On 9/6/19, the Centers for Disease Control and Prevention (CDC) announced that 450 possible cases with five deaths of acute lung disease from vaping had been reported from 33 states, including Michigan, and one territory. Although some newspaper reports have discussed infectious agents, the 9/6/2019 CDC announcement stated that “no evidence of infectious disease has been identified; therefore, lung illnesses are likely associated with a chemical exposure.”

The CDC public health case definition is shown in Table 1. Since the case reports do not require a lung biopsy, the underlying pathology of the 450 possible cases are not clear. The CDC is expected to start reporting only confirmed and probable cases so the number of reported cases in the future, at least initially, is expected to decrease. The diagnosis of six cases reported in September from Utah (Maddock et al., 2019) and five cases from North Carolina (Davidson et al., 2019) was lipoid pneumonia. All these patients had vaped cannabinoid products. Nine of these 11 patients had bronchoscopy and evaluation of their lavage fluid; all nine had lipid-containing macrophages consistent with the diagnosis of lipoid pneumonia.

On 9/6/2019, a New England Journal of Medicine article reported on 53 cases from Illinois and Wisconsin (Layden et al. 2019). The authors reported that 84% of the cases had vaped tetrahydro cannabinoid products. Only three of the patients had a lung biopsy with a range of findings: Case 1 had “mild and nonspecific inflammation, acute diffuse alveolar damage and foaming macrophages”; Case 2 had “interstitial and nonspecific inflammation, acute diffuse alveolar damage and foaming macrophages”; and Case 3 had “interstitial and peribronchiolar granulomatosis pneumonitis.” Of the 14 cases with data on lavage cells, none had increased eosinophils and only two noted moderate lipid-laden macrophages. Eighty one percent of these 53 patients had gastrointestinal symptoms in addition to respiratory symptoms.

Prior to the current concern about vaping, there have been 17 case reports in the medical literature; Acute Eosinophilic Pneumonia (4 cases), Organizing Pneumonia (3 cases), Lipoid Pneumonia (3 cases), Diffuse Alveolar Hemorrhage (2 cases), Hypersensitivity Pneumonitis (2 cases), Respiratory Bronchiolitis Interstitial Lung Disease (1 case), Pneumonia (1 case), and Bronchitis (1 case). These reports are summarized in Table 2. Unlike the current cases, the cases in previous publications did not report gastrointestinal symptoms and only one of these 17 previous cases reported the use of cannabinoid products.

<table>
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<th><strong>Table 1. CDC Case Definition for Confirmed and Probable Cases (Not for Clinical Diagnosis)</strong></th>
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<td><strong>Confirmed</strong></td>
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<td><strong>Probable</strong></td>
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<td><strong>Footnotes</strong></td>
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E-cigarettes and vaping are relatively recent forms of smoking; they were first commercially available in the United States in 2007. It has become increasingly popular with young individuals. In fact, e-cigarettes are the most common tobacco product used by high school students with 20.8% using in the prior 30 days up from about 3% in 2011 (Gentzke et al., 2019). The increased use of e-cigarettes as a nicotine delivery product as well as to deliver cannabinoids has clearly increased the population at risk. How possible changes in both legal formulations or contaminants in the products contributed to the recent cases is under active investigation. The reports in the current cases of gastrointestinal symptoms and the exposure to marijuana products may be clues to determine the etiology of the current cases. For example, vitamin E acetate oil was found in multiple cannabinoid samples and has been suggested as the cause of lipoid pneumonia in some individuals with acute lung disease associated with vaping.

E-cigarettes contain multiple types of chemicals including nicotine, carbonyls, and solvents. Previous examples of lung disease caused by chemicals that can be potentially found in e-cigarettes include microwave popcorn lung (bronchiolitis obliterans) from exposure to diacetyl and 2, 3 pentanediol flavoring agents (Van Roon et al., 2007; PS News v.18 (4), Fall 2007) and waterproof spraying lung (chemical pneumonitis and pulmonary edema) from exposure to solvents in boot or tent waterproofing products (CDC, 2006; PS News v. 19 (#1), Winter 2007-2008).

Given the uncertainty of the etiology of the lung disease associated with vaping, healthcare providers should strongly discourage their patients from vaping. To assist in determining the etiology, providers are encouraged to report all suspected cases of lung disease associated with vaping to public health officials. Ways to report are shown in Table 3. Michigan will be sharing de-identified data of the reported cases with the CDC. The CDC will be examining the cases from all states, including reviewing the epidemiology and pathological findings, along with a review of the results of the FDAs laboratory analysis of the components of the vaping products associated with the cases of lung disease.


### Table 3. Public Health Reporting Instructions

**The following information on your patient with severe pulmonary disease of unclear etiology and history of e-cigarette/vaping within the last 90 days should be reported**

Reports can be submitted in one of three ways:

1. By calling your Local Health Department (see [www.malph.org](http://www.malph.org) for directory)
2. By providing a completed reporting form to your hospital’s Infection Preventionist, who will make sure it gets to the right Local Health Department, or
3. By faxing a report to 517-335-8509. Obtain the reporting form at: [www.michigan.gov/cdinfo](http://www.michigan.gov/cdinfo)

Lung disease from chemical exposure is a reportable condition under Administrative Rules R 325.71-75. Reporting of patients with this condition falls under the HIPAA public health exception [section 1264.512 (b)]; and disclosure by you or your hospital is exempt from “patient consent, authorization, or opportunity to agree or object.”
Table 2. Seventeen Case Reports of Lung Disease and Vaping Reported Prior to 2019

**Acute Eosinophilic Pneumonia** (4) There have been four case-reports of acute eosinophilic pneumonia related to vaping; one from Hawaii (2), one from California (5), and two from Japan (1, 4). There is a much more extensive literature that acute eosinophilic pneumonia is associated with cigarette smoking (3). The 20-year-old man from California was a healthy active duty sailor who had a three-day history of a persistent cough, shortness of breath and facial flushing. His symptoms occurred within one hour after smoking an e-cigarette. He had apical ground glass opacities on a chest CT scan. He had 74% eosinophils in bronchial lavage fluid. He had significant improvement after treatment with steroids. The 18-year-old female from Hawaii had fever, non-productive cough, difficulty breathing and pleuritic chest pain. She had begun vaping in the prior two months. She had diffuse ground glass patchy airspace disease and coalescing nodules. She had 26% eosinophils in her bronchial lavage fluid and had significant improvement after treatment with steroids. One case reported from Japan was a 20-year-old man who was admitted to the hospital with acute respiratory failure He had begun vaping six months previously. He had bilateral infiltrates and pleural effusion on chest CT scan. He had 60% eosinophils in his bronchial lavage fluid. On the fourth day of steroids he was markedly improved. The other case reported from Japan was a 16-year-old male with asthma, who was hospitalized with severe cough, fatigue and shortness of breath that began after vaping for two weeks. He had ground glass opacities and was intubated, meeting the criteria for ARDS. Bronchial lavage fluid contained 14.7% eosinophils. This did not meet the diagnostic criteria for eosinophilic pneumonia but his hospitalization was consistent with acute eosinophilic pneumonia. He had resolution of symptoms and clearing of his chest CT scan by the ninth day of steroid treatment. 1) Aoyagi T, et al. Heat-not-burn cigarettes induce fulminant acute eosinophilic pneumonia requiring extracorporeal membrane oxygenation. Respir Med Case Rep 2018; 26: 87-90. 2) Artz ZL, et al. Acute eosinophilic pneumonia following electronic cigarette use. Respir Med Case Rep 2019; 27: 100825. doi: 10.1016/j.rmcr.2019.100825. 3) Di Giacomo F, et al. Acute Eosinophilic Pneumonia: Correlation of Clinical Characteristics with Underlying Cause. Chest 2017; 152: 379-385. 4) Kamada T, et al. Acute eosinophilic pneumonia following heat-not-burn cigarette smoking. Respir Case Rep 2016; 4: e0196. doi: 10.1016/j.resrep.2016.03.004.

**Hypersensitivity Pneumonitis (2)** There are two reports of hypersensitivity pneumonitis associated with vaping; one from New Hampshire (1), and one from Pennsylvania (2). The report from New Hampshire was of a 60-year-old male with weakness, chills and cough who had bilateral ground glass opacities predominantly in his upper lobes. His symptoms improved within 24 hours and resolved within 72 hours. He declined to have bronchoscopy. He had used a flavored e-cigarette prior to onset of his symptoms. The Pennsylvania report was of an 18-year-old woman with two days of progressive dyspnea, cough and pleuritic chest pain. She had a history of mild intermittent asthma. She had begun using e-cigarettes two to three weeks prior to her diagnosis. She had a history of her rash peaking off of her oral weeks before her CT scan and her chest CT scan showed “independent opacities in both lung bases, superimposed smooth interlobular septal thickening and bilateral small-to-moderate pleural effusions”. She was intubated and met diagnostic criteria for ARDS. Bronchiolavage showed cellular debris and reactive mononuclear cells. The differential of white cells in her lavage fluid was 26% neutrophils, 13% lymphocytes, 14% monocytes, 25% mononuclear cells and 22% eosinophils. All tests for viruses, bacteria and fungus were negative. She was treated with steroids and weaned from the ventilator over a five-day period. 1) Atkins G, et al. Acute Inhalational Lung Injury Related to the Use of Electronic Cigarette Delivery System (ENDS). Chest 2015; 148 (Suppl): 83A. 2) Sommerfeld CG, et al. Hypersensitivity Pneumonitis and Acute Respiratory Distress Syndrome From E-Cigarette Use. Pediatrics 2018; 141(6). pii: e20163927. doi: 10.1542/peds.2016-3927.

**Diffuse Alveolar Hemorrhage (2)** There are two case reports of diffuse alveolar hemorrhage; one from Guam of a 33-year-old man (1) and the other a 70-year-old man from West Virginia (2). The man from Guam had diabetes and a seizure disorder. He had been vaping for two months before onset of dyspnea and hemoptysis. On chest CT, he had diffuse ground glass opacities and bilateral patchy consolidation. Workup for inflammatory conditions and microbial disease was negative. Bronchial lavage and a right wedge resection lung biopsy showed “bland pulmonary hemorrhage with no evidence of capillaritis or diffuse alveolar damage”. Steroids were tapered and two weeks later his CT scan was normal. The 70-year-old had begun using electronic cigarettes four weeks prior to developing rapidly progressive dyspnea and cough. He had COPD and previously had a left upper lobectomy for lung cancer. Sequential bronchiolavage revealed increasing hemorrhagic return consistent with diffuse alveolar hemorrhage. Lavage fluid contained a large number hemosiderin–laden macrophages. Infectious and inflammatory causes were excluded. He developed refractory hypoxemia and died. Agustin M, et al. Diffuse Alveolar Hemorrhage Induced by Vaping. Chest 2018; 154(3): A6513. doi: 10.1016/j.chest.2018.03.161.

**Lipoid Pneumonia (3)** There are three case reports of lipoid pneumonia, one from Oregon (1), one from West Virginia (2), and one from the United Kingdom (3). The case from the United Kingdom was a 34-year-old woman with a three-month history of progressive shortness of breath, daily productive cough and hemoptysis who was an ex-smoker; she had been vaping for three years. She had congenital dimorphism with thrombocytopenia, iron deficiency anemia and previously had closure of a ventricular septal defect at the age of one. She had diffuse lung infiltrates on a chest radiograph and diffuse ground glass opacities and subpleural cysts on a high resolution CT scan. A video assisted thoroscopic lung biopsy showed extensive lipid-filled macrophages and deposition of cholesterol clefts with some inflammation. She was treated with 40 mg prednisone daily and advised to stop vaping but continued to vape and remained on steroids with only slight improvement in her pulmonary function test values. The individual from West Virginia was a 31-year-old male who had been vaping for four months and had diffuse ground glass opacities with “fluffy” parenchymal opacification. He had no evidence of capillaritis or diffuse alveolar damage. Steroids were tapered and two weeks later his CT scan was normal. 1) McCauley L, et al. An unexpected consequence of electronic cigarette use. Chest 2012; 141:1110–1113. 2) Viswam D, et al. Case report: Respiratory failure caused by lipoid pneumonia from vaping e-cigarettes. BMJ Case Rep 2018. doi: 10.1136/bcr-2018-224350. 3) Modis S, et al. Acute Lipoid Pneumonia Secondary to E-Cigarettes Use: An Unlikely Replacement for Cigarettes. Chest 2015; 148: 382-383.

**Organizing Pneumonia (3)** Three cases of organizing pneumonia (Bronchiolitis Obliterans Organizing Pneumonia (BOOP)) have been reported; one from New York (1), one from Ohio (2), and one from Virginia (3). Their ages ranged from 27–54 years and they had vaped for one month to several years. The 54-year-old from New York developed acute onset of dyspnea and hemoptysis six hours after vaping cannabis. He had extensive focal airspace opacities and a centriflobular pattern (“tree in bud”). His transbronchial biopsy showed organizing pneumonia. Inflammatory causes were ruled out. He rapidly recovered and was not treated with steroids. Two weeks later his repeat chest CT scan was normal. The other two patients used e-cigarettes, had abnormal chest CT scans; one with “innumerable pulmonary nodules” and the other with “multifocal discrete and confluent ground glass nodules”. Both cases had biopsy proving organizing pneumonia. Both recovered, one within days and the other within two weeks. The Ohio patient had a repeat chest CT scan two weeks later, which was normal. 1) He T, et al. “Tree-in-Bloom”: Severe Acute Lung Injury Induced by Vaping Cannabis Oil. Ann Am Thorac Soc 2017; 14: 468-470. 2) Khan MS, et al. Organizing pneumonia related to electronic cigarette use: A case report and review of literature. Clin Respir J 2018;12: 1295-1299. 3) Mannilla RD, et al. Vapor Lung: Bronchiolitis Obliterans Organizing Pneumonia (BOOP) in Patient with E-Cigarette Use. J Am Resp Crit Care Med 2016; 193: A1862.

**Other Conditions (3)** A 33-year-old male who had been treated with chemotherapy for testicular cancer was reported from Australia (1). Nine months after chemotherapy and three months after he began vaping, a chest CT scan performed as part of routine follow-up showed multiple new pulmonary nodules with “fluffy” parenchymal opacification. An open lung biopsy was interpreted as showing respiratory bronchiolitis-associated interstitial lung disease. He ceased vaping and had resolution of his radiographic findings. A 43-year-old male was reported from France with shortness of breath, fever, cough and dyspnea. He had diffuse interstitial and reticular changes on his chest CT scan and lipid laden macrophages in his bronchial lavage fluid. Testing for bacteria and viruses was negative. He had rapid improvement with steroids and cessation of vaping. The individual from Oregon was 42-years-old and had vaped for seven months. She had rheumatoid arthritis, fibromyalgia, schizoaffective disorder, and hypertension. She had ground glass opacities on her CT scan and lipid laden alveolar macrophages in her bronchial lavage fluid. Testing for bacteria and viruses was negative. She ceased vaping and a follow up chest radiograph was normal but she continued to have a reduced diffusion capacity. 1) Flower M, et al. Respiratory bronchiolitis-associated interstitial lung disease secondary to electronic nicotine delivery system use confirmed with open lung biopsy. Respirol Case Reports 2017; 5: e0230. doi: 10.1002/rcr2.230. 2) Hureaux J, et al. A case report of subacute bronchial toxicity induced by an electronic cigarette. Thorax 2014; 69: 596-597. 3) Moore K, et al. Bilateral Pneumonia and Pleural Effusions Subsequent to Electronic Cigarette Use. Open Journal of Emergency Medicine 2015; 03:18-22. doi: 10.4236/ojem.2015.33004.
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Remember to report all cases of occupational disease!

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