Implementation of OR Measure 91

Cannabis Safety Institute
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I. Background

Introduction

This position paper is a summary of the issues that the Cannabis Safety Institute considers critical in the implementation of Oregon's Measure 91. Cannabis can contain toxic contaminants that are highly dangerous via inhalation, including pesticides, and spores capable of causing invasive fungal disease. Because it is dried during production and heated during use, Cannabis is actually safer than most other agricultural crops. Nonetheless, the absence of federal standards and the size of the industry make it crucial to develop clear programs to address the dangers that do exist.

The Cannabis Safety Institute (CSI) was formed to address these issues, and to provide the expert guidance that would normally be available from federal agencies and university extension services. It is composed of scientists and regulators with extensive expertise in microbiology, food safety, toxicology, analytical chemistry, and laboratory standards. It includes PhD scientists with experience analyzing Cannabis, regulators with experience crafting and implementing Cannabis safety guidelines, a past Program Director at the NIH and the FDA, and the head of the International Laboratory Accreditation Cooperation. The CSI is a non-profit, impartial, scientific body, formed with the goal of ensuring that Cannabis legalization proceeds in a manner that is safe, and informed by rigorous and current scientific knowledge.

The CSI is producing white papers on each of the safety issues discussed here. These are co-authored by a larger group of scientists that includes food-safety microbiologists and clinicians at McGill University, Duke University, and Harvard Medical School. Completed white papers can be downloaded from the CSI website: www.cannabissafetyinstitute.org. Each of them is co-authored by a group of experts on the particular subject, and summarizes all of the available and relevant scientific information. In the cases where there are questions that cannot be answered without further experimental research, these are clearly indicated. Very few of the pressing safety issues fall into this category.

Contaminants

Microbial contamination on agricultural products is primarily a concern with high water activity foods that are consumed raw, such as lettuce. In contrast, properly cured Cannabis flowers are dried to water activity levels low enough to make it impossible for microbes to replicate. It is then heated during smoking or prior to oral ingestion. Even Cannabis in edible products must be pre-heated to convert the cannabinoids THC and CBD to their active forms. This heating process serves as a microbial kill step.

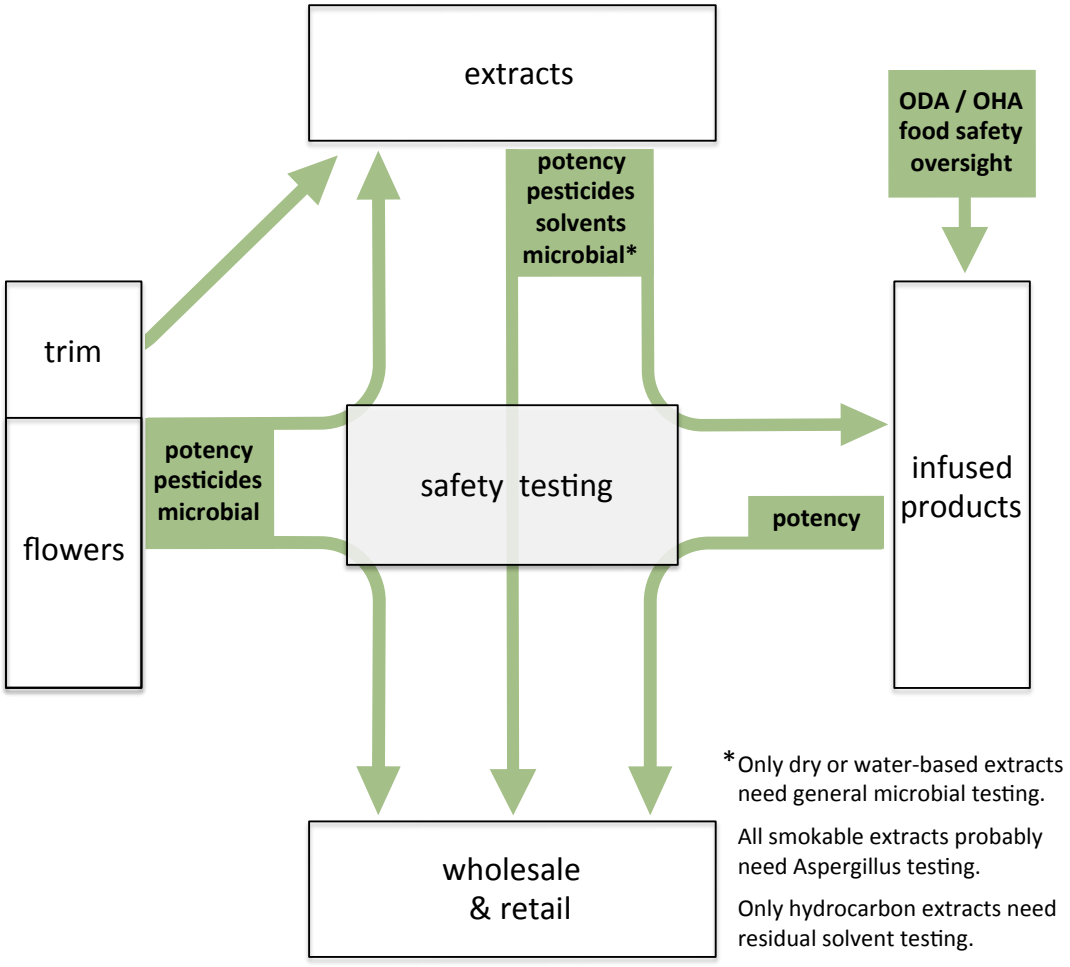
Because of these natural safeguards, most microbes cannot survive on Cannabis in a way that would let them cause disease. However, the organisms that can survive are quite dangerous. The most significant of these are a small number of mold species in the genus *Aspergillus*. This is a genus of fungi containing hundreds of different species, most of which are harmless. Four of these species, however, form spores that can cause invasive lung disease with an extremely high mortality rate in immunocompromised individuals. Aspergillus spores are not destroyed by the heat of smoking, and they can be mobilized in smoke and transferred to the lungs. Salmonella is also a threat (though an unlikely one) because it is highly infectious and can survive under extremely dry conditions.

Heavy metals are another potential contaminant of Cannabis. These can be concentrated in many plants, including Cannabis, and are found in soil contaminated by historical pesticide use or in fertilizer with high levels of poorly-sourced phosphates. If data shows that these are a concern in Oregon, then testing Cannabis for them might be necessary. We are gathering data on this subject presently, and it is one of the few unresolved issues. At present, we believe batch-testing for heavy metals should be avoided if possible. If heavy metals are a problem in outdoor-grown Cannabis, it will be a problem for an entire region, in which case it makes sense to test environmentally. If they are a problem for indoor-grown Cannabis, it may be more effective to test and ban fertilizers or nutrients with high levels of dangerous metals.

Pesticides, on the other hand, are an extremely common and very dangerous contaminant of Cannabis products. Levels will vary widely from batch to batch, and contaminated batches should not be sold. The recent sharp increase in Cannabis plants sold as cuttings, or clones, has spread many new pests throughout the Pacific Northwest, and pesticide use among growers has increased sharply in recent

years. In addition, pesticides are concentrated to extremely high levels in Cannabis concentrate products. These products are either smoked or used to infuse edible products; pesticides can be highly toxic by either route of ingestion

The diagram below is a schematic view of how Cannabis products will likely move through the market and the regulatory system, with the necessary tests at each stage indicated.



Current Testing Programs

Due to the prevalence of *Aspergillus* and pesticides, safety testing for Cannabis is critical. Many states with legal Cannabis programs of one kind or another recognize this, and have required testing. However, most of these programs lack any clear standards. In some states safety testing of medical marijuana is required by state law, but the laboratories themselves are not explicitly legal. In many states there are safety-testing laboratories, but they have no oversight and are not certified or accredited to any standard. In other states, such as Washington and Colorado, state-run certification programs for Cannabis laboratories have been created. But in the absence of the scientific and structural guidance usually provided by federal agencies such as the U.S. Food and Drug Administration (FDA) and U.S. Department of Agriculture (USDA),, these states have lacked the resources and expertise to run these programs effectively. They have failed to require laboratories to meet basic national and international laboratory standards. They have also required many tests that have no scientific basis, and failed to require testing for known toxins.

None of the states that require safety testing of Cannabis have required that concentrates be tested for pesticides. Some of these states have required testing for pesticides in flower material, without specifying the list of compounds to be tested for. None of these states have required testing for the four species of *Aspergillus* that cause invasive lung disease.

The state regulators charged with implementing new Cannabis laws have faced extraordinary logistical challenges, and only one of these is the challenge of structuring an entirely new laboratory testing system with the correct requirements and standards. On other scientific and public health issues, state regulators have the benefit of U.S. Environmental Protection Agency (EPA), USDA, and FDA oversight and assistance, and they have access to a nationwide network of research universities with experts in every conceivable field. In this case, those federal agencies are prohibited from involvement. Universities have also been prohibited from performing research on Cannabis, so basic scientific knowledge on the subject is largely unavailable. In the cases where university scientists do have relevant knowledge, they have been unable to advise regulators and policy-makers on the issue. Many universities have instructed their researchers to have no contact with the Cannabis industry, for fear of jeopardizing their federal funding.

Safety testing regulations for this massive and new agricultural crop are therefore being put in place without scientific guidance. States should not be expected to solve the long list of problems inherent in identifying the correct standards and tests for this industry, without the assistance of universities and federal agencies. This is not a small problem, and it has led to chaos in the Cannabis testing industry and in the Cannabis industry as a whole. It is risky to allow potentially dangerous products to carry guarantees that they have passed safety testing. Because of this, the Cannabis testing industry is doing more harm than good at the moment.

Research

When Colorado and Washington built the recreational Cannabis programs in their states, they were effectively working in the dark, because of how little is known about the plant. More information is available now, but this is primarily because of focused literature research, consultation with experts, and preliminary data from Cannabis testing labs. High quality peer-reviewed research is still lacking, and therefore many questions about the effects of Cannabis on public health and safety issues do not have detailed answers.

The medicinal benefits of Cannabis have been recognized with enough clarity in the last few years to drive a wave of legalization across the United States. Nonetheless, 75 years of prohibition have ensured that this plant is among the least studied of all the species with which humans interact. Colorado has recognized this recently, and approved $8 million in funding for Cannabis research. Oregon is home to many world-class research institutions and it would be an enormous mistake to miss the opportunity to take the lead in this important new research field.

It will also be impossible for the state to guide its new legal Cannabis programs intelligently if it does not have the ability to fund research and generate the new data needed to resolve policy issues. The Oregon legislature should consider the creation of a research fund administered by the state, or by a state-funded research institution, with a mandate to accept applications for research grants to study the medicinal, social, genetic, and behavioral-economic aspects of Cannabis use. A simple step in this direction would be to add a research license to the list of license types specified in Measure 91.

Laboratory Standards

Ensuring that Cannabis testing labs are held to high professional and scientific standards is essential, but also outside the purview of most state regulatory bodies. However there is an absolutely clear path toward establishing and maintaining standards for safety-testing laboratories. The majority of testing laboratories in both private industry and government are required to be accredited to one of two widely accepted standards. The most common is the internationally accepted ISO 17025 standard for testing laboratories, for which accreditation is performed by private third-party accreditation bodies. The other is the nationally accepted 2009 TNI standard, which is largely based on ISO 17025, and for which accreditation is performed by state-run National Environmental Laboratory Accreditation Program (NELAP) accreditation bodies (such as the Oregon Environmental Laboratory Accreditation Program (ORELAP) in Oregon).

So far, states have been reluctant to apply these standards to Cannabis testing laboratories, primarily because of a notion that they were too high for them to meet. We believe it is ill-advised and potentially dangerous to allow safety testing by labs unable to meet these standards. Fortunately, it is not the case that these standards are too high. Many of the existing Cannabis testing laboratories are professionally run and managed, and will be able to meet whatever standard is required of them.

Oregon, after learning from Colorado and Washington, is in a position to set standards for this industry that will guide the rest of the country. Rigorous safety testing by qualified laboratories is a crucial piece of this, but it cannot happen without clear scientific guidance on potential contaminants, testing methods, and laboratory accreditation.

Regulatory structure

In order to ensure that Cannabis in Oregon is safety-tested, lawmakers have to build a system that encourages Oregon-grown Cannabis to actually be brought into the system where testing happens. If the black market continues to thrive, then untested and potentially unsafe Cannabis will continue to be produced, sold, and exported.

The 2013 Justice Department letter known as the Cole Memo made it clear that the states would be allowed to implement legal Cannabis programs only if they meet certain clear goals. Chief among these were the removal of the black market, the protection of public health, and the avoidance of diversion of Cannabis outside of the state. These goals can only be met by considering the overall Cannabis economy in the state as a whole. We do not believe that the authors of the Cole Memo intended that they be met by a small, tightly regulated system that controls diversion from the system itself, but ignores or increases overall black market activity.

It has been suggested that legal Cannabis systems would allow economies of scale that would ultimately undercut the black market with lower retail prices. This is unlikely to be successful; taxes and regulatory costs will keep prices high, and export markets with high wholesale prices are easily accessible. The black and grey market production in Oregon is not likely to go away. The only way to ensure that it is controlled and tested is to find ways to incorporate it into the new legal regulatory structure.

We therefore urge Oregon lawmakers to find creative ways to incentivize existing Cannabis growers to join this new system. Barriers to entry should be kept low, and even small growers should be allowed to easily submit product for testing and tracking and sale within the legal system. Replacing the black market with a legal one will not happen by attracting consumers to the new legal system; it will happen by attracting *producers* to it. If Oregon's growers have a straightforward path toward joining the new system, Oregon's economy will be supported, the black market will dwindle, exports will be minimized, and public health will be protected.

Recommendations

Laboratory Standards

1. All laboratories must pass regular Inter-Laboratory Proficiency (ILP) testing covering each of the safety-related tests they perform. These ILP testing programs must themselves be administered by an organization accredited to the ISO 17043 ILP standard.

2. All laboratories must be run by a scientist with a PhD in a relevant field, or with at least 8 years of professional experience performing analytical chromatography.

3. All Cannabis testing laboratories must be accredited to the ISO 17025 standard or the 2009 TNI standard. Laboratory operation should be provisionally allowed only if laboratories have officially begun the accreditation process, and they must be required to complete it within one year.

   Either of these accreditation processes can be customized for the needs of the state, but we strongly recommend that third-party ISO 17025 accreditation be the primary standard. The basic accreditation process should be universal, and should not be a state function. There is no conflict between ORELAP and ISO 17025, and they can be utilized in parallel. But the state resources in ORELAP would be better used as an adjunct to ISO lab accreditation, or to monitor other parts of the industry that do not have independent oversight.

Microbiology Testing

4. All Cannabis flower material must be tested for these four *Aspergillus* species, each of which can cause Cannabis-mediated invasive lung disease:

   - *Aspergillus flavus*
   - *Aspergillus fumigatus*
   - *Aspergillus niger*
   - *Aspergillus terreus*

5. Cannabis flowers should also be tested for general *E. Coli,* as a quality indicator. Pathogenic forms of *E. Coli* are rare on crops, and cannot survive drying or heating. For this reason, they have been a problem only on high-moisture crops that are consumed raw. However, *E. Coli* in general is the most reliable indicator of fecal contamination and should be tested for because it can point to contamination of plants by poorly sourced soil or water, or by improper handling. Batches with greater than 100 colony-forming units per gram (CFU/gram) of *E. Coli* should not be sold.

6. Cannabis flowers should be tested for *Salmonella*. *Salmonella* is resistant to drying and highly infectious in small doses. Batches with any detectable *Salmonella* should not be sold.

7. Water activity can be used as a marker for overall microbial levels: Cannabis with water activity (A_w) levels above 0.65 A_w should be returned to producers.

8. Edible Cannabis products should be regulated by local health departments. These carry the same microbiological risks as any food product, and Cannabis extracts do not increase this risk.

9. There is no need to test Cannabis for *Pseudomonas aeruginosa*, Listeria, toxigenic *E. Coli* (e.g., H7:0157), or other bacterial pathogens besides *Salmonella*. These organisms cannot survive either the drying or heating processes which Cannabis undergoes.

10. There is no need to test Cannabis for "total yeast and mold". These tests do not correlate with either pathogens or organisms that cause allergic hypersensitivity reactions, and they do not offer useful additional information as a quality test.

11. There is no need to test Cannabis for aflatoxins. Neither living nor properly cured Cannabis can support growth or aflatoxin-production by the organisms that produce these toxins.

Pesticide Testing

12. All Cannabis flowers should be tested for relevant pesticides. Samples above 100 parts-per-billion (100 ppb) should be failed. Pesticide use is extremely common on Cannabis, and is increasing. Inhalation toxicity data is unavailable for many

compounds, and so setting tolerable limits is not feasible at this time. It is likely that inhaling high levels of most pesticides is extremely dangerous.

13. All Cannabis concentrates must also be tested for pesticides, whether or not the source material was tested beforehand. Most extraction and concentration techniques also concentrate pesticides, in some cases to extraordinarily high levels.

14. It is essential that laboratories be given a clear list of pesticides to test for. Pesticide testing is more expensive than other tests performed by Cannabis testing laboratories, and the price will be difficult for the market to bear. Accurate pesticide testing will add $200-$300 to per-batch testing costs even with an extremely narrowed list of compounds. Therefore it is essential that a list be developed that includes potentially toxic compounds that may be in use, but that does *not* include unavailable compounds.

    Such a list would imply that pesticides not on the list are acceptable for use on Cannabis. In fact, federal law prohibits the use of all pesticides on crops for which they have not been specifically approved. It is possible that there are biopesticides, pesticides used in organic production, or minimum-risk pesticides that qualify for FIFRA 25(b) exemption, that could be used with minimum harm on Cannabis. However, such use would be strictly illegal in most cases, and there is no evidence that these compounds are safe for inhalation exposure. The state of Oregon should do everything in its power to minimize pesticide use, to encourage organic Cannabis production, and to provide education on the use of Integrated Pest Management and biocontrol methodologies.

Other tests

15. Concentrates must also be tested for residual solvents, such as butane, hexane, and pentane.

16. Heavy metals, including Lead, Mercury, Arsenic, Cadmium, and Chromium can be found in soil and concentrated in plants. They should only be tested for on Cannabis if environmental or fertilizer testing is found to be impractical.

Batch Sampling and Sample-Tracking:

17. Batch sizes are a critical tool for managing the impact that safety testing will have on wholesale prices. Batch sizes should be large enough to keep the overall cost of testing under 5% of wholesale costs. The minimum batch size that could accomplish this is probably 6 lbs. Methods to combine separate batches for certain tests should be permitted when batch sizes are small – for instance, multiple small batches of different strains could be combined for a single pesticide test.

18. All Cannabis testing must be performed using statistical sampling methods, in which a laboratory employee chooses many different samples from an individual batch and homogenizes them. We recommend taking five individual one-gram samples from each pound, and then combining and homogenizing all samples from the entire batch. The appropriate volume should then be taken from this mixture for each analysis.

19. Procedures must be in place to ensure that laboratory testing results are associated only with the batch they pertain to. Every batch should be sealed in tamper-proof bags by laboratory personnel, tagged with a unique identifier, and entered into a statewide tracking system. This system needs to work with a huge variety of packaging methods, but it can be customized by bagging multiple packages, or by the use of non-removable stickers carrying testing results and tracking numbers.

Regulatory structure:

20. The many thousands of existing growers in Oregon must be incentivized to participate in the new legal structure. Barriers to entry should be kept low, and small growers should be allowed and encouraged to sell their product into the regulated system where it will be tested, tracked, and removed from the black market.

21. Research should be encouraged by the addition of a research license to the licensing structure. This should be in conjunction with the creation of a state fund to support research on Cannabis and public health, and by approaches to enable universities to perform Cannabis-related research and extension work without jeopardizing their federal funding.