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Review of NIOSH Cannabis-Related Health Hazard Evaluations and Research

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Abstract

Since 2004, the National Institute for Occupational Safety and Health (NIOSH) has received 10 cannabis-related health hazard evaluation (HHE) investigation requests from law enforcement agencies ($n = 5$), state-approved cannabis grow operations ($n = 4$), and a coroner's office ($n = 1$). Earlier requests concerned potential illicit drug exposures (including cannabis) during law enforcement activities and criminal investigations. Most recently HHE requests have involved state-approved grow operations with potential occupational exposures during commercial cannabis production for medicinal and non-medical (recreational) use. As of 2019, the United States Drug Enforcement Administration has banned cannabis as a Schedule I substance on the federal level. However, cannabis legalization at the state level has become more common in the USA. In two completed cannabis grow operation HHE investigations (two investigations are still ongoing as of 2019), potential dermal exposures were evaluated using two distinct surface wipe sample analytical methods. The first analyzed for delta-9-tetrahydrocannabinol (Δ9-THC) using a liquid chromatography and tandem mass spectrometry (LC–MS–MS) method with a limit of detection (LOD) of 4 nanograms (ng) per sample. A second method utilized high performance liquid chromatography with diode-array detection to analyze for four phytocannabinoids (Δ9-THC, Δ9-THC acid, cannabidiol, and cannabinol) with a LOD (2000 ng per sample) which, when comparing Δ9-THC limits, was orders of magnitude higher than the LC–MS–MS method. Surface wipe sampling results for both methods illustrated widespread contamination of all phytocannabinoids throughout the tested occupational environments, highlighting the need to consider THC form (Δ9-THC or Δ9-THC acid) as well as other biologically active phytocannabinoids in exposure assessments. In addition to potential cannabis-related dermal exposures, ergonomic stressors, and psychosocial issues, the studies found employees in

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Disclaimer

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Conflict of interest

The authors do not have any conflict of interest regarding this research and the cannabis industry.

cultivation, harvesting, and processing facilities could potentially be exposed to allergens and respiratory hazards through inhalation of organic dusts (including fungus, bacteria, and endotoxin) and volatile organic compounds (VOCs) such as diacetyl and 2,3-pentanedione. These hazards were most evident during the decarboxylation and grinding of dried cannabis material, where elevated job-specific concentrations of VOCs and endotoxin were generated. Additionally, utilization of contemporary gene sequencing methods in NIOSH HHEs provided a more comprehensive characterization of microbial communities sourced during cannabis cultivation and processing. Internal Transcribed Spacer region sequencing revealed over 200 fungal operational taxonomic units and breathing zone air samples were predominantly composed of *Botrytis cinerea*, a cannabis plant pathogen. *B. cinerea*, commonly known as gray mold within the industry, has been previously associated with hypersensitivity pneumonitis. This work elucidates new occupational hazards related to cannabis production and the evolving occupational safety and health landscape of an emerging industry, provides a summary of cannabis-related HHEs, and discusses critical lessons learned from these previous HHEs.

Keywords

allergen; cannabis; delta-9-tetrahydrocannabinol; Δ9-THC; diacetyl; endotoxin; marijuana; mold; 2,3-pentanedione; volatile organic compounds

Background

The NIOSH HHE program (https://www.cdc.gov/niosh/hhe/default.html) conducts a wide range of workplace investigations characterizing workplace exposures, evaluating health concerns, and providing recommendations to eliminate or mitigate hazards. Since 2004, the program has received 10 cannabis-related health hazard evaluation (HHE) requests (Table 1) from law enforcement agencies ($n = 5$), state-approved cannabis grow operations ($n = 4$), and a coroner's office ($n = 1$). Earlier requests concerned law enforcement activities, crime scene investigation, and criminal investigations regarding potential illicit drug exposures (including cannabis). While the United States Drug Enforcement Administration has banned cannabis as a Schedule I substance on the federal level, cannabis legalization at the state level has become more prominent in the USA. Four out of the last five most recent HHE requests have involved potential occupational exposures during the harvesting, cultivation, processing, and packaging of cannabis for medicinal and non-medical (recreational) use. Even though the cannabis-related HHE request numbers are small, the trend is clear. There is a need for occupational safety and health information for an emerging industry. This is a rare opportunity to study the wide array of exposures and health effects from the beginning of an industry instead of retrospectively evaluating relationships after years of exposure.

Prior to these cannabis-related HHEs and subsequent research articles, occupational safety and health research studies evaluating cannabis exposures in the workplace were severely limited. Cannabis production occupational exposure information was primarily limited to microbiological hazards derived from European industrial hemp fiber facility industrial hygiene surveys (Zuskin *et al.*, 1990; Fishwick *et al.*, 2001a,b; Martyny *et al.*, 2013). Harvesting, cultivation, processing, and manufacturing work tasks can result in personal

exposure to delta-9-tetrahydrocannabinol (Δ9-THC) as well as proteins derived from the flowers, buds, leaves, and stems of *Cannabis sativa*. Active or passive exposure to these plant-derived components in the general population has been previously shown to result in pruritus, urticaria, rhinitis, dyspnea, sinusitis, asthma, angioedema, and even anaphylaxis (Liskow *et al.*, 1971; Tessmer *et al.*, 2012). Most symptoms are experienced within half an hour of exposure (Decuyper *et al.*, 2019a,b). In occupational settings, workers that handle *C. sativa* plants have been shown to develop either allergic rhinitis (Herzinger *et al.*, 2011) or workrelated contact urticaria especially in law enforcement occupations that routinely handle *C. sativa* plants (Majmudar *et al.*, 2006; Williams *et al.*, 2008).

Fishwick *et al.* (2001b) showed that hemp production workers' endotoxin exposures, particularly in occupations that disturbed dust, exceeded the Dutch Expert Committee on Occupational Safety (DECOS) occupational exposure level of 90 endotoxin units per cubic meter (EU/m^3) (DECOS, 2010). Elevated inhalable levels of bacteria (190×10^6 colony forming units (cfu) m^{-3} and fungi (13×10^6 cfu m^{-3}) were also reported in breathing zone samples from workers that cleaned and swept the factory floor (Fishwick *et al.*, 2001b). Approximately a third of hemp workers in one facility reported work-related symptoms in high exposure occupational tasks (Fishwick *et al.*, 2001a). Soft hemp workers have a higher prevalence of chronic respiratory symptoms and byssinosis compared to control workers (Valić and Žukin, 1971; Bouhuys and Zuskin, 1976; Zuskin *et al.*, 1990, 1994). More recent studies conducted within the US law enforcement community have shown that officers removing cannabis from indoor marijuana grow operations are also exposed to elevated concentrations of viable fungi (5×10^5 cfu m^{-3}) placed in the genus *Penicillium* (Martyny *et al.*, 2013). These collective studies show that workers handling cannabis products can be additionally exposed to microorganisms that can ultimately impact respiratory health; however, the limitations associated with existing microbiological hazard identification methods (e.g. viable culture) have restricted identification to higher taxonomic ranks.

Although cannabis allergy was first reported in 1971, few peer-reviewed studies have reported the prevalence of cannabis sensitization, primarily due to the lack of available commercial extracts and the legal status of cannabis use (Decuyper *et al.*, 2017). Several European studies have recently identified and characterized *C. sativa* immunoglobulin E (IgE) binding allergens (Gamboa *et al.*, 2007; Decuyper *et al.*, 2017, 2018, 2019a,b). The most extensively studied is a 9-kDa non-specific lipid transfer protein (nsLTP) that binds human IgE and broadly crossreacts with fruits, vegetables and tobacco (Decuyper *et al.*, 2017). The International Union of Immunological Societies Allergen Nomenclature Sub-committee has designated nsLTP as an allergen named 'Can s 3' (Gamboa *et al.*, 2007; Decuyper *et al.*, 2019a,b).

These HHEs and hypersensitivity studies elucidate new occupational hazards related to cannabis production and the evolving occupational safety and health landscape of an emerging industry. The information gained in these studies may crosswalk to hemp farming and production workplaces due to their similarities. The following sections provide a summary of cannabis-related HHEs, hypersensitivity, and discuss critical lessons learned from these previous HHEs.

Summary of HHE results

National Institute for Occupational Safety and Health (NIOSH) has completed two HHE requests at cannabis grow facilities: (i) a small, 5-acre outdoor farm (referred to as the 'farm') with three employees and (ii) a modern indoor/outdoor facility (referred to as the 'indoor facility') with 13 employees and state-of-the-art processing (NIOSH, 2017, 2018; Victory *et al.*, 2018). The two worksites represent two common cannabis production facilities; although a vast majority of grow facilities will be more similar to the indoor facility. While they appear to be on opposite ends of the cannabis cultivation spectrum, both HHEs had similar cultivation, harvesting, processing activities, and findings. This section will highlight the methods used to assess hazards identified during these HHEs, as well as some pertinent results that can inform future evaluations of cannabis facilities. A summary of surface wipe sample results is presented in Table 2 and airborne sample results in Table 3.

Surface wipe sampling

Dermal Δ9-THC or delta-9-tetrahydrocannabinol acid (Δ9-THCA) exposures and corresponding health effects are largely unknown especially in an industrial cannabis setting. Unprotected dermal contact, particularly with the plant or contaminated surfaces, is a concern because previous research has illustrated dermal reactions, most notably urticarial rashes (hives), in persons handling cannabis such as forensic specialists and law enforcement officers (Majmudar *et al.*, 2006; Basharat *et al.*, 2011; Herzinger *et al.*, 2011; Ozyurt *et al.*, 2014).

At both the farm and indoor facility, a liquid chromatography and tandem mass spectrometry (LC–MS–MS) analysis for Δ9-THC with a limit of detection (LOD) of 4 ng per sample was used. In addition to the LC–MS–MS method, an experimental method was used at the indoor facility using high performance liquid chromatography with diode-array detection (HPLC–DAD) with an orders of magnitude higher LOD (2000 ng per sample). Though the HPLC–DAD method had a higher LOD, it could also analyze for multiple cannabinoids [Δ9-THC, Δ9-THCA, cannabidiol (CBD), and cannabinol (CBN)] from a single surface sample (Ambach *et al.*, 2014). Δ9-THC was detectable on surface wipe samples throughout the farm [170−210 000 nanograms per 100 square centimeters (ng/100 cm^2)] and the indoor facility [not detected (ND) to 53 000 ng/100 cm^2] (NIOSH, 2017, 2018). Surface samples were collected a 100% cotton twill wipe moistened with 3 ml of isopropyl alcohol. Sample area was determined using a 100-square centimeter template or denoted if a template could not be used. Surface wipe sample concentrations are summarized in Table 2.

Δ9-THC air sampling

Δ9-THC air sampling was not conducted during either HHE at the grow facilities. The farm allowed employees to use cannabis during work hours and during breaks. This non-occupational consumption would have greatly interfered with the air sampling aimed at characterizing occupational exposure, and would have most likely led to a gross overestimation of Δ9-THC airborne exposures. At the indoor facility, the decision to not collect Δ9THC airborne samples was based, in part, on a previous study of 30 indoor grow operations that indicated potential airborne Δ9-THC exposures were unlikely with all Δ9-

THC air samples below detection limits (0.10 μm per sample) except one with a result of 0.70 μm per sample (Martyny *et al.*, 2013).

Microbiological hazards

Cultivation and processing workers employed at cannabis farms are likely to share similar occupational safety and health concerns encountered in other agricultural and manufacturing workplaces (CDPHE, 2017). In addition to these shared agricultural and manufacturing hazards, NIOSH has shown that cannabis workers are additionally exposed to a broad spectrum of microbiological hazards specific to cultivation, processing, and hand trimming occupational tasks (NIOSH, 2017, 2018; Green *et al.*, 2018). These microbiological hazards have predominantly included prokaryotic bacteria, eukaryotic fungi, as well as cell wall components such as bacterial lipopolysaccharide (endotoxin) derived from Gram-negative bacteria (Green *et al.*, 2018; Couch *et al.*, 2019).

Utilization of contemporary gene sequencing methods in NIOSH HHEs has improved the understanding of microbial communities sourced during cannabis cultivation and processing activities. In the HHE at the farm, 16S gene sequencing resulted in the identification of over 600 bacterial operational taxonomic units (OTUs) and Actinobacteria diversity was shown to be highest in personal air samples compared to outdoor area samples (NIOSH, 2017; Green *et al.*, 2018). In contrast, Internal Transcribed Spacer region sequencing revealed over 200 fungal OTUs and personal air samples were predominantly composed of the cannabis plant pathogen, *Botrytis cinerea*: the source of gray mold disease (Williamson *et al.*, 2007). In addition to cannabis plant pathogens, workers have most recently been shown to be exposed to fungal species placed in the phylum Basidiomycota and included *Wallemia* species and even environmentally sourced species placed in the class Agaricomycetes (NIOSH, 2018). Each of these fungal sources has been previously identified as aeroallergens and causative agents of adverse health effects in several agricultural settings (Jarvis, 1962; Popp *et al.*, 1987; Groenewoud *et al.*, 2002; Jeebhay *et al.*, 2007; Ampere *et al.*, 2012; Bekci *et al.*, 2014). These data have suggested that cannabis cultivation and processing workers that engage in harvesting, bud stripping, and hand trimming occupational tasks are potentially exposed to a diverse spectrum of microbiological hazards.

Endotoxin exposures [breathing zone: ND to 85; area: ND to 94 EU/m^3] were evaluated at both facilities and increased exposures were associated with harvesting activities at the farm and grinding tasks at the indoor facility (NIOSH, 2017, 2018; Couch *et al.*, 2019). All endotoxin levels were well below the DECOS exposure limit of 90 EU/m^3 at the indoor facility (DECOS, 2010). However, a cultivator's breathing zone full-shift sample that involved a grinding task (85 EU/m^3) was elevated when compared to the same cultivator's previous sample (15 EU/m^3) the day before which included similar tasks but no grinding tasks (NIOSH, 2018). For the farm, precipitation appeared to reduce endotoxin exposure. Average breathing zone concentrations on days without precipitation (arithmetic mean = 22 EU/m^3; standard deviation 6.7 EU/m^3) were higher than days with precipitation (arithmetic mean = 3.9 EU/m^3, standard deviation 1.5 EU/m^3) with otherwise similar work conditions and tasks (NIOSH, 2017).

Volatile organic compounds

At the indoor facility, volatile organic compound (VOC) screening was conducted during both visits by collecting whole air samples using 450 ml evacuated canisters a with restricted flow controller (less than 30 s, 15-min, and 6-h duration) followed by gas chromatography/mass spectrometry (GC/MS) analysis (LeBouf *et al.*, 2012). The canister VOC screening results identified diacetyl (ND to 23 ppb) and 2,3-pentanedione (ND to 25 ppb), with the highest concentrations (diacetyl = 23 ppb, 2,3-pentanedione = 25 ppb) measured near the decarboxylation oven using short task samples collected as the decarboxylation oven was opened after a cycle containing cannabis material (NIOSH, 2018). Subsequent sampling using a validated OSHA method identified low full-shift diacetyl concentrations (ND to 0.51 ppb) for cultivators while the only detectable area OSHA method result (0.26 ppb) was collected near the decarboxylation oven (OSHA, 2017). Diacetyl and 2,3-pentanedione are naturally occurring substances that have also been identified during roasting, grinding, and other coffee-related processes (Bailey *et al.*, 2015; Gaffney *et al.*, 2015; Pierce *et al.*, 2015; Duling *et al.*, 2016; McCoy *et al.*, 2017). In the cannabis industry, decarboxylation is the process of removing a carboxyl group from Δ9-THCA, to activate it to Δ9-THC, the psychoactive ingredient in cannabis (Citti *et al.*, 2018;Hadener *et al.*, 2019). While decarboxylation occurs naturally as the plant ages after harvesting, it is accelerated by the application of heat. Exposures were below the NIOSH recommended exposure limit for both diacetyl (5.0 ppb) and 2,3-pentanedione (9.3 ppb) for the evacuated canister and traditional industrial hygiene sampling using a validated Occupational Safety and Health Administration method (NIOSH, 2016; OSHA, 2017).

Terpenes are a class of VOCs that have a distinctive odor and gives cannabis its characteristic smell; however, little is known about occupational exposures to terpenes and possible health effects (Eriksson *et al.*, 1996, 1997; Wolkoff *et al.*, 2013). The most likely occupational hazard is not necessarily terpenes themselves, but their interaction with ozone and hydroxyl radicals to form highly oxidized species (ketones and aldehydes) associated with adverse health effects such as irritation, occupational asthma, and pulmonary airflow limitation (Weschler, 2000; Jarvis *et al.*, 2005; Singer *et al.*, 2006; Anderson *et al.*, 2012). These interactions are particularly concerning in cannabis facilities that use ozone generators as a means to neutralize odors and sterilize equipment. At the indoor facility, area ($n = 10$) terpene samples were collected using an 60 milliliter (ml) polytetrafluoroethylene impinger filled with 25 ml of deionized water, derived with 100 μl aqueous 250 mM *O*-tert-butylhydroxylamine hydrochloride, and analyzed by electron impact ionization/liquid-chemical ionization ion trap mass spectrometer in splitless mode (Jackson *et al.*, 2017). While a number of both mono- and sesquiterpenes (including alpha-pinene) were identified at the indoor facility, no terpene ozonolysis products were identified using an impinger method analyzed via GC/MS (Jackson *et al.*, 2017; NIOSH, 2018).

Ergonomic stressors

At the farm facility, an ergonomic evaluation examined harvesting and processing activities such as cola (large branch) removal, big leafing (removing outside leaves with small percentages of cannabinoids), destemming (removing stems), and final hand trimming (performed for flower products) (NIOSH, 2017). During cola removal, harvesters did not

remove netting (used to allow airflow within the plant) resulting in horizontal reaching, trunk bend, and creating pressure on the lower spine. For processing activities (big leafing, destemming, and final hand trimming), tasks requiring hand forces were found to be low when evaluated with a digital pinch force gauge but the quantity of hand movements and the time needed to perform the activities could potentially lead to adverse musculoskeletal health effects. The indoor facility manufactured only extracts and used mostly automated methods for destemming product for mechanical grinding. Therefore, an ergonomic evaluation was not performed at this facility.

Psychosocial factors

Of 13 employees at the indoor facility, 12 were interviewed about job stress, psychosocial factors at work, and work-related health concerns (NIOSH, 2018). A majority of the employees reported low to moderate job stress and described a heavy workload as the main contributor to their stress. Most employees reported performing tasks that were not part of their job description, and some employees also noted issues with coworkers not doing their job properly or being absent. Being a relatively small operation with a large production quota created challenges, whereby the demands put on the employees outweighed their available resources. This is a classic scenario for increased job stress (NIOSH, 1999). These interviews highlighted that cannabis operations should hire the appropriate number of staff to adequately distribute workload and ensure individuals' roles are clearly defined so that each employee is comfortable with their job duties and expectations.

Secondhand cannabis smoke

With increased availability of cannabis, environmental exposures to secondhand cannabis smoke for law enforcement officers, home healthcare aids, employees in cannabis-related workplaces that allow open consumption, and the general public remains a hazard of concern (Brooks *et al.*, 2017; Wilson *et al.*, 2017; Iglesias *et al.*, 2018; NIOSH, 2019a,b). NIOSH received an HHE request concerning law enforcement officers' secondhand cannabis smoke exposures at a music concert. Area and breathing zone Δ9-THC air sampling was conducted with a 37-mm polytetrafluoroethylene filter cassette (flow rate of 3 l min^{-1}). Results were analyzed with HPLC (ultraviolet light detector) with a minimum detectable limit 40 nanograms per cubic meter (ng/m^3) and minimum quantification limit of 140 ng/ m^3 (NIOSH, 2019a,b). The method is an internally developed NIOSH contract laboratory method developed in accordance with International Organization for Standardization 17025 requirements. Sixty-six percent (19 out of 29) of breathing zone samples (range: ND to 330 ng/m^3) and 100% ($n = 8$) of area samples (range: 53–480 ng/m^3) had detectable Δ9-THC concentrations. It is important to note that the concert venue was an open-air arena (NIOSH, 2019a,b).

Hypersensitivity reactions to cannabis

In addition to HHE requests, NIOSH has conducted research evaluating hypersensitivity reactions to cannabis. In North America, hypersensitivity has also been reported in patients that have handled or consumed cannabis (Tessmer *et al.*, 2012). In Colorado, where medical and recreational cannabis use are legalized, clinicians have observed a recent increase in

patients sensitized to cannabis classifying it as a mild allergen (Silvers and Bernard, 2017). However, the profile of IgE reactivity appears to vary compared to European study populations. In a collaboration with the University of Toronto, NIOSH investigators identified and characterized high molecular weight allergens from different sources of *C. sativa* including roots, leaves, buds, and flowers (Nayak *et al.*, 2013). The most common allergens identified in sensitized individuals included a 23-kDa oxygen-evolving enhancer protein 2 and a 50-kDa protein identified to be the photosynthetic enzyme ribulose1,5-bisphosphate carboxylase/oxygenase (Nayak *et al.*, 2013). Interestingly, sensitization to Can s 3 was not observed in the analysis indicating that subjects in North America may have varying exposures to broad cross-reactive antigens such as nsLTP derived from fruit or vegetable sources. To date, the prevalence of occupational sensitization to *C. sativa* in the emerging US cultivation and processing workforce continues to remain relatively unknown. As the US workforce continues to expand with this emerging industry, the incidence of hypersensitivity reactions is likely to increase, especially in the industrial cultivation workforce.

Lessons learned

Δ9-THC versus Δ9-THCA

Due to known psychoactive properties, Δ9-THC has been a focus of potential occupational exposures within the cannabis industry. However, because so little is known about occupational exposures to Δ9-THC and/ or Δ9-THCA and corresponding potential health effects, let alone other cannabinoids such as CBD, care should be taken in future epidemiological studies to differentiate the two exposures.

From an exposure assessment standpoint, one would expect higher levels of Δ9-THCA in live and recently harvested cannabis material. In contrast, higher levels of Δ9-THC would be expected in cannabis material that has been decarboxylated through either aging or heat treatments. As described previously, surface wipe samples have been collected during HHEs using two different analytical methods with the starkest difference being the LOD between the two. The LC–MS–MS method had a LOD of 4 ng per sample while the four cannabinoid HPLC–DAD method had a LOD of 2000 ng per sample. For the exposure assessor, a decision must be made between selecting a method with a low LOD for only Δ9THC or a method with an orders of magnitude higher LOD, but capable of measuring four different cannabinoids. The decision is ultimately driven by the purpose of sampling, such as identifying potential workplace contamination or differentiating between potential cannabinoid exposures. Future work to develop and validate a multiple phytocannabinoid LC–MS–MS method should yield LOD values for all measured cannabinoids similar to that of the Δ9-THC only method. In addition to surface and/or dermal sampling, future research should also consider airborne Δ9-THCA and Δ9-THC levels to better characterize total potential exposures in commercialized grow operations, particularly in companies that have workplace policies in place forbidding the use of cannabis while at work.

Cannabis occupational exposures compared to non-medical or medicinal use

In general, exposures to cannabis in the occupational environment differ from personal exposures from non-medical (recreational) and medicinal cannabis use. Employees working in cannabis cultivation and processing facilities are exposed to cannabis through inhalation of plant materials and dermal exposures by touching the plant directly or indirectly by touching surfaces contaminated with plant material or residue containing cannabinoids. The degree of biological uptake of cannabinoids through dermal absorption, either through direct contact or contact with contaminated surfaces, has not been clearly characterized in occupational settings. Because of dermal contact and surface contamination, ingestion is another possible route of exposure especially with hand-to-mouth activities such as eating, drinking, and smoking without proper handwashing prior to consumption.

Individuals that use cannabis for medicinal purposes most commonly do so through ingestion of Δ9-THC-containing materials (e.g. pills, oils, and edibles), or by inhaling cannabis smoke through combustion. Similarly, individuals exposed to cannabis during non-medical (recreational) use are exposed most commonly through combustion or ingestion of edibles but may also be exposed through a wide variety of consumer products such as electronic cigarettes (vaping), drinks, lotions, etc.

The nature of occupational and non-medical/medicinal exposures is distinct. Employees exposed to cannabis during cultivation and processing are typically exposed to raw cannabis and its organic material. It is only during the final stages of processing that heat is applied to cannabis. Conversely, non-medical and medicinal users combust the raw cannabis material, activating Δ9-THC and inhale it deeply into their lungs. Thus, health effects are directly related to inhalation of smoke and the psychoactive effects of Δ9-THC. Occupational exposures (Δ9-THC, CBD, etc.) may result in lower level inhalation hazards and more frequent skin contact with cannabinoids and plant proteins compared to non-medical and medicinal users. However, this may differ for employees in cannabis-related workplaces that allow open consumption.

For employees that participate in non-medical and/or medicinal use, exposures from personal use will not only add to the biological burden of occupational exposures but may exceed occupational exposures. Research into associations between occupational cannabis exposures and health effects will need to develop exposure metrics to account for these notable non-medical and medicinal exposures.

Ventilation challenges

Ventilation assessment was not a primary focus of the two completed HHEs and was not formally evaluated at either facility. However, indoor grow facilities face a balance of creating environments for optimal growth and yield while providing safe working conditions. Currently, ASHRAE (formerly known as The American Society of Heating, Refrigerating, and Air-Conditioning Engineers) does not have specific guidance for indoor cannabis grow facilities. Carbon dioxide (CO_2) enrichment, ozone generation, high intensity grow lights (high operating temperatures), odors, and microbial contamination prevention techniques (intake filtration, outside or makeup air restrictions, etc.) all contribute to the

need for often complex ventilation systems with multiple fail-safes for both worker and crop protection. During enrichment, CO_2 levels are typically below 2000 parts per million (ppm) which is below the NIOSH recommended exposure limit of 5000 ppm for CO_2 (NIOSH, 2019a,b). However, fumigation by CO_2 can reach concentrations above the NIOSH Immediately Dangerous to Life or Health limit of 40 000 ppm (NIOSH, 2019a,b).

Due to high costs associated with creating these microenvironments and prevention of outside contamination, indoor grow facilities may restrict the introduction of outside air, especially during CO_2 enrichment and fumigation as well as ozone generation. It is paramount to have an effective workplace entry restriction program to include physical barriers to entry, a hazard communication program and a monitoring system for oxygen and CO_2 concentrations to warn employees of potential hazards in these workplaces.

Medicinal/non-medical cannabis and industrial hemp

Medicinal and non-medical cannabis and industrial hemp are all classifications of cannabis plants from primarily three species: *C. sativa*, *Cannabis indica*, and *Cannabis ruderalis*. The most notable distinctions among the species being concentrations of Δ9-THC and other cannabinoids. While hemp was previously banned in the USA, the Agriculture Improvement Act of 2018 (commonly referred to as the U.S. Farm Bill) removed industrial hemp (contains less than 0.3% of Δ9-THC) from the U.S. Drug Enforcement Administration's Controlled Substances List and allowed for cultivation and sale of hemp as an agricultural commodity (Agriculture Improvement Act of 2018). Similarities between the hemp industry and the two cannabis-related industries (medicinal and non-medical) may allow a crosswalk of identified exposure characterization information to the industrial hemp industry in the USA. However, specific industrial hemp exposure characterizations should be performed applying and building upon previously elucidated cannabis occupational safety and health information.

Conclusion

An emerging cannabis industry (medicinal, non-medical, and industrial hemp) with an increasing worker population necessitates the need for occupational safety and health research to further identify potential hazards, characterize exposures, and to evaluate associations between exposures and adverse health effects. In addition to potential cannabis-related dermal exposures, ergonomic stressors, and psychosocial issues, employees in cultivation and processing facilities may be exposed to allergen and respiratory hazards through inhalation of organic dusts including fungus, bacteria, and endotoxin as well as VOCs such as diacetyl and 2,3-pentanedione. These hazards are most evident during the decarboxylation and grinding of dried cannabis material, where elevated job-specific concentrations of VOCs and endotoxin have been measured. While a number of these occupational safety and health hazards are similar to other agricultural workplace settings, there are cannabis industry-specific health hazards that should be further characterized. Lessons learned through these HHE investigations (Δ9-THC versus Δ9-THCA, occupational exposures compared to non-medical and/ or medicinal use, ventilation challenges, and

medicinal/ non-medical cannabis information crosswalk to the industrial hemp industry) aide in shaping future exposure assessment studies.

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Table 1.

Cannabis or cannabis-related HHEs.

Year	Location	HHE requestor	Concern	General activity
Ongoing	Cannabis grow/manufacturing	Management	Pesticides/nutrients, electrical hazards, trimming	Cultivating, grinding
Ongohg	Cannabis grow/manufacturing	Management	Ozone, noise, respiratory protection, cleaning products, ergonomics	Cultivating, grinding, decarboxylation, extracting, trimming, packaging, retail
2019	University Event Venue	University Department of Environmental Health and Safety	Secondhand cannabis smoke	Law enforcement officers providing security/crowd control
2018	Medicinal cannabis grow/ manufacturing	Union	Identify occupational safety and health hazards	Cultivating, grinding, decarboxylation, extracting, packaging
2017	Cannabis Farin	Union	Identify occupational safety and health hazards	Cultivating, trimming, packaging
2016	Clandestine ‘spice’ Laboratory	Law Enforcement Agency	Synthetic cannabinoids	Raid and processing of clandestine site
2013	County Coroner’s Office	Management	Residue drug particles (air/surface) from drug evidence laboratory	Autopsy and related activities Cross-contamination
2011	Law Enforcement Drug Vault	Police Department	Potential health effects from stored drugs	Drug storage
2009	Criminal Investigation Section	Police Department	Cancer excess	Drug storage
2004	Border Protection	Federal Government	Exposures using drugs as training aides	Chopping cannabis bales

Ann Work Expo Health. Author manuscript; available in PMC 2020 August 10.

Table 2.

Surface wipe concentration results (ng/100 cm^2).

	Samples (*n*)	Farm	Indoor facility
Δ9-THC[a]	Farm (27) Indoor (18)	170−210 000	ND to 53 000
Δ9-THC[b]	18	N/A	ND to 17 000
Δ9-THCA[b]	18	N/A	ND to 140 000
CBD[b]	18	N/A	ND to 3700
CBN[b]	18	N/A	ND to 6400

N/A, not sampled.

[a]LC–MS–MS: LOD = 4 ng per sample.

[b]HPLC–DAD: LOD = 2000 ng per sample.

Table 3.

Summary airborne exposure results from cannabis cultivation operation HHEs.

		Samples (*n*)	Sample time (min)	Farm	Indoor facility
Endotoxin (EU/m^3)	Breathing zone	Farm (12)	Farm (409–486)	2.8 to 37	ND to 85
		Indoor (7)	Indoor(250–489)		
	Area	Farm(11)	Farm (409–525)	ND to 15	1.6 to 94
		Indoor(12)	Indoor (60–477)		
Microbial diversity (% relative abundance)				Fungal	Fungal
		Farm(26)	Farm (335–489)	*Botrytis cinerea* (34%) Bacterial	Agaricomycetes (30%) Bacterial
		Indoor (37)	Indoor (287–335)	Actinobacteria (45 %)	N/A
VOCs (Parts per billion)	Diacetyl				
	Breathing zone				
	Full shift[a]	13	183–527	N/A	ND to [0.51]
	Full shift[b]	14	156–542	N/A	ND
	Task[b]	8	4–15	N/A	ND to 23
	Area				
	Full shift[a]	8	298–561	N/A	ND to [0.26]
	Full shift[b]	10	360–480	N/A	[1.6] to 12
	Task[b]	9	0.5–15	N/A	[0.7] to 6.7
	2,3-Pentanedione				
	Breathing zone				
	Full shift[c]	13	183–527	N/A	ND
	Full shift[b]	14	156–542	N/A	ND to [4.2]
	Task[b]	8	4–15	N/A	ND to 25
	Area				
	Full shift[c]	8	298–561	N/A	ND
	Full shift[b]	10	360–480	N/A	ND to 9.3

Ann Work Expo Health. Author manuscript; available in PMC 2020 August 10.

	Samples (*n*)	Sample time (min)	Farm	Indoor facility
Task[b]	9	0.5–15	N/A	ND to [5.1]

N/A, not sampled; [], results in brackets were below their respective limit of quantification.

NIOSH REL and STEL: diacetyl = 5.0 ppb (8-h TWA) and 25 ppb (15 min); 2,3-pentanedione = <9.3 ppb (8-h TWA) and 31 ppb (15 min).

[a]OSHA Method 1013 (diacetyl/acetoin).

[b]NIOSH Method 3600.

[c]OSHA Method 1016 (2,3-pentanedione).