

Implementation of OR Measure 91

Cannabis Safety Institute
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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. These and other potential public health issues make it critical to implement careful safety testing regulations for Cannabis.

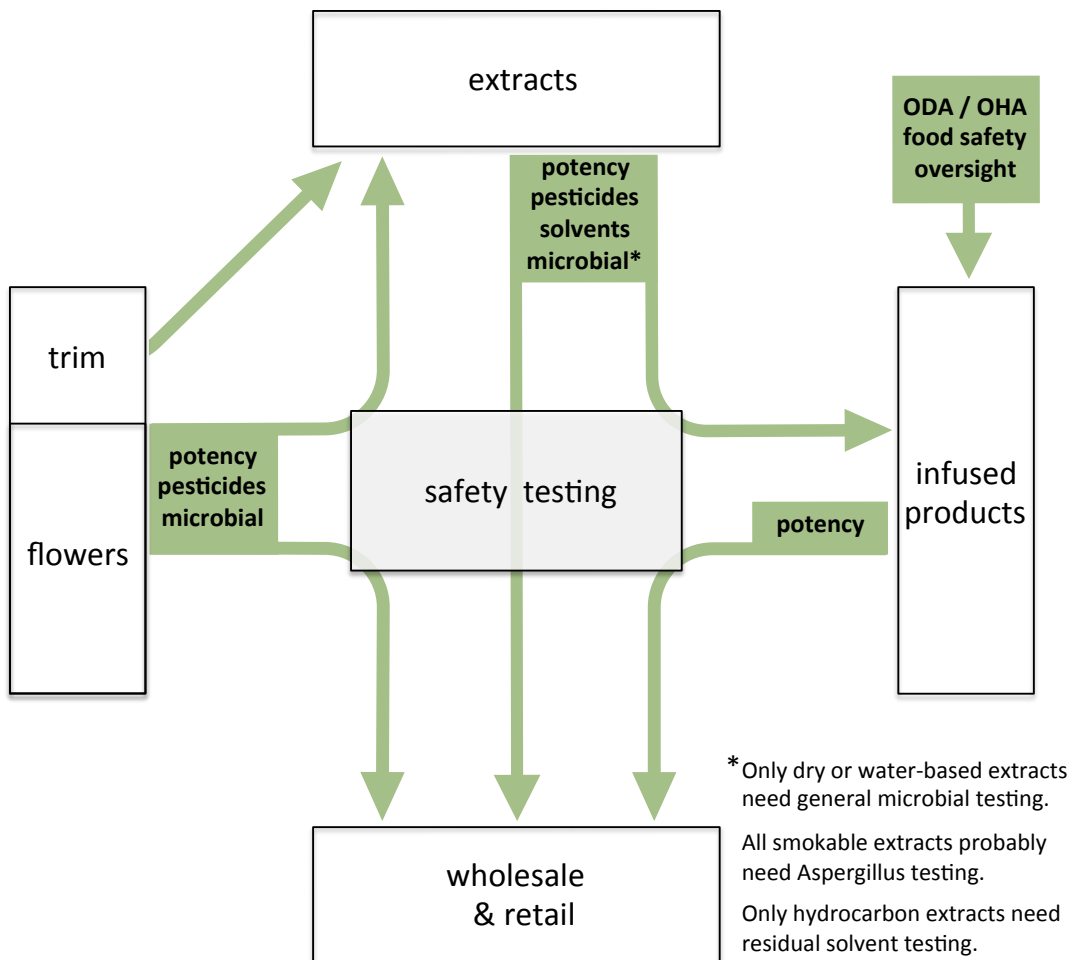
The absence of both federal regulatory structure and adequate academic research has made it quite difficult to implement these policies. State regulators in Washington, Colorado, and other states, have not had access to the relevant scientific data to assess what testing should be performed. They have also not had any framework for regulating the commercial Cannabis testing labs that now 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.

Safety testing

The Cannabis industry is already somewhat mature in Oregon. It consists of a supply chain based on plant material, but leading to many products in addition to cured flowers. Each of these products has their own particular set of safety issues, and need to be considered independently. The diagram below is a schematic of the region of the supply chain that produces retail products, and the general safety testing requirements for each of them.



Microbiology

Microbiologically, Cannabis is quite safe compared to other agricultural products. Nonetheless, there are a number of microbial tests that should be performed on Cannabis. The most important of these would be a screen for several species of *Aspergillus* mold. These form heat-resistant spores capable of causing invasive lung disease that has a known clinical association with Cannabis smoking. The mortality rate from these infections is extremely high in immunocompromised individuals.

The CSI has shared this data with regulators in Colorado, and they have recently adjusted their Cannabis regulations to require testing for *Aspergillus*, *Salmonella*, and *E. coli*.

Recommendations:

- Research is needed to determine what the actual fungal and bacterial load is on Cannabis – although we can identify certain tests that must be performed, it is impossible to set threshold levels without additional data.
- Microbiology testing, in general, should be required by statute, with the specification that a list of specific tests be developed in the rule-making process. The available data indicate that Cannabis testing should include *Salmonella*, general *E. Coli*, and four *Aspergillus* species, but it is critical that these rules be responsive to new research findings.

Pesticides

Pesticides 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

Identifying a list of pesticides to be tested for on Cannabis is extremely challenging. The data used to establish safe exposure levels on other

crops does not apply to inhalation exposure. All other agricultural industries have access to pesticides specifically approved for them by the EPA, but this will likely not be the case for Cannabis in the next few years. The CSI has completed a comprehensive study of pesticide levels on Cannabis and Cannabis products in Oregon, and is developing a list of pesticides that should be tested for. Pesticide testing is expensive, and unnecessary tests should not be performed. On the other hand, many toxic compounds are available commercially and it is important to screen for those that may be used.

Washington State has recently released a list of approved pesticides for use on Cannabis. We do not recommend this approach. Pesticide use as a whole should be strongly discouraged, and education on Integrated Pest Management and biocontrol approaches should be made available to growers. Regulatorily, what is needed is a list of *banned* pesticides, so that safety testing laboratories can operate effectively.

Recommendations:

- Pesticide testing should be required by statute. The OLCC should be directed to develop a list of banned pesticides that Cannabis must be tested for, and this list should include other related classes of chemicals as well, such as fungicides and plant-growth regulators.

Heavy metals

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. We have collected some data on this subject, and will have reasonable recommendations on the subject by May, but they will not be founded on a large pool of data.

Recommendations:

- Research is needed to determine whether heavy metal contamination is an issue on Cannabis grown in Oregon, either outdoors or indoors.
- Heavy metals testing should not be required by statute, but the OLCC should be empowered to require it if necessary.

Extraction solvents

Many Cannabis extract products are made using hydrocarbon solvents such as pentane, butane, and hexane. These can be toxic if not properly purged from the final product.

Extracts made with CO₂, water, or alcohol, do not need to be tested in this way. However, water-based extracts in particular may need to be tested for microbiological contamination. Hydrocarbon and CO₂ extraction methods are most likely sterilizing.

Recommendations:

- Hydrocarbon-based extracts should be tested for residual solvents.
- The OLCC should be empowered to require additional tests for specific types of extracts and concentrates, as necessary.

Laboratory standards

In the last two years, a Cannabis testing industry has arisen in many states with medical or recreational Cannabis programs. Initially these performed market-driven potency testing, and more recently they have begun to provide state-mandated safety testing as well. The majority of these labs are unregulated, operate with non-standard methodologies, and are subject to no oversight or proficiency testing whatsoever.

It is critical to public health and safety that Cannabis testing labs be held to the same scientific and professional standards that all other analytical laboratories are held to. There is a nationwide industry of analytical chemistry labs, both public and private, that perform food, water, agricultural and environmental testing. The accuracy and reliability of these labs is ensured by accreditation to national or internationally accepted standards such as ISO 17025 or the 2009 TNI standard.

Accreditation to these standards can be performed by third-party private accreditation bodies, or by state programs with the correct expertise. Oregon is fortunate to be home to the Oregon Environmental Laboratory Accreditation Program (ORELAP), a state body that accredits laboratories to the more rigorous TNI standard.

ORELAP is highly qualified to ensure that Cannabis testing labs are run appropriately, although to perform this work they will need funding for additional staff and instrumentation.

Recommendations:

- All Cannabis testing labs must be required to obtain TNI accreditation through ORELAP or another TNI accreditation body, as well as commercial licensure by the OLCC.
- Action should be taken immediately to ensure that laboratories currently testing for the OMMP program are using adequate methods, are run by qualified scientists, and are at least provisionally eligible for the accreditation process.

Sampling and tracking

A critical component of Cannabis safety testing is methodology for batch sampling and for associating test results with the batches they pertain to.

Both potency and contaminant levels can vary widely between different areas of a single Cannabis plant. Test results are not significant unless they take this into account and utilize statistical sampling methods. These require that laboratory staff take multiple representative samples spread across a batch, homogenize them, and use the resulting mixture to perform analyses. Batch sizes and sampling protocols need to be set based on values that represent a reasonable balance between the sensitivity levels of test methodologies and the need to keep testing costs to reasonable levels. If batch sizes are too high, even highly sensitive chemical detection devices will not have adequate discrimination to identify certain contaminants. If batch sizes are too low, the costs of testing will be unnecessarily burdensome, which will have negative impacts on the critical goal of minimizing the black market Cannabis economy. All Cannabis that is not brought into the regulated system will be untested and unsafe as well as illegal.

It is also important that test results be unequivocally linked with the batches to which they pertain. There are many possible ways to address this, and they will depend on the nature of the overall tracking system in place. It is possible that large highly-regulated production facilities will be capable of tracking this data internally as long as it is

also entered into a statewide system. It is also possible, especially with smaller operations, that it will be necessary for batches to be sealed into containers with unique ID numbers and test results printed on them. Whatever system or system is decided upon, it needs to ensure that retail products are labeled correctly and that batches that fail contaminant testing are destroyed or appropriately redirected for processing.

Recommendations:

- Statistical sampling protocols should be required in statute. The specifics of these protocols should be developed in the rule-making process, and laboratories should be required to obtain accreditation for their sampling procedures.
- Tracking of test results should be identified as a priority in statute, but specified in detail in rules.

Oversight

The above sections outline the various issues related to Cannabis laboratory testing. These are scientific issues and should be managed by a scientific body. The Oregon Health Authority (OHA) – through ORELAP – will be responsible for laboratory accreditation. They should be responsible for all of these other issues related to laboratory testing as well. The rationale for leaving some level of detail out of statute (for instance, lists of specific chemical compounds to test for) is that these are constantly being informed by new research and they need to be responsive to such new findings.

A scientific organization such as the OHA has the expertise necessary to rapidly and efficiently respond to new scientific information. This is particularly critical in the Cannabis industry, where public health research on issues such as pesticides and plant-born infections is almost non-existent. Because of its resources and expertise, OHA is also uniquely positioned to engage in the critical public health research programs necessary to guide Cannabis testing programs and the Cannabis industry itself. As will be discussed in the final section of this document, it is extraordinarily difficult to perform this kind of research in either academic or commercial settings. Allowing – and funding – the OHA to engage in Cannabis research would solve several problems simultaneously and put Oregon at the forefront of the now nationwide struggle to regulate Cannabis appropriately.

Recommendations:

- The OHA should be given oversight of every aspect of Cannabis safety testing.
- The OHA should be instructed to create its own Rules Advisory Committee, parallel to the OLCC Rules Advisory Committee, specifically responsible for determining scientific and public health policy relating to Cannabis.
- The OHA should be instructed to create a Cannabis Research Program capable of structuring and funding both in-house and outside research programs with goals related to public health and Cannabis. This program should operate in addition to any other public or commercial research programs that are created, and work in collaboration with them whenever possible.
- The OHA should be funded as necessary to carry out all of these programs.

Regulatory Framework

Ensuring that Oregon develops a safe Cannabis industry cannot be done simply by specifying relevant contaminants and requiring adequate laboratory standards. The regulatory structure of the industry has to be taken into account for several reasons. A failure to appropriately license the different segments of the industry would encourage the growth and existence of these businesses in the black market. Any Cannabis that remains on the black market is unlikely to be tested, and will carry higher pesticide and microbial loads and so will pose a threat to public health that the regulated system should be working to avoid. Likewise, a failure to understand the economic forces at work, and to properly incentivize producers, will lead to the continued existence and growth of the black market.

In addition, there is little chance that Oregon's Cannabis industry will be safe and sustainable if there is not aggressive support for the completion of the basic scientific research that has not been done until now. Much of this research deals with basic safety and contaminant issues that cannot be addressed without further data.

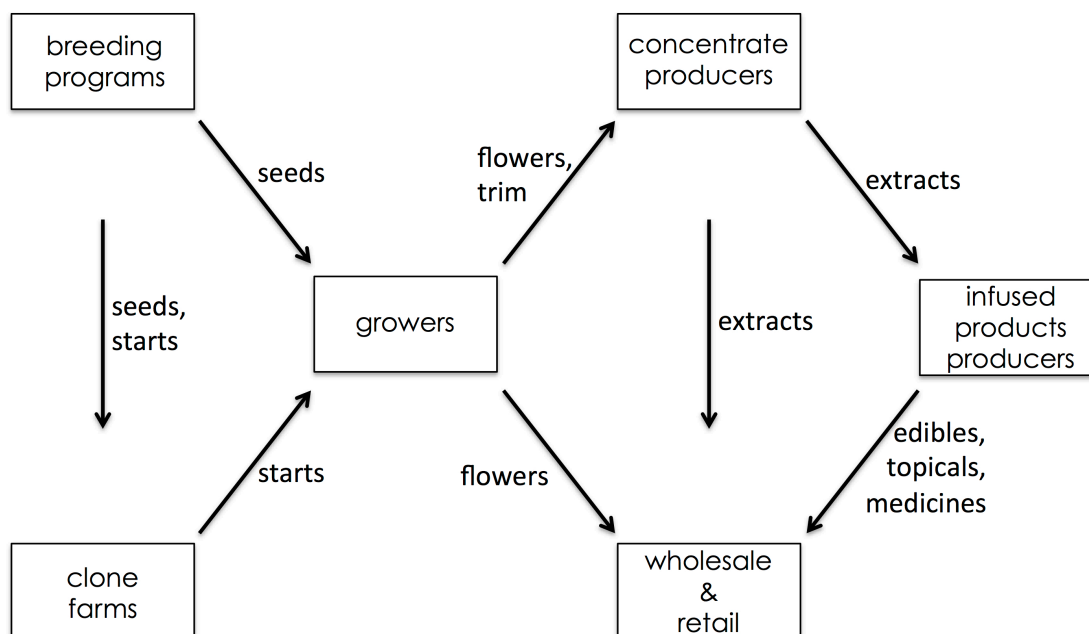
Supply chain structure

The black market cannot be addressed without a realistic understanding of the existing structure of the entire Cannabis industry. CO and WA have structured their Cannabis programs as if the production pipeline for plants did not require starting material. Where modifications to this point of view were allowed, they were one-time exceptions that failed to grasp the overall structure of this essentially mature agricultural industry.

Cannabis plants are grown either from seed or from cuttings (clones). Flower producers typically do not produce their own seeds or clones, although they are capable of doing so in small amounts. At present, clones can be purchased at many dispensaries, and businesses that specialize in producing clones are becoming increasingly common. Clones (rather than seeds) dominate Cannabis production in urban areas, but they also carry plant diseases and have contributed to the recent sharp increase in pesticide use. The consensus within the industry is that clone farms utilizing sterile tissue culture technique will be the dominant supplier of starts in the next few years. This is a technology that most producers will not be able to bring in-house.

In certain areas, growers prefer to start plants from seed. In the last decade breeders have produced hundreds of distinct Cannabis varieties and distributed them through seed companies. Oregon in particular is home to several world-class medicinal Cannabis breeding programs. The medicinal varieties driving the recent intense interest in Cannabis are the result of long-term breeding programs that have only recently born fruit. The Cannabis plant is extraordinarily diverse, and therefore has great genetic potential for varietal development. Many more new cultivars with a range of medicinal properties will be developed in the next few years as Cannabis breeding becomes modernized. These will largely be distributed through seed companies.

If Oregon hopes to be a model of effective Cannabis regulation for the rest of the country, it needs to provide a licensing structure that is appropriate for the actual needs of the industry. These different business types are highly stratified and will likely become more so under typical market pressures. If no available license type protects seed or clone producers under state law, then genetic innovation will suffer, and this portion of the economy will remain rooted in the black market. License structures that are based on plant counts or square feet of flowering canopy are not appropriate for clone farms growing many thousands of starts in agar dishes. Nor are they appropriate for breeding programs that require many thousands of plants to be grown, crossed, selected, and analyzed. The diagram below outlines the actual structure of the Cannabis industry supply chain.



Recommendations:

- A *Nursery License* specific to providers of clones and seeds should be provided for in statute. It is not necessary to create two separate licenses for these two different types of business, because they are fundamentally similar in practice. Neither of them should be allowed to sell Cannabis flowers, but they both require high plant counts in order to be able to supply raw starting material to flower producers.
- Any mature flower material produced in the course of the operation of these businesses should be destroyed, donated for research purposes, or donated to low-income medical patients.
- Measure 91 specifies a tax of \$5 per clone. Seeds, however, should not be taxed, as there is no consistent and reasonable way to do so. Seeds are genetically variable, and often non-viable, so the number of mature plants a given lot will produce is impossible to determine.
- Flower production facilities often engage in some cloning or breeding. This should not be prohibited, but if it is for commercial purposes it should require co-licensing.

Economic 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 local retail prices elevated, and export markets with high wholesale prices are easily accessible. The Cannabis production in Oregon that is currently supplying the black and grey markets is not going to cease. 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:

- Oregon already produces much more Cannabis than Oregonians can consume. Everything possible should be done to incorporate existing production into the legal system. Everything possible should also be done to minimize additions to the existing production capacity in Oregon.
- Priority for production licenses should be given to existing growers that are Oregon residents.
- Barriers to entry into the legal recreational Cannabis system, should be minimized for existing growers that are Oregon residents.
- Barriers to entry into the legal recreational Cannabis system should be minimized for home growers with excess material. There should be a straightforward path toward testing and retail for this product so that it does not reach the black market.
- Grow sizes should be capped. This cap should be based on total production rather than plant count. Plants vary by as much as

tenfold in productive capability. Flowering canopy square-footage is a preferable method for defining grow size, but this too can be misleading because of the various styles and heights of growing arrangements and plant type.

- Any overall tracking system should be a “flower-to-sale” system rather than a “seed-to-sale” system, for these reasons:
 1. The need for a rational method for defining the production capacity of a facility (given the lack of correspondence between seed, clone, or plant numbers and the amount of final product).
 2. The need to minimize barriers to entry for small existing growers.
 3. The technical difficulty and lack of meaningful information involved in tracking immature plants.
 4. The importance of focused and effective tracking of final products along with their testing results, and the fact that testing serves as the first rational quantitation point in the supply chain.
 5. The fact that the black market will not be fed by diversion from the regulated system, but rather by product that is never brought into the system in the first place. Seed-to-sale tracking systems in other states have inadvertently functioned as barriers that kept product *out* rather than *in*.

Cannabis research

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, after 75 years of prohibition 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.

The Cannabis plant produces a series of small molecules (phyto-cannabinoids) that interact with the endocannabinoid receptors in the human metabolic, immune, and nervous systems. These receptors are

poorly understood, as are most of the phytocannabinoids (of which there are at least 108). A basic scientific understanding of the medicinal properties of Cannabis will require concerted research programs in both plant biology and clinical pharmacology.

Because Cannabis remains federally illegal, it is extraordinarily difficult to conduct this research. If this were not the case, land-grant universities would provide extension work to aid agricultural producers. State and federal agriculture departments would study relevant pesticides and issue guidelines. Clinical researchers at medical schools would perform pharmacological studies on human subjects. Plant biologists at research universities would study the genetics, development, and pathogens of the plant. Microbiologists would investigate the dangers associated with plant-born human pathogens. Together these lines of research would lead to optimal medical care for patients and a healthy agricultural industry.

None of these institutions, in any state, have been able or willing to participate in Cannabis research. Universities are almost entirely reliant on federal funding, and they fear that involvement in Cannabis research would put that funding at risk. If academic researchers are going to engage in Cannabis research they will need to sever ties with universities. Colorado recently approved \$9M for Cannabis research under a Medical Marijuana Research Grant Program run by the Colorado Department of Public Health and Environment. These funds are still not accessible to university-appointed investigators.

Research can also be performed by commercial entities that will not have this same set of concerns. If such companies were able to operate in a manner that was consistent with state law, they would be likely to move important Cannabis research forward. However, commercial research is usually proprietary, and it is not the proper setting for public health research that needs to be widely disseminated.

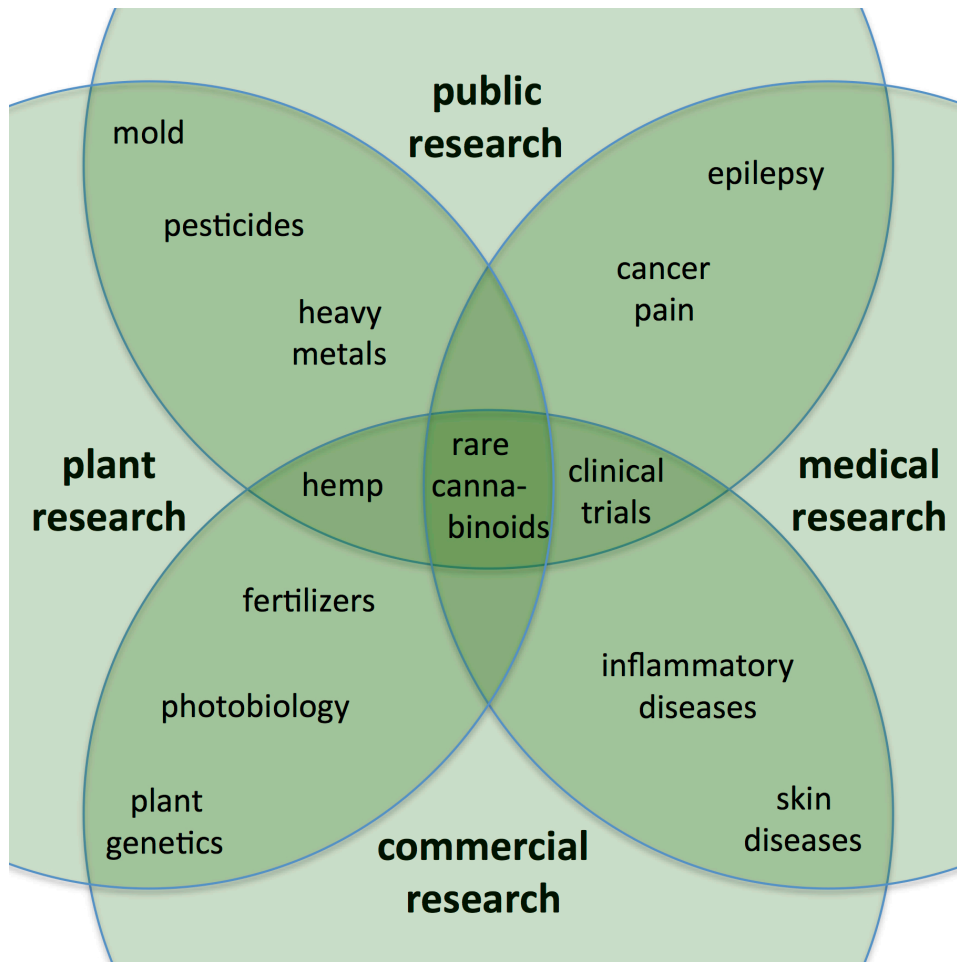
Research that is largely for the public good needs to be financed and structured publicly. For this reason, the vast majority of all research in the U.S. is financed by the NIH. Without NIH support, if Oregon wants this critical work done it will have to structure and fund it at the state level. One way to do this would be to create a public Cannabis Research Institute that could receive state funds for Cannabis research without endangering federal funding for Universities. Researchers would potentially have to leave their university appointments altogether in order to participate.

Another way to facilitate such research, especially the crucial studies that need to be performed on contaminants of Cannabis, would be to house it in an already existing state body, such as the OHA. The OHA is well-equipped to undertake such research, and will be deeply involved in managing the Cannabis testing laboratories in any case.

It is quite possible that there could be fruitful cooperation between the public and commercial entities on research projects. But whether Cannabis research is done in a commercial setting, or in the setting of a state-sponsored Institute, it will require the use and possession of Cannabis plants and products in a way that does not fit easily into the license types created by Measure 91 to apply to commercial flower producers. It will therefore require separate licensing, and should also be subject to separate oversight, ideally by the OHA itself.

The first section of this document outlines a number of health threats on Cannabis for which we do not presently have adequate information to guide more than the most basic safety-testing regulations. Clinical research on Cannabis lags even further behind. If Cannabis research is not enabled in Oregon with both public programs and a private license structure, it will not be possible for either academic or commercial research to move forward. The medical properties of Cannabis will remain inadequately explored, and the agricultural Cannabis industry will not be able to operate efficiently or safely.

The intersections between public and commercial research, and between plant and medical research, are complex (as illustrated below). This figure lists only a handful of the pressing research goals related to Cannabis, and it does not describe the way that each individual project depends on others. All of this research can be done with a combination of state and commercial support. It is likely that none of it can be done in a federally-funded university setting.



Recommendations:

- A bill creating A Cannabis Research License to promote commercial research projects involving both medical and agricultural subjects.
- A bill instructing The OHA to create a Cannabis Research Program. This program should empower the OHA to structure and fund external research in the form of an Institute capable of performing public health research. It should additionally empower the OHA to structure and fund internal Cannabis research projects.
- Funding should be allocated for both internal and external OHA Cannabis research programs, and structured so as to encourage the participation of qualified scientists and the engagement of industry partners.