:
https://www.cdc.gov/tobacco/basic_information/e-cigarettes/pdfs/Lab-Clinical-Specimen-Collection-Storage-Guidance-Lung-Injury-508.pdf

- Bronchoalveolar lavage (BAL) fluid: The decision to perform a bronchoscopy is at the discretion of the clinical treatment team. BAL fluid should undergo culture and routine centrifugation followed by cellular analyses and cytopathology, including lipid and other staining, as clinically indicated at the local institution. Samples may be obtained at any time during the clinical course, however, it is preferable to obtain BAL fluid prior to initiation of antimicrobial or steroid therapy. If initiated, please note the course, duration, and timing relative to BAL collection.

- Remaining uncentrifuged BAL fluid and centrifuged supernatant should be labeled as such and retained.
- Up to 10 unstained cytology slides should be briefly fixed in formalin and retained for future evaluation.
- Excess cell pellet after cytopathologic evaluation can be divided in half, with half being fixed in formalin and stored at room temperature and half frozen at -20ºC or lower.
- Place remaining uncentrifuged fluid and centrifuged supernatant into sterile vials with external caps and internal O-ring seals. If there is no internal O-ring seal, then seal tightly with available cap and secure with Parafilm®. Label each sample container with the NYS PCC case ID, sample type, subsection of lung lavage, date of sample collection, and **freeze** samples at -20ºC or lower.

- Blood Samples (Plasma): Collect up to 12 mL of blood in (3) 4-mL purple/lavender top (K2 – EDTA) tubes, or (3) 3 mL tubes. Mix tube contents by inverting them 8-10 times. Label tubes in order of collection. Place a barcode label on tube vertically. Spin tubes for 15 minutes at 1000 to 1300 g-force to separate plasma from whole blood. Aliquot plasma into cryotubes and apply labels that include the NYS PCC Case ID. **Freeze** samples at freezer temperatures of -20ºC or lower.
  - **If a centrifuge is not available**, label blood tubes as directed and store whole blood samples at 1ºC to 10ºC. **Do not freeze**.

- Urine samples: Store 40 to 60 mL of urine in a screw-cap urine cup. Place a barcode label vertically on the cup. Label the cup with the NYS PCC Case ID. Indicate the collection (i.e. “clean catch” or catheterization). **Freeze** urine samples at -20ºC or lower.

Additionally, specimen submission guidance for pathologic evaluation of tissue specimens from **probable** and **confirmed** cases has been issued by the CDC (10/1/2019). The full version of this CDC guidance is available at: https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease/healthcare-providers/pdfs/specimen-submission-req.pdf

Characterizing tissue pathology seen in cases of lung injury associated with e-cigarette or vaping product use is important to further understand the spectrum of pathology and the pathogenesis of lung injury. Evaluation of both fresh and fixed tissues can help improve our understanding during this outbreak.

The decision to perform a lung biopsy is at the discretion of the clinical treatment team. If available, the CDC encourages submission of lung biopsy tissue specimens as described below. Autopsies should be considered for cases with a fatal outcome, with collection and submission of autopsy tissues.

- Lung tissue specimens: Fresh lung tissue, formalin-fixed (wet) lung tissue, and formalin-fixed, paraffin-embedded (FFPE) tissues from biopsy procedures will be

accepted. Lipid staining can only be performed on-formalin-fixed (wet) lung tissues prior to routine tissue processing and paraffin embedding as this involves the application of alcohols which removes lipids. Label specimens with the NYS PCC Case ID. Ship formalin-fixed (wet) tissue and FFPE tissue blocks at room temperature. Fresh tissue must be shipped frozen.

- Autopsy tissue specimens: Formalin-fixed (wet) tissues and FFPE tissue blocks from autopsy will also be accepted by the CDC for evaluation. Respiratory tissues should be thoroughly sampled, including lung parenchyma, trachea, and bronchi. 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:
    - Liver
    - Kidney
    - Heart
    - Representative sampling of tissues from all other major organs including brain is recommended, especially any organs with gross or microscopic pathology.
    - Label all samples with the NYS PCC Case ID and ship **frozen**. Formalin-fixed (wet) tissues and FFPE tissue blocks can be sent at room temperature.

- 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.