



**NUDE NICOTINE**

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## **Acute Lung Failure & Lipoid Pneumonia – Addressing the “Vaping Illness”: Diagnostic Criteria & Harmful Constituents in Hemp & Cannabis Products:**

### **Subtitle:**

A Scientific Review of the Status of Literature, Medical Reports, & Industry-Practices of the Addition of/Exposure to, Harmful Constituents by Inhalation in Hemp & Cannabis Products.

**Written by Jake Rubenstein**

**President & Chairman of the Board – Nude Nicotine, Inc. & N.N. Analytics, Inc.**  
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### **Brief Executive Summary:**

This review shall serve as a guide and directive for local, state, and federal authorities, more specifically the CDC & CDC Emergency Center, to institute a set of diagnostic criteria for Vapor-Induced Exogenous Lipid Pneumonia (V-ELP), caused by the inhalation of non-polar lipids. This directive speaks to clinicians and radiologists. It allows target product identification and mandates analytical testing for a set of potentially-harmful constituents (HPHCs) involved in the production of cannabis or hemp products.

Moreover, this is a call-to-action to local government officials to separate “flavor bans” from the important public health risk – black market cannabis and hemp vapor products. As evident from the analytical testing reports, clinical, and radiological criteria, the cases of Illness presented are not rooted in the formulation or usage of nicotine-containing eLiquids. “Flavor bans,” in our professional opinion, do not address this lung illness, and should be separated in conversations about what is Appropriate for the Protection of Public Health (APPH). In a separate argument, flavored tobacco products should never be sold in a location with exposure to, or directly to, children under the legal smoking age. However, this scientific dissertation is focused on clinical, radiological, and analytical criteria of a “vaping illness” and is not intended to enforce a political agenda.

Nicotine-containing products used an Electronic Nicotine Delivery System (ENDS), historically, have never used non-polar components in their vaporized liquids due to the water-soluble

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chemistry of the three ingredients constituting over 95% of solution volume of all nicotine-containing e-liquids: propylene glycol (PG), vegetable glycerin (VG), nicotine. These compounds' inhalation toxicology is well known to the medical literature as GRAS for inhalation within the parameters of the testing environments. Prior to 2019 there were very few adverse effects, even as the electronic industry grew to its first peak in 2015. The few isolated cases were traced to exposure to an e-liquid that was not manufactured to proper standards. However, in the start of 2019, and especially in the summer of 2019, a large amount of lipoid pneumonia cases began to evolve from those "vaping" (Vaping is the act of inhaling vapor produced by a vaporizer or electronic cigarette)

However, in 2019, particularly the summer of 2019, a large amount of lipoid pneumonia cases began to appear in patients who were known "vapers." Upon closer clinical, radiological, and sometimes pathological scrutiny, these patients had been exposed to lipids not found in traditional e-cigarettes. According to the reports, in 82% of these cases THC or CBD products turned out to be the culprit of oil-exposure leading to V-ELP rather than those bought from a reputable vendor or manufacture.

### **Hypothesis:**

It has become clear that the HPHCs connected to the cases of acute lung failure associated with vaping is linked to a new class of lipoid pneumonia. These HPHCs - triglycerides, vitamins, and oils – are atomized in an electronic cigarette or vaporizer, most often from THC and CBD products. The sources of exposure of aerosol containing these contaminants can be attributed to the improper use of topical products labeled as "oils" in a vaporizer, or the presence of these HPHCs in the product formulation itself. In a New England Journal of Medicine review of patient case studies, over 80%\* were found to have consumed Hemp or Cannabis Vape Products procured from the black or grey market. Hemp and Cannabis industry stakeholders do not test for, consider, or provide ingredients list disclosure of their products sold to consumers. These HPHCs are commonly added by the manufacture to "cut," dilute, and/or lower the cost of their final product while maintaining an oil-like consistency; they do so without regard to the potential adverse effects of the inhaled aerosol of these compounds.

\**Pulmonary Illness NEJM*, September 2019 – DOI: 10.1056/NEJMoa1911614

### **Proposal:**

Nude Nicotine recommends the establishment of triage and diagnostic tools, both in the hospital and in the laboratory (clinical/radiological with tandem chemical analysis) to identify patients exposed to this new class of lipoid pneumonia, V-ELP.

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### **SECTION 1: Background:**

In the late months of August 2019, the nation began to see its first cases of a mysterious “Vaping Illness” with patients presenting to the emergency room in acute lung failure. Each of these patients presented similar symptoms and could all attest to have vaporized eLiquids of many kinds. To stop the spread of an unknown contaminant in the vaporization space, the CDC needed to act quickly. They issued a nationwide Health Alert Network (HAN) statement on August 30<sup>th</sup>, 2019, titled: “Severe Pulmonary Disease Associated with Using E-Cigarette Products”

<https://emergency.cdc.gov/han/han00421.asp>

As a result of this ongoing investigation, the CDC released the following statement:

*“While this investigation is ongoing, if you are concerned about these specific health risks, consider refraining from using e-cigarette products.”*

This broad statement sent the nation into panic in September. Vapers across the nation were not encouraged to continue vaping out of fear of an unknown contaminant in the supply stream. The source, product line(s), and origins were unknown. However, there seemed to be a statistically significant link within the growing case reports of illnesses. A very large cohort of patients within these case studies (over 80%\*) admitted to using CBD or THC vaping products in addition to traditional ecigarettes with nicotine.

*\*Pulmonary Illness NEJM, September 2019 – DOI: 10.1056/NEJMoa1911614*

*“The mean monthly rate of visits to the ER for severe respiratory illness as identified by syndromic surveillance between June 1 and August 15, 2019,... was twice the mean monthly rate that occurred between June 1 and August 15, 2018 ( 7.4cases per 10,000 visits vs. 3.8 cases per 10,000 visits), in Illinois counties.”*

Moreover, these case studies were appearing more rapidly in states without legal access to cannabis or hemp products on the legal market.

*(Pulmonary Illness NEJM September 2019 – DOI: 10.1056/NEJMoa1911614 ) – “On July , the WDHS issued an alert to clinicians describing the clinical syndrome and requested that similar cases of pulmonary disease associated with e-cigarette use be reported to public health authorities. The WDHS was subsequently contacted by a physician in Illinois seeking clinical treatment guidance for a patient with similar clinical presentation and e-cigarette product exposure, and the WDHS promptly notified the IDPH in July. A joint WDHS–IDPH public health investigation was initiated sometime in August to identify additional case patients and to characterize the pulmonary clinical syndrome related to*

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*the use of e-cigarettes and related products. The CDC was consulted for technical assistance early in the investigation, and a CDC epidemiologic assistance field team (Epi-Aid) was deployed to the WDHS and IDPH on August 20, 2019."*

The most important finding, however, is within the dates of the supposed V-ELP cases. The references section in the CDC's warning, as well as the Status of the Literature, does not list case material more current than the Summer of 2019.

One of the only notable cases before the summer of 2019, was a non-conclusive study, relating to a similar illness using vaping products (undisclosed if nicotine or THC vaping)\*

*\*Respiratory Bronchitis, Respirol, April 2017 – doi: 10.1002/rcr2.230*

This has not been an issue pre-spring/summer 2019. Previous cases were of other types of pneumonia associated with exposure to a specific chemical, or class of chemicals (popcorn lung – diacetyl, diketones)\*. As the example, diketones, like diacetyl, and acetyl propionyl, are chemicals present on the FDA's list of harmful chemicals (HPHCs – harmful or potentially harmful chemicals) within the 21 CFR Part 1100. Nude Nicotine and N.N. Analytics support this analysis on a qualifying basis for introduction to the market as per FDA ruling.

*"Occupational exposure to 2,3-butanedione (BD) vapors has been associated with severe respiratory disease leading to the use of potentially toxic substitutes... (Toxicol Pathol. 2016 Jul; 44(5): 763–783. Published online 2016 Mar 29. doi: [10.1177/0192623316638962](https://doi.org/10.1177/0192623316638962))*

However, this exposure has not led to a specific death in any clinical case using an ENDS with nicotine eLiquid in the Status of the Literature....

### ***SECTION 2: An overview of lipid pneumonia, its risk factors, and the newly-identified subset of lipid pneumonia related to the "Vaping Illness:"***

#### **Lipoid pneumonia Medical Overview:**

(Citation – Lipoid pneumonia: an overview – DOI: 10.1586/ers.10.74) –

*"Exogenous lipid pneumonia is related to inhalation or aspiration of fatty substances, whereas in endogenous lipid pneumonia, intra-alveolar lipid accumulation occurs as a result of obstruction, chronic lung infection/disease or a lipid storage disorder."*

The definition of the subset of lipid pneumonia we will use for the oil-soluble aerosol exposure from vaping cannabis or hemp products is Exogenous Lipoid Pneumonia (ELP).

*"In the case of exogenous lipid pneumonia due to inhalation/ aspiration, mineral oils/fat enter the tracheobronchial tree without stimulating the cough reflex and impair the mucociliary transport system... Once inside the alveoli, it is*

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*difficult to expectorate the lipid.... [and] oil is taken up by macrophages after emulsification. Because alveolar macrophages cannot metabolize the fatty substance, the oil is repeatedly released into the alveoli after death of the macrophages... The oil released elicits a giant-cell granulomatous reaction (hence also called lipid granulomatosis), chronic inflammation, and alveolar and interstitial fibrosis."*

(Pulmonary Lipid-Laden Macrophages and Vaping – DOI:

10.1056/NEJMc1912038) *"A notable and consistent feature of the cases we report is the presence of lipid-laden macrophages seen with oil red O staining in BAL samples that are not attributable to aspiration of exogenous lipid material. In addition, the diffuse parenchymal opacities seen on CT scans did not have low attenuation (in Hounsfield units) consistent with classic lipid pneumonia. Although the pathophysiological significance of these lipid-laden macrophages and their relation to the cause of this syndrome are not yet known, we posit that they may be a useful marker of this disease."*

### **Clinical Criteria:**

(Citation – Lipoid pneumonia: an overview – DOI: 10.1586/ers.10.74) – *"Blood investigation results are usually normal. However, leukocytosis and an increased erythrocyte sedimentation rate may occur"*

### **Radiological Criteria:**

(Citation – Lipoid pneumonia: an overview – DOI: 10.1586/ers.10.74) – *"The typical findings include homogenous dense consolidation, often with air bronchograms and sometimes a fine, 'spun glass' appearance may be observed [34]. The most common findings described on CT scan include airspace consolidations, areas of ground-glass attenuation, airspace nodules and 'crazy-paving' pattern [38]. Consolidations are usually heterogeneous and their negative density values, as low as -30 to -150 HU, are a diagnostic criterion for lipid pneumonia.... Other radiological abnormalities that can be seen in these patients include pneumatoceles, pneumomediastinum, pneumothorax and pleural effusions."*

### **Disease Progression & Resolution:**

(Citation – Lipoid pneumonia: an overview – DOI: 10.1586/ers.10.74) – *"The radiologic manifestations of acute exogenous lipid pneumonia usually show a partial to complete resolution over time after stopping exposure to lipids. Resolution of opacities is usually observed within 2 weeks to 8 months, however,*



*they may be progressive or static in some cases, even after stopping the exposure and symptomatic improvement... There can be scarring of lung parenchyma, which can cause persistence of radiological shadow... Fibrosis and coalescence of oil can result in nodules and masses with irregular margins, closely mimicking lung cancer”*

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ELP described this case subset perfectly - cases from aspirating oils and non-polar compounds that are not able to be hydrolyzed by semi-basic environment of alveolar mucosa.

*(Exogenous lipid pneumonia - doi: 10.1002/rcr2.356) – “Repeated oral administration of plant-based oil for cultural reasons was reported by 10 of 11 caregivers. Cough (12/12), tachypnoea (11/12), hypoxia (9/12), and diffuse alveolar infiltrates on chest radiography (12/12) were common at presentation. Chest computed tomography revealed ground-glass opacification with lower zone predominance (9/9) and interlobular septal thickening (8/9). Bronchoalveolar lavage specimens appeared cloudy/milky, with abundant lipid-laden macrophages and extracellular lipid on Oil-Red-O staining (12/12)”*

**An example from industry – inhalation of aerosol containing lipids can result in a similar form of ELP:**

*(Pulmonary Lipid-Laden Macrophages and Vaping -DOI: 10.1056/NEJMc1912038) “Further work is needed to characterize the sensitivity and specificity of lipid-laden macrophages for vaping-related lung injury, and at this stage they cannot be used to confirm or exclude this syndrome. However, when vaping-related lung injury is suspected and infectious causes have been excluded, the presence of lipid-laden macrophages in BAL fluid may suggest vaping-related lung injury as a pro visual diagnosis.”*

**THC use and prevalence of patients affected is high compared to nicotine use:**

*(Pulmonary Illness NEJM September 2019 – DOI: 10.1056/NEJMoa1911614 ) – “80% reported use of THC products, and 7% reported use of CBD products (Table 2). A total of 37% of the patients reported using THC products only, whereas 17% reported using nicotine-containing products only.”*

Report of brand – “Dank Vape” – 59% prevalence of use – high likely target for analytical testing of HPHC profile reported by Nude Nicotine/NN Analytics

<https://www.dankvapes.org/>

<https://www.dankvapes.org/product/mimosa-dankvapes-dank-carts->

[vape-pen/](#)

**Diagnosis is not related to viral or bacterial factors – negative testing**

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(Tree-In-Bloom – March 2017 – AnnalsATS Volume 14 Number 3) “An upper respiratory viral panel was negative and HIV serology and rheumatologic tests were all negative. Microbiologic culture was negative for all samples.”

(Pulmonary Illness NEJM September 2019 – DOI: 10.1056/NEJMoa1911614 ) – “All the patients who received antibiotics on an outpatient basis had reported progression of respiratory symptoms, which had prompted subsequent hospital admission.”

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### **Approximately 50% of patients exhibited lipid pneumonia:**

(Pulmonary Illness NEJM September 2019 – DOI: 10.1056/NEJMoa1911614 ) – “A total of the cytology reports on bronchoalveolar-lavage specimens noted lipid-laden macrophages with oil red O stain; the other reports did not comment on the use of oil red O stain. Of the samples with noted lipid-laden macrophages, reports listed moderate lipid-laden macrophages”

**Technique = bronchoalveolar-lavage AKA BAL** ([J Cytol.](#) 2014 Jul-Sep; 31(3): 136–138.)

*“Bronchoalveolar lavage (BAL) is a diagnostic procedure by which cells and other components from bronchial and alveolar spaces are obtained for various studies. One of the main advantages of BAL is that it can be done as a day care procedure. Material obtained by BAL can give a definite diagnosis in conditions such as infections and malignancies.”*

### **Technique = measurement of ground-glass opacity (GGO) - doi:**

10.3978/j.issn.2218-6751.2013.09.03)

(Pulmonary Illness NEJM September 2019 – DOI: 10.1056/NEJMoa1911614 ) – “Ground-glass opacities in both lungs were characteristically observed on CT, sometimes with subpleural sparing. Of the 48 patients who underwent CT imaging, 4 cases of pneumomediastinum, 5 pleural effusions, and 1 case of pneumothorax were present (in 8 patients). One patient had both a pneumomediastinum and a pneumothorax, and one patient had both a pneumomediastinum and pleural effusion.

### **Other conditions to consider for CT scan to determine the need for a definitive PET scan.**

- Pneumomediastinum
- Pleural effusion
- Pneumothorax



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### **SECTION 3: Background to Patient Disclosure of illicit (or socially unacceptable) substance use - Reporting for THC and CBD cannot be considered completely accurate:**

As noted by Bachhuber et al, a gentle approach to patient counselling is required to reveal specific products that the patient might have been exposed to. Illicit substances, like THC, or if not illicit, socially-unacceptable use of THC and CBD products lead to a large cohort of users who do not disclose the use of, or extent-of-use-of hemp and cannabis products.

Citation: (Pulmonary Illness NEJM September 2019 – DOI: 10.1056/NEJMoa1911614 ) – *“Information on product use is based on reports by the patients, and patients may be reluctant to report illicit drug use.”*

Citation: (Protecting Privacy or Protecting the Public March 2010 – Health Policy & Ethics): *“According to a recent report published by the National Institute of Medicine, “[T]he HIPAA Privacy Rule does not protect privacy as well as it should, and ... as currently implemented, it impedes the conduct of important health research.” There is no question that these privacy protections are important and serve the public interest. In today’s tense climate of fears of identity theft, privacy violations, and other unwanted personal intrusions, however, it is easy for the public, and regulators, to lose sight of how easily the increasingly broad body of restrictions limiting access to medical and public health data can undermine efforts to better understand and improve public health.”*

Another example of the same phenomenon outside of industry: (Harvard Men's Health Watch) – MSM HIV Reporting Statistics

*“Yet, so far, most of the available data are from animal experiments or observational studies that rely on people's willingness to report their marijuana use. “And since most users are recreational, it's tough to accurately measure dosage and frequency,” says Dr. Mukamal. It's no surprise, then, that the science is so cloudy. For instance, an analysis published in 2015 in The Journal of the American Medical Association examining almost 80 trials involving nearly 6,500 people found that most of these studies suggested that marijuana use was associated with relief of some symptoms, but the findings were inconsistent.”*

#### **Example within-industry:**

Bachhuber et al – <https://dx.doi.org/10.1089%2Fcan.2017.0051> - Willingness to Participate in Longitudinal Research Among People with Chronic Pain Who Take Medical Cannabis: A Cross-Sectional Survey:

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*“For respondents' indicating a willingness to participate in the proposed study (for any length of time), we presented a list of potential reasons why and asked participants to check all that apply. Similarly, for respondents not willing to participate, we displayed a list of potential reasons why not and asked respondents to check all that apply.”*

*“Of 405 respondents (estimated response rate: 30%), 54% were women and 81% were white non-Hispanic. Neuropathy was the most common pain condition (67%) followed by inflammatory bowel disease (19%). Of respondents, 94% (95% CI 92–97%) thought that the study should be done, 85% (95% CI 81–88%) would definitely or probably enroll if asked, 76% (95% CI 72–81%) would participate for ≥1 year, and 59% (95% CI 54–64%) would respond to questions at least daily. Older age was the only factor associated with lower willingness to participate, lower willingness to participate for ≥1 year, and lower willingness to respond to questions at least daily.”*

### **Outside example –**

HIV patients on the “down-low” – (Focusing :down low” – [J Natl Med Assoc.](#) 2005 Jul; 97(7 Suppl): 52S–59S.)

### **Case Study of Chronic Marijuana Smoker with almost identical symptoms to ELP, but without oil-red stain.**

Example that BLA is required to investigate:

*“38-year-old male with no past medical history who came for an evaluation due to a cough with hemoptysis and shortness of breath that started immediately after smoking marijuana. The patient was afebrile, and his blood pressure was 122/81 mmHg. His heart rate was 79 beats/min and his oxygen saturation was 90% in room air.*

*Examination of his lungs indicated bibasilar rales... A bronchoscopy with bronchoalveolar lavage (BAL) was initially bloody, but subsequently became clear (Figure 4). BAL cell counts showed leukocytes at 120 cells/mm<sup>3</sup>, with 98% neutrophils, and red blood cells at 28,250,106 cells/mm<sup>3</sup>. A transbronchial biopsy revealed chronic inflammation.”*

(Citation: Hashimi et al – A Case Report of Cannabis Induced Hemoptysis – doi: 10.1097/MD.0000000000003232)

(Citation: Can J Respir Ther. 2015 Winter; 51(1): 7–9. - ...Vapourized cannabis and respiratory risk)

### **Marketplace practices for Cannabis and Hemp Manufacturers of Vaporized Oils:**

Commonplace diluents are used in vaporized THC and CBD eLiquid for manufacturers to obtain a certain terpene profile, viscosity, or diluted concentration to maximize on cost. These practices are, unfortunately, commonplace. Multiple manufacturers use high concentrations of monoterpenes, not sourced from cannabis, but from other plants,

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vegetables, and oils, to “flavor” their product. In addition, some manufacturers will dilute their product to maximize on cost, or “thicken” the product to hide the fact that they have diluted its concentration of the API, CBD or THC.

THC and CBD products are, unfortunately, also mislabeled in relation to their API. The early-adopters of CBD and THC vaporization technology used total percentage of the distilled oils (THC distillate and/or CBD distillate) to hide the fact that this was not the true concentration of the API in the product. Most, if not all manufacturers of these THC and CBD vaping products, label their packaging with this concentration, most often between 80-95%. In fact, the CBD/THC distillate used in these products is mostly of fair to excellent quality, free of the HPHCs noted above. The distillation process of CBD and THC, if conducted properly, eliminates the presence of these HPHCs, if even present in the starting extract (very low possibility), by way of boiling point separation. However, manufacturers dilute this distillate to a VERY low percentage, sometimes as low as 10-30%. The diluting agents are labeled below and represent the majority of the HPHCs that are causing acute lung failure by way of the lipid pneumonia mechanism. Between 2015-2019 as the industry matured, more grey-market and black-market THC and CBD vaporization products entered the market as well as among dealers on the street. These products were manufactured to the same disappointing labelling standard. Consumers purchasing products claiming to be “pure” THC or CBD were in fact pure before they manufactured the product. The oil itself was pure. But the manufacturing process introduced a plethora of HPHCs as the product formulators diluted and flavored their products. This trend has led to a reporting of “highly pure” cannabis or hemp products, which in fact, have been contaminated by diluents and have gone undisclosed. This is a direct supporting statement to the case study cited previously – Tree-In-Bloom – March 2017 – Annals ATS Volume 14 Number 3.

### ***Section 5: How can we define compounds that, upon exposure, can lead to lipid pneumonia:***

#### **Octanol: Water Partition Coefficient:**

Definition of a compounds partitioning into oil (lipophilicity) or water (hydrophilicity), or a range in between.

It is worth noting that small molecule drugs in the LogP <2 range exhibit high solubility in lung mucosa, but their solubility is through a different mechanism:

Transcellular pathway – integration into the lipid bilayer of cell membranes.

Water soluble compounds diffuse by way of the:

Pore-diffusion @ cellular tight-junctions

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(Citation – Patton et al – The Lungs as a Portal of Entry for Systemic Drug Delivery – doi: 10.1513/pats.200409-049TA)

### **Section 4: What compounds in Vaping products can be classified as lipoid-pneumonia**

Please see list below labeled “Diluents Used:”

#### **Diluents used:**

##### **High concentrations of monoterpenes**

Lab Effects Terpene Diluent:

<https://labeffects.com/the-cut-terpene-diluent/>

TERPS USA Terpene Diluent:

<https://terpsusa.com/>

[https://www.walmart.com/ip/Terps-USA-Terpene-Diluent-5ml/721327851?wmlspartner=wlp&selectedSellerId=1875&adid=22222222227294701892&wl0=&wl1=g&wl2=c&wl3=359256829915&wl4=pla-778373868945&wl5=9061204&wl6=&wl7=&wl8=&wl9=pla&wl10=113137471&wl11=online&wl12=721327851&veh=sem&gclid=Cj0KCQjw5zsBRD8ARIsAJfI4BhkKcLJv4m3YbTVkrFU0YhcTGzedMevhgLeEtX0DWnjsaTeEgoknb4aAssIEALw\\_wcB](https://www.walmart.com/ip/Terps-USA-Terpene-Diluent-5ml/721327851?wmlspartner=wlp&selectedSellerId=1875&adid=22222222227294701892&wl0=&wl1=g&wl2=c&wl3=359256829915&wl4=pla-778373868945&wl5=9061204&wl6=&wl7=&wl8=&wl9=pla&wl10=113137471&wl11=online&wl12=721327851&veh=sem&gclid=Cj0KCQjw5zsBRD8ARIsAJfI4BhkKcLJv4m3YbTVkrFU0YhcTGzedMevhgLeEtX0DWnjsaTeEgoknb4aAssIEALw_wcB)

##### **Solutions marketed as diluting agents, “cutters,” and/or “thickeners”**

Floraplex – mostly Phytol

<https://www.buyterpenesonline.com/product-category/terpenes/diluent/>

<https://www.buyterpenesonline.com/terpenes-for-sale/terpene-diluent/>

##### **Mineral Oil (CAS 8012-95-1):**

National Library of Medicine HSDB Database Case Report: Inhalation of Mineral Oil:

*“We report a case of acute exogenous lipoid pneumonia in a 34-year-old fire-eater. Six hours after inhalation of liquid paraffin, dyspnea, cough, fever, hemoptysis, and chest pain developed in this patient. Chest-computed tomography showed nodular infiltrations with ground glass opacities (GGO) in the right middle lobes, GGO alone in the right lower lobes, and consolidations with GGO in the left lower lobes. Lipid-laden alveolar macrophages in bronchoalveolar lavage fluid were detected by lipid staining (Sudan III stain, oil-red-O stain) and transmission electron*

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*microscopy. The symptoms and lung infiltrations were improved by treatment with prednisolone, together with antibiotics and urinastatin.”*

(Citation:

<https://toxnet.nlm.nih.gov/cgi-bin/sis/search/a?dbs+hsdb:@term+@DOCNO+1922>)

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**Vitamin E (tocopherols)**

**Vitamin E-acetate**

**MCT Oil**

**Coconut Oil**

**Other Cooking Oils**

### **Section 6: Alternative hypothesis to product contamination:**

Improper packaging as “FOR TOPICAL USE ONLY” – Topical Products are being inhaled in vaporizer devices:

Similar to eLiquid bottles – “boston round” 30-60mL with a dropper cap – markedly similar to eLiquid packaging. If a user mistakes this for their eLiquid, or by way of the packaging, assume it is intended for vaporization is a critical error. Aerosolization of oils and oil-soluble compounds is a direct source of the lipid pneumonia – extremely similar lung case studies to aspirated mineral oil in infants as cited:

*(Exogenous lipid pneumonia - doi: 10.1002/rcr2.356) – “Repeated oral administration of plant-based oil for cultural reasons was reported by 10 of 11 caregivers. Cough (12/12), tachypnoea (11/12), hypoxia (9/12), and diffuse alveolar infiltrates on chest radiography (12/12) were common at presentation. Chest computed tomography revealed ground-glass opacification with lower zone predominance (9/9) and interlobular septal thickening (8/9). Bronchoalveolar lavage specimens appeared cloudy/milky, with abundant lipid-laden macrophages and extracellular lipid on Oil-Red-O staining (12/12)”*

### **Conclusions & Recommendations:**

It has become clear that the HPHCs connected to the cases of acute lung failure associated with vaping is linked to a new class of lipid pneumonia. These HPHCs - triglycerides, vitamins, and oils – are atomized in an electronic cigarette or vaporizer, most often from THC and CBD products. The sources of exposure of aerosol containing these contaminants can be attributed to the improper use of topical products labeled as “oils” in a vaporizer, or the presence of these HPHCs in the product formulation itself. Hemp and Cannabis industry stakeholders do not test for, consider, or provide ingredients list disclosure of their products sold to consumers. These HPHCs are commonly added by the manufacture to “cut,” dilute, and/or lower the cost of their final product while maintaining an oil-like consistency; they do so without regard to the potential adverse effects of the inhaled aerosol of these compounds.

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Moreover, this is a call-to-action to local government officials to separate “flavor bans” from the important public health risk – black market cannabis and hemp vapor products. As evident from the analytical testing reports, clinical, and radiological criteria, the cases of illness presented are not rooted in the formulation or usage of nicotine-containing eLiquids. “Flavor bans,” in our professional opinion, do not address this lung illness, and should be separated in conversations about what is Appropriate for the Protection of Public Health (APPH). In a separate argument, flavored tobacco products should never be sold in a location with exposure to, or directly to, children under the legal smoking age. However, this scientific dissertation is focused on clinical, radiological, and analytical criteria of a “vaping illness” and is not intended to enforce a political agenda.

### **Now:**

Products samples are tested for HPHCs in the same manner as the Product Testing recommendations listed below. This protocol is recommended to be added to the FDAs HPHC list, as defined in the 21 CFR Part 1100, as well as applied to any, and all inhalation products, whether by smoke, or by vapor, adherent to ISO 20768:2018, 20778:2018, 3308:2012, & 7210:2018 mandated requirements.

There should be a focus on the procurement and analysis of hemp & cannabis vapor cartridges, vape “oils,” and other products intended for (or appearing to be intended for) vaporization. The state-regulated testing requirements for cannabis and hemp testing must quickly enact this protocol (as being-developed) as mandated testing before sale on the market. Regulated cannabis and hemp markets do not currently employ any testing for these constituents, while ENDS nicotine-containing products do. Nude Nicotine, Inc. & N.N. Analytics, Inc. applaud the FDAs foresight of these chemicals as HPHCs in other industries; we recommend applying these to 21 CFR Part 1100 HPHC testing mandates.

### **Ongoing:**

Collection of samples from street vendors to put out (DO NOT BUY LIST)  
Prosecution & Legal Action against “grey market” and “black market” cannabis & hemp vapor product producers, as well as those ENDS products not currently registered with the FDA.

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### **Triage #1: Diagnostic Criteria for Patient Exposure –**

recommend the following analytical procedures to triage patients exposed to hemp & cannabis products exhibiting shortness-of-breath, wheezing or coughing, nausea, vomiting, and/or elevated heart-rate:

- 1) Pulse Oximeter measurement (SPO2)
- 2) Blood pressure and heart rate monitoring – examine for elevated heart rate and/or depressed blood pressure
- 3) CT Scan to reveal possible pneumomediastinum, pneumothorax, or pleural effusion

If SPO2 readings are below 96% and CT scan reveals abnormal lung function as indicated in point #2, admit patient, and submit for more-extensive diagnostics as-indicated in Triage #2

### **Triage #2: Clinical Techniques for evaluating the chemistries of HPHCs in cannabis & hemp products from Triage #1 –**

recommend the following analytical procedures to examine BAL fluid for HPHCs that can expose a patient to ELP:

- 1) BAL Sampling of patient – BAL fluid is sampled, stained with oil-red, and examined via microscopy for the presence of oil-soluble droplets. An estimation of density and size are taken to evaluate remediation techniques.

### **Triage #3: Methodologies for Patient Counselling & Treatment to Reveal Products containing HPHCs –**

As noted by Bachhuber et al, a gentle approach to patient counselling is required to reveal specific products that the patient might have been exposed to. Illicit substances, like THC, or if not illicit, socially-unacceptable use of THC and CBD products lead to a large cohort of users who do not disclose the use of, or extent-of-use-of hemp and cannabis products.

Teens and underage users should never be coerced into disclosing their use, rather approached without family, and in a calm setting, to ensure to the patient that full-disclosure is in the best interest of their health, without punishment from parents. Underage patients do require admission and by a parent or guardian, whom are required to be disclosed this information. This is a sensitive topic. In whatever way possible, doctors, nurses, hospital staff, parents, and family alike must approach the underage patient with love, care, and kindness – never judgement based on what substances they have been exposed to.



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In the same manner, adults with family present and whom would rather not immediately disclose their substance use should be treated carefully and kindly.

These approaches are necessary if the goal is two-fold:

- 1) Eliminating the patient's use of the cannabis and/or hemp vaping products identified
- 2) Collecting samples, brand names, points of purchase.
- 3) In addition to identifying patient symptom remediation and subsequent elimination of exposure, collecting the names of others that the patient knows or may know to have been exposed to the hemp/cannabis vaping product in-question is critical.

#### **Triage #4: Chemical Analysis Criteria for Product Testing with Results from Triage #1-3:**

Nude Nicotine and Nude Nicotine Analytics recommend the following analytical procedures to examine all vaping products, specifically those containing cannabis or hemp, to evaluate for HPHCs form that can expose a patient to ELP:

Product (solid/liquid) testing:

Nude Nicotine Analytics Method ID – "VOL-DB-MS" –

Refinement of AOCS Official Method 5a-40: Free Fatty Acids in Crude and Refined Fats and Oils – applied to vaporized liquids in e-cigarette devices:

- 1) Basic hydrolysis with 1.75M Ethanolic KOH @65C for 2hrs
- 2) GC/MS Analysis of non-polar constituents – VOL-DB-MS
  - a. Salimon J, Abdullah BM: A study on the thermal properties and solid fat content of Malaysian rubber seed oil. The Malaysian Journal of Analytical Sciences 2009, 13:1-7.
- 3) HPLC Analysis of non-polar constituents – VOL-C18-PDA
  - a. Salimon J, Abdullah BM: A study on the thermal properties and solid fat content of Malaysian rubber seed oil. The Malaysian Journal of Analytical Sciences 2009, 13:1-7.
- 4) %FFA Analysis by Neutralization
  - a. The reactions typically employed to obtain total lipid by esterification of the lipid components into their corresponding FAMES are not capable of discerning the FAMES produced from FFAs in the sample from FAMES produced from TAGs in the sample. Standard methods such as AOCS Official Method Ce 2-66.
  - b. AOCS: Official Methods of Analysis. Association of Official Analytical Chemist, Arlington, Cd 9F93.20,, 16 1997.



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(Citation: Hydrolysis Optimization - doi: [10.1186/1752-153X-5-67](https://doi.org/10.1186/1752-153X-5-67) – Salimon et al.: Hydrolysis optimization and characterization study of preparing fatty acids from Jatropha curcas seed oil. Chemistry Central Journal 2011 5:67.)

(Citation: Christie, W.W.; Gas chromatography and lipids. The Oily Press, Bridgewater, UK, (1989), pp. 184. - Lipids, chemical analysis I. Title 547.7'7046)

(Citation: <https://doi.org/10.1093/chromsci/bms093> - Kail et al. Determination of Free Fatty Acids and Triglycerides by Gas Chromatography Using Selective Esterification Reactions)

Target analytes:

- Alpha-Tocopherol (E307 – Vitamin E)
- Hexadecanoic acid (75-10-3)
- Dodecanoic Acid (143-07-7)
- Decanoic Acid (334-48-5)
- Octanoic Acid (124-07-2)

Emissions (Aerosol Testing):

Protocols are developed with protocols adherent to N.N. Analytics' procedures utilizing ISO 20768:2018, 20778:2018 mandated requirements. Additional document controls and product chain-of-custody-requirements are also embodied for 21 CFR Part 1100 (2019):

Patent Pending by Nude Nicotine, Inc. & N.N. Analytics, Inc.

Products samples are tested for HPHCs in the same manner as the above Product Testing recommendations. This protocol is recommended to be added to the FDAs HPHC list, as defined in the 21 CFR Part 1100, as well as applied to any, and all inhalation products, whether by smoke, or by vapor, adherent to ISO 20768:2018, 20778:2018 3308:2012, & 7210:2018 mandated requirements