



COLORADO
Department of Revenue



August 10, 2015

Marijuana Equivalency in Portion and Dosage

*An assessment of physical and pharmacokinetic relationships
in marijuana production and consumption in Colorado*

Prepared for the Colorado Department of Revenue

The authors are grateful for suggestions and assistance from Lewis Koski, Ron Kammerzell, Jim Burack, Dr. Franjo Grotenhermen, M.D., Dr. Kari Franson, M.D., and all the businesses that hosted the team and contributed information to this study. Any omissions or errors are the sole responsibility of the report team.

This report was commissioned under Colorado HB 14-1361. The Colorado Department of Revenue retained the University of Colorado, Leeds School of Business, Business Research Division, in partnership with the Marijuana Policy Group, and BBC Research & Consulting, to produce an unbiased and scientific report for the purpose of rulemaking by Colorado stakeholders.

Version 12 / August 10, 2015

Corresponding author:

Adam Orens

aorens@mjpgroup.com

Authors

Adam Orens

Miles Light

Jacob Rowberry

Jeremy Matsen

Brian Lewandowski

MPG

Marijuana Policy Group



Leeds School of Business
UNIVERSITY OF COLORADO BOULDER

BUSINESS RESEARCH DIVISION

BBC
RESEARCH &
CONSULTING

Marijuana Equivalency in Portion and Dosage

*An assessment of physical and pharmacokinetic relationships
in marijuana production and consumption in Colorado*

Table of Contents

EXECUTIVE SUMMARY	6
Physical Equivalency	6
Pharmacokinetic Equivalency	7
Market Price Equivalency	8
OVERVIEW AND MOTIVATION	11
Production, Price, and Dosing Equivalencies	11
Use of Metrc™ Data	12
PREVAILING MIP PRODUCTION TECHNIQUES	13
THC vs. THCa	13
Production Technique Summary	13
Hydrocarbon Extraction Process	14
Carbon Dioxide Extraction Process	15
Butter and Cooking Oils	15
Other Solvents	16
PHYSICAL EQUIVALENCY CALCULATIONS	17
Alternate Methodology	21
PHARMACOLOGICAL EQUIVALENCIES	23
Enumeration of THC Uptake Methods for Marijuana	23
THC, THCa, 11-OH-THC and THC-COOH	24
Identification of THC Uptake and Benchmarking	24
Role of the Blood-Brain-Barrier (BBB)	27
Constructing Dosing Equivalencies for Marijuana Products	28
Identification of Parameter Values	30
A Worked Example	33
Resulting Equivalency Tables	34
Oils, Tinctures, Lotions, and Less Common Uptake Methods	35

MARKET PRICE COMPARISON	36
REFERENCES	41
TERMS & ACRONYMS	44

Executive Summary

The original legislation to legalize and regulate marijuana in Colorado does not explicitly restrict marijuana concentrates and infused edibles. Over time, these marijuana products have become more popular, prompting new legislation to remedy the omission. House Bill 14-1361 now stipulates limits upon marijuana flower portions, “or their equivalent.”

This study provides scientific and data driven evidence in order to understand these equivalencies. The results provide comparisons between marijuana flower, concentrates and infused products specifically for Colorado’s marijuana market.

Equivalency can be viewed from three perspectives: production, dosing, and market price. The first perspective relates to physical production, where infused edibles or concentrates are traced back into their corresponding weight of flower or trim inputs. This enables the conversion from non-flower products into a common flower-based denominator, so that aggregate use can be measured across different marijuana product types.

The second perspective uses pharmacology to develop a dose-equivalent measure across product types. The results equate the dosing effects between inhaled and ingested marijuana products. Finally, the third perspective uses Colorado potency and market data to convert marijuana retail prices into their unit-THC equivalents. These THC-based prices are then compared across product types. A powerful and reassuring finding is that Colorado’s market prices reflect, almost identically, the dosing equivalencies found in the pharmacological review. The pricing perspective is a new methodology, made possible by analyzing recently collected data from Colorado’s retail marijuana market.

The information contained in this report is specific to Colorado in 2015. Production techniques are constantly evolving, and the marijuana included in this study was

grown in Colorado and may not share similarities with product in other regions. Overall, the study is designed to meet the requirements of Colorado House Bill 14-1361 and focuses solely on the retail adult-use marijuana market in Colorado.

PHYSICAL EQUIVALENCY

Physical equivalencies were calculated in two ways – a THC equivalency, and a physical production equivalency. Physical equivalencies were calculated for the major concentrate and infused product manufacturing techniques, including butane hash oil, CO₂ oil, ethanol, and water. Physical production equivalency is calculated by isolating the marijuana trim and shake inputs and determining a yield ratio. The THC methodology provides an equivalent amount of THC in various forms of marijuana products based on recent state testing information Table ES-1 shows equivalency factors for both methodologies by solvent type.

The physical equivalencies in Table ES-1 show that between 347 and 413 edibles of 10mg strength can be produced from an ounce of marijuana, depending on the solvent type and production method. For concentrates, between 3.10 and 5.50 grams of concentrate are equivalent to an ounce of flower marijuana.

The THC equivalency factors in Table ES-1 can be interpreted as showing units with equivalent amounts of THC based on recent state testing data. For instance, given the uniform dosage amounts of edibles in Colorado, 434 edibles of 10mg strength and one ounce of flower marijuana at average potency have an equivalent amounts of THC. For concentrates, between 6.91 and 8.50 grams of concentrate (depending on solvent) and an ounce of flower marijuana at average potency have an equivalent amount of THC.

Table ES-1. One Ounce Equivalents by Solvent Type

	1-Ounce Flower Equivalents			
	Physical Equivalency		THC Equivalency	
	Amount	Amount	Amount	Amount
	Edibles	Concentrate (g)	Edibles	Concentrate (g)
Solvent Type	(10mg)	(Avg. Potency)	(10mg)	(Avg. Potency)
Butane	391.07	5.46	434.35	6.91
CO2	346.96	4.84	434.35	8.07
Butter/Lipid	413.49	N/A	434.35	N/A
Ethanol	N/A	5.44	N/A	7.37
Water	N/A	3.10	N/A	8.50

Source: Author calculations based on metrc™ data.

The conversion factors described above are the first of their kind. They can be useful for state-level production management. The conversions allow units of infused edibles and concentrates to be denominated by flower weight, and then added to flower sales, in order to determine retail market demand and supply.

PHARMACOKINETIC EQUIVALENCY

An important compliment to the physical THC relationships identified in this study is the pharmacological perspective. If the purpose of the equivalency legislation is to limit transactions or possession to a reasonable “dose” of concentrates and marijuana products for residents and non-residents, then the medical effects described here will be useful to construct a set of equivalencies between marijuana product types.

Pharmacokinetic equivalency incorporates findings from medical and pharmacological publications to inform marijuana stakeholders about the dosing process. The authors created a new mathematical construct that can compare ingested and smoked marijuana products in a consistent manner.

The pharmacokinetic model compares inhaled and ingested products using a dose ratio. The calculations are based upon different uptake routes and speeds for the psychoactive compounds related to marijuana use (e.g., THC and 11-OH-THC). Other compounds, such as cannabinoids, are not included here because the legislation relates only to retail use. The base pharmacokinetic equivalency ratio is 1 to 5.71. This means that one milligram of THC in edible form, is equivalent to 5.71 milligrams of THC in smokable form.

Table ES-2. Pharmacokinetic Dosage Equivalency

	Average THC Potency	Effective Uptake Ratio	1 Gram Equivalent	1 Ounce Equivalent
Buds/Flower	17.1%	1.00	1 Gram	1 Ounce
Edibles	N/A	5.71	3 Servings	83 Servings
Concentrates	62.1%	1.00	0.28 Grams	7.72 Grams

Source: Author calculations based on metrc™ data.

Table ES-2 shows the pharmacokinetic equivalencies, and the corresponding serving equivalencies, using data from Colorado.

Pharmacokinetic equivalencies indicate that 83 ten-milligram infused edible products is equivalent to one ounce of marijuana flower in Colorado. About 7.72 grams of concentrate is equivalent to an ounce of flower marijuana.

MARKET PRICE EQUIVALENCY

For comparison, a third equivalency approach was developed by the study team. This is the “market price equivalency” method. As with the physical equivalencies, this methodology was previously not possible. We use metrc™ data to convert retail store market prices into a price per unit of THC across different products. These new THC-based prices reflect the inherent value of each product from a psychoactive dose viewpoint. They reveal the price that consumers are willing to pay for the psychoactive experience (the high) yielded from each type of product.

Table ES-3 below shows representative marijuana product pricing in Colorado’s retail market. The top portion shows

typical prices for the products themselves. The middle portion shows the price after conversion—in cents per milligram THC (¢/MG_{THC}). Finally, the bottom portion computes the price-ratio between products using the THC price measure.

Table ES-3 shows the price of marijuana flower, or buds, is \$14.03 when purchased by the gram, or \$264 when an ounce is purchased. When converted to THC, the same product costs 8.25 cents per milligram THC when purchased by the gram, and 6.10 ¢/MG_{THC} for an ounce, reflecting some volume-pricing. Similarly, a typical 100mg THC edible product costs \$24.99, a 40mg product is \$19.81, and a single-serve 10mg THC edible costs \$6.60. When converted, the THC price for these products equals 24.99 ¢/MG_{THC}, 35.00 ¢/MG_{THC}, and 66.00 ¢/MG_{THC} respectively, for these goods. Finally, concentrates cost \$55.00 for a typical 1 gram wax portion, and a typical 500mg vaporizing cartridge costs \$66.00. The THC prices are 8.46 ¢/MG_{THC} and 18.86 ¢/MG_{THC}, respectively.

Using the THC prices, the edibles to flower price ratio is 3.03 (edible THC per flower THC) for the 100mg edible product, 3.00 for the 80mg product, and 4.24 for the 40mg product. The 10mg single-serving ratio is 8.00, which we believe reflects a minimum price for small portions.

The ratio for wax/shatter is 1.03 for a 1 gram container, and 2.28 for a 500mg vaporizer cartridge. The higher price ratio for vaporizing equipment may reflect higher packaging costs.

In general, the price ratios shown in Table ES-3 are notable because they match—quite closely—to the pharmacokinetic equivalency ratios. This means that although the market participants may not have completed their own pharmacokinetic research, they naturally have gravitated toward this result, based simply upon trial and error.

The remainder of this report provides details regarding the data, the methodologies, and previous scientific findings used to construct our results.

Table ES-3. THC Market Price Equivalencies

THC Market Price Ratios in Colorado					
Indicative Prices by Weight (\$)					
Buds/Flower		1 Gram	1/8 Oz	1/4 Oz	1 Ounce
	Most Common	\$14.03	\$41.27	\$82.54	\$264.14
	Discounted	\$12.38	\$33.03	\$66.06	\$239.43
Edibles		100 MG	80 MG	40 MG	10 MG
	Edible Variety	\$24.99	\$19.81	\$14.00	\$6.60
Concentrates		1 Gram	500 MG	250 MG	
	Wax / Shatter	\$55.00	--	--	--
	Vape Cartridge	--	\$66.00	\$46.00	--
Equivalent Market Price (Cents per MG THC)					
Buds/Flower		1 Gram	1/8 Oz	1/4 Oz	1 Ounce
	Most Common	8.25	6.94	6.94	6.10
	Discounted	7.28	5.55	5.55	5.53
Edibles		100 MG	80 MG	40 MG	10 MG
	Edible Variety	24.99	24.76	35.00	66.00
Concentrates		1 Gram	500 MG	250 MG	
	Wax / Shatter	8.46	--	--	--
	Vape Cartridge	--	18.86	26.29	--
THC Market Price Equivalencies (Price Ratios in THC Units)					
Buds/Flower		1 Gram	1/8 Oz	1/4 Oz	1 Ounce
	Most Common	1.00	1.00	1.00	1.00
Edibles		100 MG	80 MG	40 MG	10 MG
	Edible Variety	3.03	3.00	4.24	8.00
Concentrates		1 Gram	500 MG	250 MG	
	Wax / Shatter	1.03	--	--	--
	Vape Cartridge	--	2.28	3.19	--

Note: 1. Prices taken from a sample of online retail menus for Colorado stores.

2. Ratios may not necessarily apply to other states..

Source: Colorado Storefront menus, calculations by the report study team.

Overview and Motivation

The original legislation to legalize and regulate marijuana in Colorado for adult use did not include explicit purchase restrictions on marijuana concentrates and infused edibles. As these marijuana products grew more popular in 2014, up to 35 percent¹ of statewide retail sales, legislation was enacted under House Bill 14-1361 to remedy the omission. The legislation does so by stipulating limits upon marijuana flower portions, “or their equivalent.”

This study provides unbiased, scientific information that can be used to suggest appropriate equivalencies between flower and alternative marijuana products. It is a summary of how different marijuana products are produced and consumed in accordance with House Bill 14-1361, which requires the state to conduct a study to establish equivalencies.

The information in this study can be used to convert concentrate and infused products into their flower weight equivalents from both a production and consumption viewpoint. From a production viewpoint, the findings can be used to translate marijuana product unit sales into their weight equivalent. This will improve the measurement of aggregate marijuana demand, by using a common denominator. From a consumption viewpoint, the findings here can be used to establish an equivalent “dose” amount between non-flower products and flower weight. Overall, the study is designed to meet the requirements of House Bill 14-1361 and focuses solely on the retail adult-use marijuana market. Issues related to medical marijuana are not addressed in this study.

PRODUCTION, PRICE, AND DOSING EQUIVALENCIES

This study investigates marijuana equivalencies from three perspectives: production, price, and dosing.

The first perspective is from a physical production viewpoint, where servings of infused edibles or concentrates are converted into the respective weight of marijuana flower or trim needed as inputs to production. To construct these equivalencies, average yield and potency is estimated by the consultants after a series of interviews with Marijuana Infused Product (MIP) manufacturers, and by analyzing the state’s Marijuana Enforcement Tracking Reporting Compliance (metrc™) database to isolate input and output packages at MIPs for various concentrates and infused edibles. This metric will provide a bridge between concentrate and infused edible output and plant material inputs.

The second perspective computes equivalencies from a dosing viewpoint. The dosing perspective provides stakeholders with a pharmacological model that equates the dosing effect between inhaled and ingested marijuana products. The pharmacological approach resolves the disparity between weight-based THC content in marijuana products, so that a dose-equivalent measure can be established.

Finally, the third perspective computes the market price of THC across product types in the Colorado marketplace. The pricing perspective is a new methodology. It was made possible by manipulating recently collected data from Colorado’s retail marijuana market. By using statewide inventory and testing data, the study team can convert retail marijuana store price for flower, concentrates, and infused edibles into a price with a common denominator—THC. The study team found that the pricing structure in stores reflects, almost exactly, the pharmacokinetic dosing equivalencies found in this report. This suggests that although no individual has explicitly measured the dosing effect of different products, that the marketplace reflects the dosing value for each product implicitly.

¹ Based upon statewide retail sales, May – September 2014.

SECTION I
SECTION II
SECTION III
SECTION IV
SECTION V

SECTION I	The science and data related to marijuana, its use, and regulation are inherently complex. The purpose of this report is to synthesize state-level marijuana data with existing manufacturing and medical research in order to construct easy-to-understand ratios between marijuana product types. The resulting information can be used to establish a set of rules that are defensible, operable, transparent and systematic. Over time, as new information evolves, these findings may be reviewed and adjusted to reflect the most current research available.
SECTION II	This analysis and report is developed for use by stakeholders in Colorado's retail marijuana market. It is assumed that the reader of this report is an informed, intelligent public policy official or individual with experience and understanding of Colorado's retail and medical marijuana markets. The objective of this report is to provide a clear and understandable synthesis of relationships between marijuana product types.
SECTION III	USE OF METRC™ DATA This study would not have been possible before the state inventory tracking system was established. The system allows a viewpoint of the entire state marketplace from “seed to sale”, providing a powerful data arena from which to determine key statistics, such as potency levels, production ratios, and consumption rates, to name a few. Colorado's inventory tracking platform, metrc™, requires data to be uploaded from every cannabis business. As a result, there is some underlying variability due to user input error by MIPs, cultivations, and retail stores.
SECTION IV	
SECTION V	During this study and during previous studies over the past 18 months, the study team has reconciled most disparities by conducting thorough checks, and through vendor interviews to ensure that data is being interpreted correctly. Over the course of this research, the investigators applied generally accepted statistical methods to

remove outliers and questionable records. The sample sizes used in the analysis represent the largest samples we could pull from the system that we believed would give reliable results.

The report is organized as follows: Section II provides a summary of prevailing MIP production techniques, followed by the calculation of production equivalencies in Section III. In Section IV, a pharmacokinetic model is developed and dosing equivalencies are defined. Section V explains the market price equivalency methods and findings, and Section VI provides a brief summary of the study findings. Following Section VI is a dictionary of marijuana terms used here, as well as a reference list for the interested reader.

Prevailing MIP Production Techniques

This section provides descriptions of marijuana infused product concentrate production techniques used in commercial MIPs in Colorado. The information contained in this section was obtained through a series of interviews conducted between April 24 and June 18, 2015.

The voluntary industry outreach process consisted of 11 in-person interviews, facility tours, and phone interviews with MIP operators and testing facilities. No identifying information of specific facilities is included in this report to protect the privacy and intellectual property of interviewees. The interviews consisted of the following business types organized by primary production process:

- Butane/hydrocarbon concentrates (4);
- Carbon dioxide concentrates (2);
- Butter-based edibles (2);
- Butane/hydrocarbon edibles (2); and
- Carbon dioxide edibles (1).

In addition to the individual interviews, the study team attended two industry group meetings at the request of the Marijuana Industry Group (MIG) and the Cannabis Business Alliance (CBA). The meetings allowed member businesses to ask questions and provide their input to the study in group format.

PRODUCTION TECHNIQUE SUMMARY

Several cannabinoid extraction techniques are used in the production of marijuana concentrates and edibles. The majority involve using a solvent process where solvents are introduced to marijuana plant material to form a concentrate. The solvents are then removed

through various refining techniques to produce a refined oil in various consistencies. Potential solvents include hydrocarbons, carbon dioxide, butter/cooking oils/lipids, ether, ethanol, isopropyl alcohol, water, and dry extraction methods. Several extraction methods involving hydrocarbons and carbon dioxide were borrowed from long-standing methods used in the fragrance and food industries.

Over the course of the interviews, it became apparent that while any of the aforementioned solvents can produce a marijuana concentrate or other infused product, commercial producers prefer hydrocarbon, carbon dioxide, and butter/lipid extraction processes. Interviewees cited solvent costs, efficiencies in production,

THC vs. THCa

Marijuana flower is often said to contain THC, but this is not technically true. The plant contains “THCa”, which is not psychoactive in its natural state. THC is created through decarboxylation.

Decarboxylation is the process of heating THCa, which naturally occurs in cannabis plants, to activate THC that can be absorbed in the body through ingestion. In the process, the THCa loses carbon and oxygen molecules, and about 12.3 percent of its weight.

This weight reduction is calculated using the molecular weight of THCa and THC.

Although the report authors refer to both THC and THCa throughout the report, the reader can interpret the terms as synonymous.

SECTION I
SECTION II
SECTION III
SECTION IV
SECTION V

and output product quality as reasons for using these preferred solvents.

Metrc™ data confirmed that these three solvents account for over 93 percent of edibles production in the state. The interview participants used variations on the three major solvent processes shown above. Each process is described in more detail below.

HYDROCARBON EXTRACTION PROCESS

Hydrocarbon extraction uses any number of hydrocarbons as the principal solvent. Butane and propane are the most common solvents used in commercial operations. When cannabis plant matter comes in contact with the hydrocarbons; cannabinoids, terpenes, and other compounds dissolve into the solvent. The hydrocarbon solvent and cannabinoid mixture is purged using vacuum ovens to remove the solvents.

The purging process leaves only cannabinoids and other desired compounds in a refined concentrate. Hydrocarbon concentrates are often called butane hash oil

(BHO), shatter, or wax. All of these products refer to slightly different refining techniques that occur after the BHO is extracted from the plant matter. BHO and other variants contain a high concentration of THCa, often between 60 percent and 95 percent, depending on the amount of refinement and quality of inputs.

If BHO is used to make infused edible products, it must be decarboxylated. Decarboxylation converts the THCa in cannabis plants into psychoactive THC. Decarboxylation requires heating the BHO to 240°F–250°F until bubbling dissipates to achieve desired results. BHO sold for smoking or vaporizing does not require decarboxylation.

Table II-1 shows information on weight yields and THCa potency for hydrocarbon extractions obtained during the industry outreach process. Weight yield is the ratio of output weight to input weight. THCa potency is obtained from metrc™ as part of the mandatory testing for potency and safety. Table II-1 presents THCa for all establishments regardless if the end product is a concentrate or edible.

Table II-1. Butane Extraction Weight Yields and THCa Potency

	Product Type	Primary Input	Input Potency (% THCa)	Weight Yield (%)	Output Potency (% THCa)
MIP 1	BHO Wax/Shatter	Trim	12-20	12-22	60-80
MIP 2	BHO Wax/Shatter	Trim	15-20	10-25	70-95
MIP 3	BHO Wax/Shatter	Trim	10-20	10-20	65-90
MIP 4	BHO (edibles)	Trim	10-17	15-20	65-80

Source: MIP interviews April - June 2015.

CARBON DIOXIDE EXTRACTION PROCESS

Carbon dioxide (CO₂) fluid extraction techniques have been used for various industrial applications in the food and cosmetic industries. CO₂ at very high (supercritical) or low (subcritical) pressures is used to extract cannabinoids from plant material. Different combinations of temperature and pressure are used in the extraction. CO₂ is a popular solvent due to its lack of toxicity and its perception as a less dangerous form of cannabis concentrate. CO₂ oils are a popular ingredient in vaporizing concentrates for use with a stationary vaporizer or a portable vaporizer pen.

CO₂ fractionations² at different pressures in the production process can yield different product consistencies and compositions. Plant waxes remain in varying amounts in the raw extraction, which is often refined further using various techniques involving an ethanol wash or refrigeration techniques called winterization.

² Fractionation is a separation process in which a certain quantity of a mixture (gas, solid, liquid, suspension or isotope) into a number of smaller quantities (fractions) in which the composition varies according to a pressure or temperature gradient.

The refining process removes plant waxes, chlorophyll, or other undesirable elements.

Similar to BHO, CO₂ oil contains THCa concentrations between 60 percent and 85 percent, depending on the amount of refinement and quality of inputs.

CO₂ extractions must be decarboxylated to make edible products. An increasing number of edible products are made with decarboxylated CO₂ oil as the active ingredient. The decarboxylation process with CO₂ oil is similar to BHO.

Table II-2 shows weight yields and THCa potency for CO₂ extractions obtained during the industry outreach process. Table II-2 presents THCa for all establishments regardless if the end product is a concentrate or edible.

BUTTER AND COOKING OILS

Perhaps the most widely known method for extracting cannabis for edible preparations involves the use of butter, coconut oil, and other cooking oils. Cannabinoids are fat soluble, and MIPs add cannabis to butter and other oils and the mixture is heated to 240°F–250°F.

Table II-2. CO₂ Extraction Weight Yields and THCa Potency

	Product Type	Primary Input	Input Potency (% THCa)	Weight Yield (%)	Output Potency (% THCa)
MIP 1	CO ₂ Oil	Trim	12-17	10-15	80-85
MIP 2	CO ₂ Oil	Trim	15-17	8-12	70-80
MIP 3	CO ₂ Oil (edibles)	Trim	10-15	8-10	60-65

Source: MIP interviews April - June 2015.

Some MIPS vary this process by decarboxylating the plant material before adding it to the butter. Then plant material is strained and the butter is brought back to room temperature.

MIPs are required to test each batch of cannabis butter or oil for potency. After a batch of butter is made and tested for potency, the MIP may add additional butter or oil if necessary to adjust the potency in accordance to its recipe. Then the cannabis butter or oil is measured in the recipe to determine the appropriate potency for each batch of baked edible products. The butter MIP operators indicated that they have formed relationships with wholesale suppliers for trim, and they generally know the potency range of their raw cannabis butter, but natural variation exists in each package of plant material used to produce butter-based edibles.

Table II-3 shows weight yields and THC potency for butter and oil extractions obtained during the industry outreach process.

OTHER SOLVENTS

Marijuana concentrates and infused products can also be manufactured using a host of other solvents, including isopropyl alcohol, ethanol, vegetable glycerin, water, and dry/solventless (kief).

While these methods are employed in Colorado for some commercial production, no MIPS in the interview group reported use of these methods on a commercial scale. These extraction methods are in use for small production batches and represent less than 7 percent of the market.³ The interviewees often referred to these products as a “cottage” or “artisanal” market.

In the following section, metrc™ data is used to provide production equivalency calculations for alcohol and water based extraction methods in addition to the methods encountered in the interviews (hydrocarbon, CO₂, and butter/oil).

3 Based upon author calculations from metrc™ data.

Table II-3. Butter and Oil Extraction Weight Yields and THCa Potency

	Product Type	Primary Input	Input Potency (% THCa)	Weight Yield (%)	Output Potency (% THC)
MIP 1	Butter edibles	Trim	10-15	3-4	1.9-2.5
MIP 2	Butter edibles	Trim	15-22	2.75-3.25	2.0-2.8

Source: MIP interviews April - June 2015.

Physical Equivalency Calculations

In this section, metrc™ data is used to identify statewide average conversions of marijuana plant inputs into marijuana product outputs. Together with the MIP production structure defined above, these two sections combine to produce conversion rates between plant-based inputs and infused or concentrated outputs.

The study team developed two types of physical equivalency calculations: a simple THC conversion and a more nuanced physical conversion. The physical conversion traces the marijuana through the concentrate and edible production process and matches inputs (marijuana plant material) with outputs (concentrates and infused products). The THC conversion presents a more basic equivalency that quantifies equal amounts of THC in marijuana concentrates, edibles, and plant material. The equivalencies are organized by the major solvents used in production.

Inventory tracking data is used to trace the path between cultivation centers, marijuana infused products (MIP) manufacturers, and final retail centers. Disparate data sources needed to be translated and combined in order to complete this task. For example, marijuana packaging data provides information about product contents and source, facility information is used to categorize package owners and transfers. Transfer manifests provide an accounting of shipments of intermediate and final products between facilities, and testing results are used to establish potency among product types.

After plants are harvested and cured, marijuana flower and trim are registered as “packages.” The packages are transferred to retail stores for sale or to MIPs for further processing. Package records contain identifying information about package contents and the facilities on either end of a package transfer.

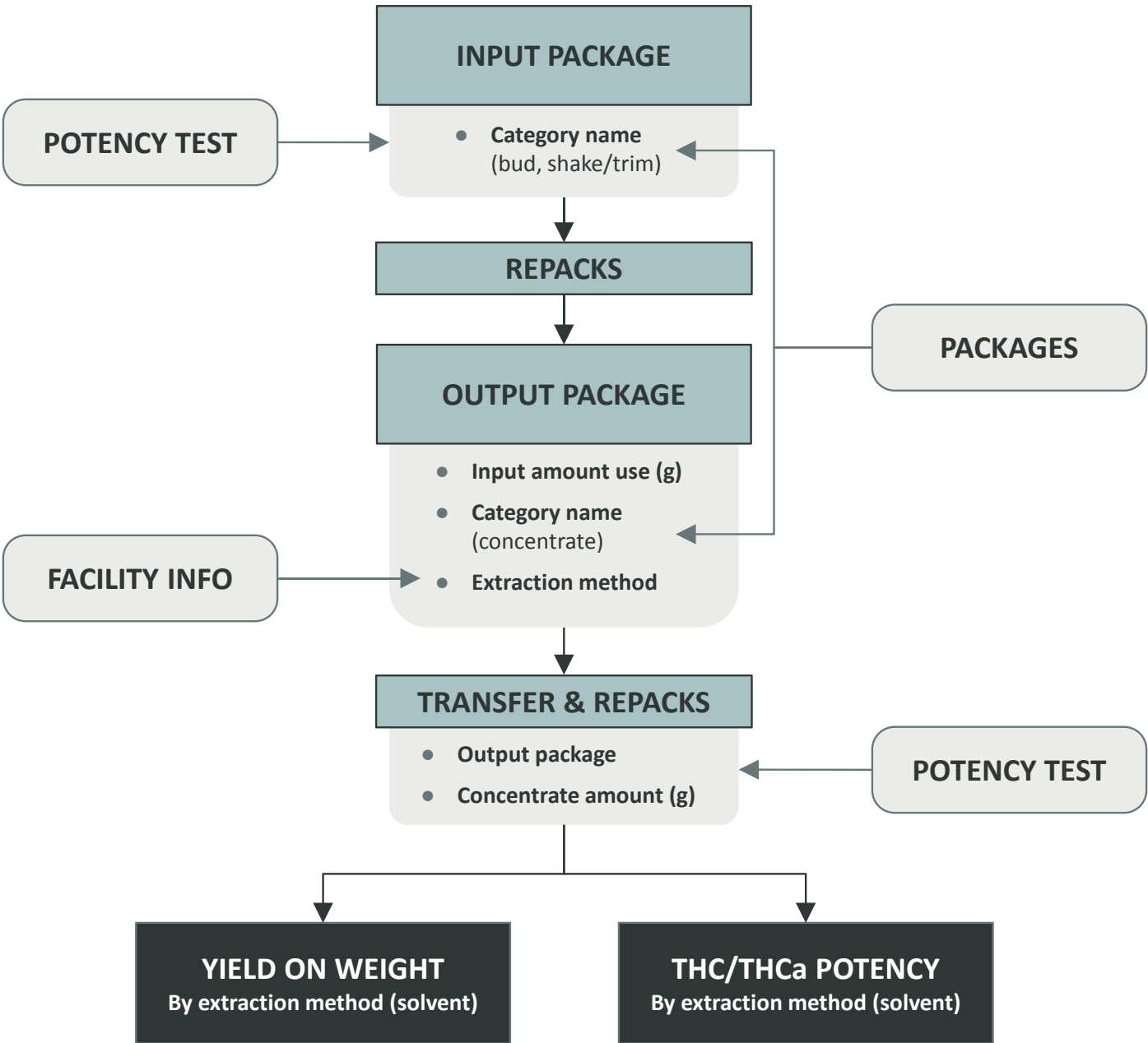
The study team built a genealogy of packages that traces them through the production process and correlates input packages of trim and flower to output packages of marijuana concentrates and infused products at MIP facilities.

Once an input and output package is linked, the study team mines the state inventory data to obtain identifying information about the production process and package contents. Equivalency calculations are provided for extraction processes that use butter and cooking oils, butane/hydrocarbons, CO2, water, and alcohol/ethanol as primary solvent. The calculations provide information on the yield on weight and input/output THC amounts for each production process.

For example, in butane hash oil (BHO) manufacturing, if a production batch starts with 1,000 grams of trim and yields 180 grams of BHO, then we calculate a weight yield of 18 percent. The study team then queries the testing database to obtain THCa and THC figures for trim, flower, concentrates, and edibles to obtain potency information for production inputs and outputs. The process diagram in Figure III-1 shows the data collection process in metrc™ for weight yield and potency.

SECTION I
SECTION II
SECTION III
SECTION IV
SECTION V

Figure III-1. Physical Equivalency Calculation Process



The calculation process provides the weight yield and potency figures in Table III-2. Table III-2 provides the mean weight yield, 95 percent confidence interval range and sample size for each solvent type included in the analysis. Table III-2 also provides information on potency testing for each solvent type. Marijuana flower and shake/trim potency is also included.⁴

The figures in Table III-2 show between 9.7 and 17.1 percent concentrate weight yield rates on non-butter solvents with relatively narrow confidence intervals.

Using butane as an example, a 1,000-gram production batch of trim yields on average 171 grams of BHO with a mean potency of 71.7 percent THCa. These calculations have a sample size of over 11,500 for weight yield and over 5,600 for potency.

⁴ Testing results display combined THCa and THC for each solvent type. Butter and oil potency is listed as amounts of THC due to decarboxylation. All other solvent types contain almost exclusively THCa.

Table III-2. Marijuana Concentrate Yield and Potency

Solvent	Yield Calculations				Potency Calculations				Bud %	Shake/ Trim %
	Mean Weight Yield	95% Lower Bound Weight Yield	95% Upper Bound Weight Yield	(n)	Mean THC/ THCa %	95% Lower Bound % THC/ THCa	95% Upper Bound % THC/ THCa	(n)		
Butane	17.11%	16.76%	17.46%	11,514	71.67%	71.20%	72.14%	5,606	11.43%	88.57%
CO₂	15.18%	14.80%	15.55%	7,257	61.39%	60.27%	62.51%	1,950	3.51%	96.49%
Butter	504.50%	484.69%	524.32%	599	2.57%	2.04%	3.09%	216	9.72%	90.28%
Water	9.72%	9.01%	10.43%	1,270	58.30%	56.34%	60.26%	266	9.91%	90.09%
Alcohol/ Ethanol	17.06%	14.37%	19.76%	241	67.17%	64.08%	70.25%	201	16.46%	83.54%
Flower					17.47%	17.41%	17.53%	26,023		
Shake/Trim					15.53%	15.26%	15.80%	1,591		

Source: Author calculations based on metrc™ data.

The butter “yield” rate differs from other solvents because it is a different production process. The butter yield results can be interpreted as the weight of cannabis butter produced per weight of plant input. For example, 100 grams of cannabis in a production batch would yield on average 502 grams of cannabis butter at a mean THC of 2.57 percent or 25 mg of THC per gram of butter.)⁵

The yield and potency figures described above are inputs to the physical equivalency calculations. For concentrates sold or transferred directly to retail stores, the figures in Table III-2 provide the information for an equivalency. For marijuana edibles, these figures are supplemented by several intermediate calculations shown in Table III-3.

All figures from Table III-2 are converted from percentages into milligrams per gram, as shown in Table III-3. This conversion is necessary because edibles in the adult use

5 The butter yield rate was the most difficult to interpret because of the many weight units that can be used to describe the prepared cannabis butters. There is also the possibility that some manufacturers report the output units after additional non-psychoactive butter is added to the cannabis butter. The 5-to-1 yield ratio is somewhat higher than what was discussed in our interviews. The authors have elected to use the metrc™ data due to the amount of data (1,623 records) that support the figures in Table III-2.

Table III-3. Edibles Intermediate Calculations

Solvent	mg THC/g Solvent	g Solvent per 10 mg Edible	g Trim per 10 mg Edible
Butter	25.70	0.39	0.08
Butane	716.70	0.014	0.08
CO ₂	613.90	0.016	0.09

Source: Author calculations based on metrc™ data.

retail market are sold in two standard sizes (10mg and 100mg)⁶ based on the amount of THC contained in the edible product.

The calculations in Table III-3 show the average potency of each solvent used in edibles production, the amount of solvent necessary to produce an edible product with 10mg of THC, and the amount of marijuana plant material necessary to produce 10mg edible product. On average, between .08 and .09 grams (or 80–90 mg) of plant material is required to make an edible product containing 10mg of THC.

Table III-4 shows equivalency calculations based on the physical approach described in Table III-3. Equivalencies are organized by solvent type and shown for edibles and concentrates. The process estimates the amount of plant material used in each 10 mg and 100 mg edible package and provides a calculation of the amount of edible packages that can be produced from an ounce of dried marijuana flower.

For concentrates available directly for sale, the study team provides estimates of the amount of plant material used to make one gram of concentrate at average potency for each solvent type. Similar conversions for an ounce and a quarter-ounce of marijuana flower are provided.

Table III-4 provides estimates of the amount of trim used in each production process and then converts trim amounts to flower equivalents using a THC-based conversion factor derived from the testing data presented in Table III-2.⁷

6 Two dosages are outlined in state statute. One is 10mg., which represents a standard dose of THC. The second is 100 mg., which contains 10 servings and represents the maximum amount of THC allowed in an edible retail marijuana infused product.

7 Trim has on average 15.53 percent THC and flower has on average 17.47 percent THC; therefore, a conversion ratio is calculated at 1.125.

Table III-4. Physical Equivalency Calculations

Product Type	Solvent	Purchase Amount	Trim Used in Production	Flower Equivalency Ratio	Ounce Equivalent	Quarter-Oz Equivalent
Edible	Butter	10 mg	0.08 g	0.07 g	413.49 each	103.37 each
Edible	Butter	100 mg	0.77 g	0.69 g	41.35 each	10.34 each
Edible	Butane	10 mg	0.08 g	0.07 g	391.07 each	97.77 each
Edible	Butane	100 mg	0.82 g	0.72 g	39.11 each	9.78 each
Edible	CO ₂	10 mg	0.09 g	0.08 g	346.96 each	86.74 each
Edible	CO ₂	100 mg	0.92 g	0.82 g	34.70 each	8.67 each
Concentrate	Butane	1 g	5.84 g	5.20 g	5.46 g	1.36 g
Concentrate	CO ₂	1 g	6.59 g	5.86 g	4.84 g	1.21 g
Concentrate	Ethanol	1 g	5.86 g	5.21 g	5.44 g	1.36 g
Concentrate	Water	1 g	10.29 g	9.15 g	3.10 g	0.77 g

Source: Author calculations based on metrc™ data.

The physical equivalencies in Table III-4 show that about between 347 and 413 edibles of 10 mg strength can be produced from an ounce of marijuana, depending on the solvent type and production method. For concentrates, between 3.10 and 5.50 grams of concentrate are equivalent to an ounce of flower marijuana.

The conversion factors described above can be useful for state-level production management. The conversions allow units of infused edibles and concentrates to be expressed in equivalent flower weight, and then added to flower sales, in order to determine retail market demand and supply.

ALTERNATE METHODOLOGY

A second, simpler methodology is presented in Table III-5 that employs THC as the common unit for conversion between the various forms of marijuana products. This methodology calculates an equivalent amount of THC in various forms of marijuana products based on the testing information shown in Table III-2.

The equivalency factors in Table III-5 can be interpreted as showing units with equivalent amounts of THC. For instance, given the uniform dosage amounts of edibles

in Colorado, all 10mg strength edibles have an amount of THC equivalent to 60 mg (0.06 g) of flower marijuana at the average potency. A conversion rate of 1.14 is applied to convert THC in infused products back to THCa in flower due to weight loss in the decarboxylation process involved in manufacturing edibles.⁸

⁸ Decarboxylation is the process of heating THCa, which naturally occurs in cannabis plants, to activate THC that can be absorbed in the body through ingestion. In the process, the THCa loses a carbon dioxide molecule and about 12.3 percent of its weight. Conversion calculation from THC back to THCa uses 1/(1-.123) or 1.14. This weight reduction is calculated using the molecular weight of THCa and THC obtained from Steep Hill Labs <http://steephilllab.com/resources/cannabinoid-and-terpenoid-reference-guide/>.

For retail concentrates equivalency calculations, the THC/THCa conversion is not necessary because concentrates are not decarboxylated for direct retail sale. The THC in one gram of concentrate is equivalent to between 3.05g and 3.75g of marijuana flower at average potency. Ounce and quarter-ounce equivalents are also provided in Table III-5.

Table III-5. Simple THC Equivalency Calculations

Product Type	Solvent	Purchase Amount	THC Amount	THCa Amount	Flower Equivalency Ratio	Ounce Equivalent	Quarter-Oz Equivalents
Edible	Butter	10 mg	10 mg	11.40 mg	0.07 g	434.35 each	108.59 each
Edible	Butter	100 mg	100 mg	114.03 mg	0.65 g	43.43 each	10.86 each
Edible	Butane	10 mg	10 mg	11.40 mg	0.07 g	434.35 each	108.59 each
Edible	Butane	100 mg	100 mg	114.03 mg	0.65 g	43.43 each	10.86 each
Edible	CO ₂	10 mg	10 mg	11.40 mg	0.07 g	434.35 each	108.59 each
Edible	CO ₂	100 mg	100 mg	114.03 mg	0.65 g	43.43 each	10.86 each
Concentrate	Butane	1 g	0.72 g	0.72 g	4.10 g	6.91 g	1.73 g
Concentrate	CO ₂	1 g	0.61 g	0.61 g	3.51 g	8.07 g	2.02 g
Concentrate	Ethanol	1 g	0.67 g	0.67 g	3.84 g	7.37 g	1.84 g
Concentrate	Water	1 g	0.58 g	0.58 g	3.34 g	8.50 g	2.12 g

Source: Author calculations based on metrc™ data.

Pharmacological Equivalencies

An important compliment to the physical THC relationships identified in this study is the pharmacological perspective. If the purpose of the equivalency legislation is to limit transactions or possession to a reasonable “dose” of concentrates and marijuana products for residents and non-residents, then the medical effects described here will be useful to construct a set of equivalencies between marijuana products.

There are several methods to consume marijuana such as intravenous, oral mucosal, ingested, transdermal, and inhaled. The two most popular methods for consumption are ingestion and inhalation. We focus upon these two methods in this study. The remaining methods are either reviewed briefly or are provided as references for the interested reader.

The reader should understand that this section does not represent a clinical study. Instead, this section uses findings from other studies to inform marijuana stakeholders about the dosing process, and it provides a new mathematical construct that can compare ingested and smoked marijuana products in a consistent manner. Therefore, this report should be considered to be a policy-driven study that leverages medical literature to provide scientific evidence during the construction of dose equivalencies between various marijuana products.

This section focuses upon the psychoactive components of marijuana, primarily THC and related chemicals, and does not focus upon the medicinal effects of marijuana because the findings and resulting regulations will be applied only to Colorado’s retail marijuana market, under House Bill 14-1361.

ENUMERATION OF THC UPTAKE METHODS FOR MARIJUANA

The psychoactive component of marijuana, THC (and

THC derivatives) can be delivered to the recipient in a number of ways. Each method translates into a different net amount of THC entering the bloodstream and the brain.

- **Flower smoking:** Over the past 30 years, smoking has been the most common method to consume marijuana. Based upon 2014-15 data, the THC content in Colorado retail flower lies between 8-22 percent, with a mean estimate of roughly 17 percent. Therefore, one gram of marijuana flower contains 170 milligrams of THC, on average. However, a large portion of that THC is destroyed during the smoking process. In this report, we itemize the uptake rates and the potential loss of THC through smoking, during the process of inhalation, exhaling, and blood-clearance. The process is further complicated by the transfer process of THC from the blood plasma, into the brain itself.
- **THC ingestion:** Alternatively, THC can be infused into edible products such as baked goods or candies, and then eaten. By state law, each serving of edibles is limited to no more than 10 milligrams of THC content. THC, when ingested, will be absorbed at different levels, depending upon other foods in the stomach, and upon the chemical nature of the pre-existing foods. As with smoked products, a majority of the THC is not absorbed by digestion. Various studies, which will be discussed below, suggest that between 6-20 percent of the THC content in an edible product is metabolized and absorbed into the bloodstream. However, ingestion and processing by the liver has been found to create an important THC byproduct that subsequently boosts the psychoactive effect of THC. This research will be discussed later in this section.

SECTION I	SECTION II	SECTION III	SECTION IV	SECTION V
-----------	------------	-------------	------------	-----------

- Concentrate smoking or “dabbing:”** This method also uses smoking as the uptake method, but the material contains very high concentrations of THCa.

The typical THC content in concentrated forms of marijuana varies between 60-80 percent, although rates as high as 95 percent have sometimes been observed. By heating and smoking these concentrates, the uptake ratios are similar to smoking marijuana flower, but the ratios of THC to flower-based cannabinoids may be different, creating a different type of psychoactive effect.

THC, THCA, 11-OH-THC AND THC-COOH⁹

The underlying chemistry for marijuana, and its psychoactive elements is complex and beyond the policy scope of this report. A large number of clinical studies and medical findings are cited later in this section. This subsection provides a brief and concise overview of the main psychoactive component in marijuana, THC. In addition to THC, there are cannabinoids, typically labeled using a root form, CBD, and then enumerated, such as “CBD-A” or “CBD-B.” Many cannabinoids contain psychoactive elements as well, but the type of effect caused by those cannabinoids is not typically as strong as THC.

Because this study is designed for the retail market, and not the medical market, only the psychoactive THC and THC related chemicals are considered.

The reader is reminded that marijuana flower (or buds) does not contain THC itself, but instead contains THCa (Tetrahydrocannabinolic Acid), a precursor to THC. The

⁹ Please note that this sub-section is an overview of report findings. In order to be concise, only a few of the specific technical references and citations are provided here. Instead, most citations are provided, combined, and enumerated during the longer, technical exposition at the bottom of this section.

relationship between THCa and THC is explained at the beginning of this report.

THC itself is the primary psychoactive component in marijuana, but there are also related chemicals that have been found to have an amplification effect upon the base blood levels of THC. In particular, when THC is ingested, it is then oxidized and converted by the liver into the active metabolite named 11-hydroxy-THC (11-OH-THC) [see 23, 25], and 11-nor-9-Carboxy-THC (THC-COOH), a secondary, non-psychoactive metabolite.¹⁰ Recent studies have found that 11-OH-THC penetrates the brain barrier more quickly than regular THC, causing a markedly-higher psychoactive effect. We cite a number of studies below, to estimate the relative potency of 11-OH-THC versus regular THC in blood levels, in order to more accurately characterize the psychoactive effects between ingestion and inhalation of THC.

IDENTIFICATION OF THC UPTAKE AND BENCHMARKING

This section describes THC uptake, delivery methods, and related dosing. The dosing relationships between uptake methods (smoking and ingesting) can be quite different from the physical weight relationships that were identified in the first half of this report. One relationship is pharmacokinetic, while the other is purely physical.

Comparing Peak Effect vs. Aggregate Effect

It is also important to recognize the differences between “peak effects” or “aggregate effects.” The former measure identifies the most intense moment experienced by a subject during a dosage event with marijuana. This can

¹⁰ THC-COOH is a non-psychoactive metabolite formed in the liver when THC is ingested or smoked. Due to its inactive nature, it is not factored into equivalency calculations See source 9 in references section.

be characterized as the “peak intensity” of the high. The latter measure calculates the integral, or area under the curve where the curve relates to blood-levels of THC and 11-OH-THC over time.

Typically, smoking produces a higher peak effect, as THC enters the blood stream through lung tissue. But THC levels are also quickly reduced when smoked, as the body works to clean contaminants from the bloodstream. Conversely, edible products absorb much more slowly, so that the effect is delayed compared to smoking. However, the digestion and oxidization process last much longer.

For example, Figure IV-1 shows the THC and related chemicals in the blood stream over time. As shown,

THC concentrations peaked 90 minutes after ingestion, and 11-OH-THC peaked slightly later, at approximately 110 minutes. Levels of these psychoactives remained elevated for approximately 300 minutes, or five hours, and non-active THC-COOH remained elevated for 1,400 minutes (almost 24 hours).

In contrast, smoking concentrations were much higher, and shorter. Figure IV-2, taken from the “California NORML Guide Interpreting Drug Test Results,”¹¹ combines results from smoking and ingested THC to reveal the relative magnitude of blood plasma levels.

¹¹ Sourced from: <http://www.canorml.org/healthfacts/drugtestguide/drugtestdetection.html#fn03>. Last visited on June 13, 2015.

Figure IV-1. An Example of Blood Plasma Concentration Rates of THC Derivatives Over Time, After Oral Ingestion of Marijuana Products. From Nadulski et. Al. (2005).

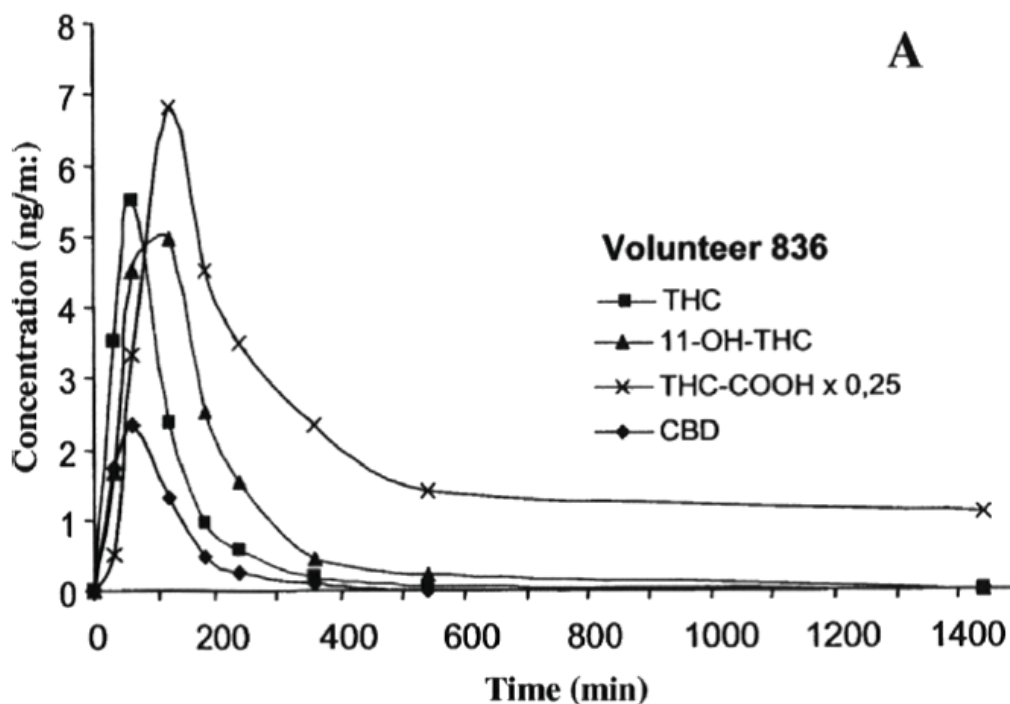


Figure IV-2. Comparison of Inhaled Versus Ingested THC Elements

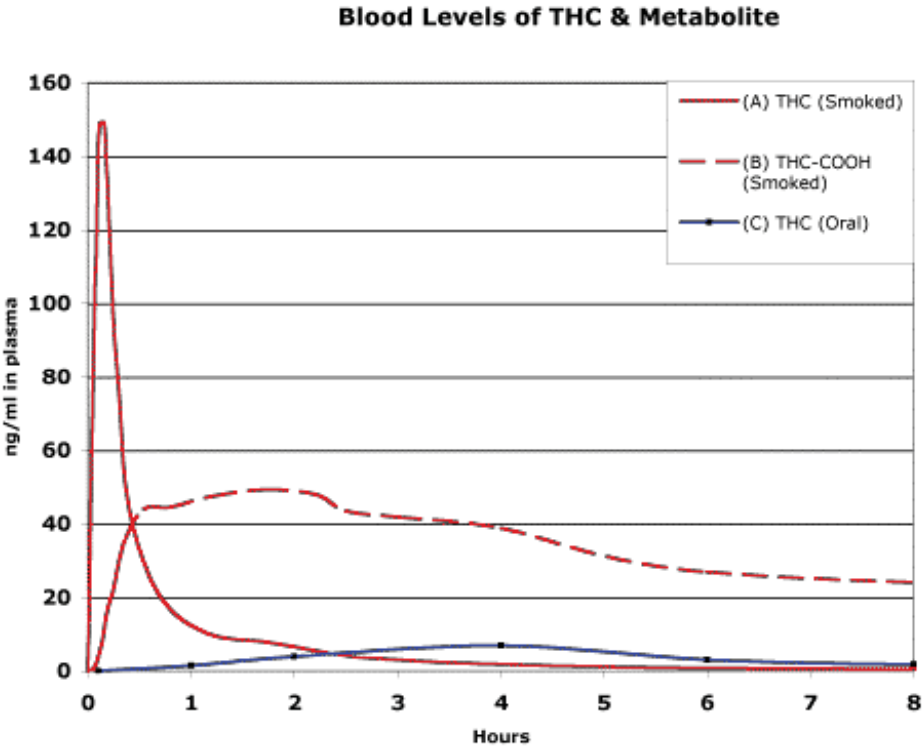
References:

(A-B) Smoked dose based on data from M. Huestis , J. Henningfield and E. Cone,M. Huestis , J. Henningfield and E. Cone. [08] M. Huestis , J. Henningfield and E. Cone, "Blood Cannabinoids. I. Absorption of THC and Formation of 11-OH-THC and THCCOOH During and After Smoking Marijuana", Journal of Analytic Toxicology, Vol. 16: 276-282 (1992).

(C) Oral dose based on data from B. Law et al. ([03] B. Law et al, "Forensic aspects of the metabolism and excretion of cannabinoids following oral ingestion of cannabis resin," J. Pharm. Pharmacol. 36: 289-94 (1984).)

Figure IV-2 shows that THC plasma concentrations are more than 10 times higher for smoked cannabis compared to ingested cannabis. The more recent findings from Nadulski, et. Al. (2005) suggest that while THC and 11-OH-THC levels peak much earlier than suggested by Law, et al. (1984), the relative magnitudes are similar. Peak levels were 5-6 ng/mL in the Nadulski study, and approximately 8 ng/mL in the Law study.

These findings suggest that either smoked marijuana experiences are significantly more intense, or—as scientists suggest—that 11-OH-THC produces an extenuated effect, compared to base THC. It also suggests that the relationship between blood-plasma THC levels do not necessarily correspond to psychoactive effects in a strictly-linear fashion.



Indeed, for the psychoactive effects to occur, the THC must penetrate the blood-brain barrier and connect directly to the brain. This means that even though blood-plasma THC levels are 10 times higher when smoking versus ingesting THC, the psychoactive effect may not be 10 times as intense, because THC is not necessarily reaching the brain at the same rate as it flows in the blood plasma.

As discussed earlier, 11-OH-THC has an extenuating effect. According to Perez-Reyes, et. al. [26], it has been found to penetrate the brain membrane approximately four times faster than THC. This suggests 11-OH-THC will contribute more rapidly to the psychoactive effects than THC. Also, by elongating the amount of time that THC is elevated in the blood plasma when THC is ingested and processed by the liver, there is more time for the THC

to penetrate the brain membrane and therefore a higher ratio of absorption of THC and other psychoactives into the brain fluid.

Together, this suggests that lower concentrations of THC in blood plasma do not necessarily imply that consumers are experiencing a lower intensity of psychoactivity. Instead, the level of THC and 11-OH-THC, combined with the time these metabolites have to penetrate the blood brain barrier, will determine the comparative psychoactive effects between inhaling and ingesting marijuana products.

The different rates of tissue absorption are shown more clearly in Figure IV-3. Here, blood plasma levels are the immediate recipients of THC, yielding high rates of THC concentration. However, rate of brain absorption from the

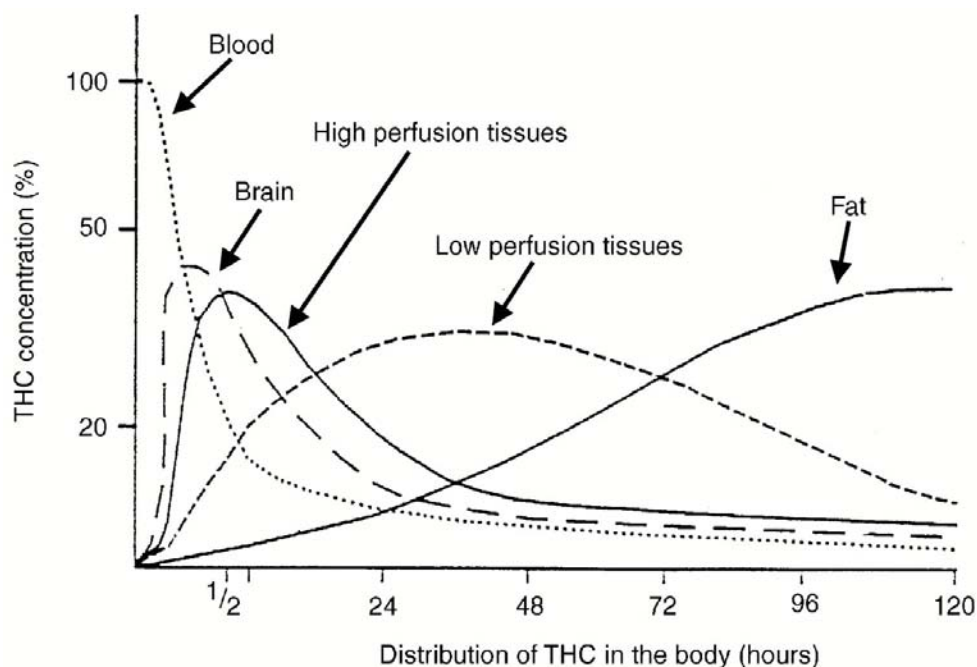
blood is slower, as discussed earlier. Next, the so-called “High perfusion” tissues begin absorbing THC, followed by “Low perfusion” tissues, and finally, fat tissues.

ROLE OF THE BLOOD-BRAIN-BARRIER (BBB)

A barrier, or sheath, separates the brain from the human body blood stream. There are several descriptions of the BBB.¹² In general, the BBB is a highly selective permeable

¹² See, for example: Blood-Brain Barrier: Drug Delivery and Brain Pathology, edited by David Kobilier, Shlomo Lustig, Shlomo Shapira, 2012. Springer Science & Business Media, Dec 6, 2012. A clear description for the lay person can also be found on Wikipedia: https://en.wikipedia.org/wiki/Blood%E2%80%93brain_barrier. Accessed on June 16, 2015.

Figure IV-3. Distribution of THC in the Body. Blood and Brain Absorption Rates Differ Significantly.



References:

Nahas, G. G. (1975) Marijuana: toxicity and tolerance. In Medical Aspects of Drug Abuse (ed. R. W. Richter), pp. 16-36. Baltimore, MD: Harper & Row.

SECTION I	barrier that separates the circulating (pulmonary) blood from the brain extracellular fluid that circulates in the central nervous system. The blood–brain barrier is formed by brain endothelial cells, which are connected by tight junctions with a high electrical resistivity. The BBB allows water and some gases to pass through, as well as lipid-soluble molecules. It also allows the selective transport of molecules, such as glucose and amino acids that are crucial to neural functioning. The BBB will often prevent the entry of lipophilic, potential neurotoxins by way of the so-called active transport mechanism. A small number of regions in the brain do not have a blood–brain barrier.
SECTION II	The BBB is an important factor that limits the flow of THC between the body’s blood plasma and the brain, where it creates the psychoactive effects. Where THC is allowed to penetrate the BBB, the rate of penetration is slow. In contrast, scientists have found that the rate of penetration for 11-OH-THC is much faster.
SECTION III	The selective permeability of the BBB causes a competition. On the one hand is the BBB/THC passage rate allowed by the BBB, and on the other hand is the metabolic clearance rate for toxins in blood-plasma. The BBB slowly allows THC to pass through the membrane, causing the psychoactive effects. But at the same time, the body’s metabolism will purify the blood stream, rapidly removing the THC from blood-plasma.
SECTION IV	This competition causes a decrease in THC effectiveness from inhalation, compared to the slower, steadier THC supply from ingestion. As shown in Figure IV-2, the concentration of THC in the blood stream is much higher when inhaled than when ingested. But due to blood plasma clearance, the ratio quickly falls to relatively low levels (e.g., in 30 minutes).
SECTION V	The limitations incurred by the BBB suggest that much of the THC in the blood-plasma is therefore lost, because the BBB slows conversion of blood-plasma THC into

“effective” THC within the brain itself. The share of THC that actually passes through the BBB and into the brain during the short period when blood-plasma levels are high is estimated to be approximately 35 percent. Just over one-third of the THC in the blood plasma is captured by the brain before it is cleaned out by the body’s pulmonary system.

CONSTRUCTING DOSING EQUIVALENCIES FOR MARIJUANA PRODUCTS

This is the first time that data from an official marijuana market is combined with medical research to develop scientifically-based relationships between marijuana products. The estimates reflect the best-available data and knowledge as of the report publication. Over time, we hope that further research can be used to improve upon the methods here, and to refine the estimates as knowledge of the subject matter continues to improve.

In order to synthesize the various pharmacokinetics of marijuana uptake into a simple, actionable metric, we suggest using a THC conversion factor. The conversion factor for purposes of dosing will compare the amount of weight-based THC contained in smokable products, such as marijuana flower and concentrates, with the amount of weight-based THC contained in ingested THC products such as edibles.

For example, if the THC conversion factor for dosing equals 1:5, this means that one milligram of THC in edible form (ingested) is roughly equal, from a dosing perspective, to 5 milligrams of THC in a smokable form. This section will provide a basic conversion factor model that synthesizes the scientific findings discussed earlier, in order to construct the THC conversion model.

The THC conversion factor is based upon a combination of findings. Among them are: the typical THC loss rate during the smoking process; the typical loss rate of THC for ingested products; the absorption rate of THC vs. 11-OH-THC in the brain; and the estimated comparative psychoactive intensity of THC versus 11-OH-THC.

For clarity, the uptake relationship can be parameterized and displayed mathematically. The following equations explain the relationship between each pharmacokinetic finding and the overall impact of that finding upon the equivalency factor between inhaled and ingested products.

First, the effective uptake of THC or THC derivatives from inhalation can be simplified using the following formula:

$$U^I = (cw)\alpha_{IN}\alpha_{EX}\beta$$

The total uptake U , is the product of the flower weight, w , times the THC/THCa content. This yields the THC weight available for inhaling. This amount is then scaled by the share of THC captured during the inhalation, α_{IN} , and also by the share of THC retained in the lungs after exhalation, α_{EX} . These inputs determine the level of THC that will ultimately be absorbed into the subject's blood plasma. Finally, the share of THC that passes through the BBB from the blood-plasma is denoted by β . The product of these parameters reveals the effective THC uptake from inhalation of activated THC.

The uptake ratio for the THC content alone can be obtained by simply dividing by the marijuana flower weight and THC concentration (cw). After doing this, we denote u^I to be the uptake conversion factor. It is:

$$u^I = \frac{U^I}{(cw)}$$

For edibles, a similar approach can be used. Edibles come in various shapes and sizes, but are required to contain 10 milligrams or less of THC per serving. This allows for a direct uptake comparison of THC content into effective THC uptake from ingestion.

In edibles, the metabolism of THC into 11-OH-THC is an important consideration. It is also important to acknowledge that the slow, steady release of THC and 11-OH-THC into the blood stream allows most, if not all, of the THC derivatives to pass through the BBB. Thus, the equation below implicitly assumes a blood-brain THC retention share of 100 percent for edible marijuana.

$$U^E = \theta\omega(1 + \gamma)$$

The total uptake equivalent, U^E , is a function of the THC absorption rate in the stomach, θ , and amount of THC in the product, by weight, ω . Next, the absorbed portion of THC is metabolized into two components, THC and 11-OH-THC, where THC enters the blood stream linearly, but 11-OH-THC, which can pass the BBB more rapidly, receives a conversion factor, γ .

As with inhaled THC, the share ratio of THC uptake can be constructed simply by dividing by the weight of the THC content in the product:

$$u^E = \frac{U^E}{\omega}$$

Finally, a simple equivalency ratio can be derived from the share-value uptake ratios. This equivalency ratio, R , is used to denote the relative psychoactive effect that is embodied in edible versus smokable marijuana products.

$$R = u^E / u^I$$

Symbol Table

Symbol	Description	Relevant Literature
U, u	Uptake equivalent amount of THC, in weight terms, and unit-free terms, for edibles (E), and for inhalation (I).	Calculated as a function of parameterized values from this report.
C	THC concentration rate in marijuana flower.	Based upon testing observations from Colorado retailers and dispensaries.
W	Weight of marijuana flower.	
α_{IN}, α_{EX}	Share of captured THC during marijuana smoke inhalation, and after exhalation, respectively.	Scientific laboratory studies of marijuana smoking. See See [20], [30], [31].
β	Brain fluid retention rate from blood plasma.	
θ	Absorption rate of THC when ingested in the form of an edible product.	[25], [24], [21], [19], and [13] are studies on oral consumption of marijuana, and its effects upon the human body.
ω	Weight of THC in edible form, in milligrams.	
y	Effective impact of 11-OH-THC that is metabolized by the liver.	Pharmacokinetic studies by [5], [1], [2], [21], and [26].
R	Equivalency ratio – the equivalent dose impact of 1 milligram of THC in edible form, in milligrams of THC in smokable form.	Calculated as a function of parameterized values from this report.

For the purposes of this study, R is the key ratio that can be used to compare edible products with smokable products, from a policy standpoint.

IDENTIFICATION OF PARAMETER VALUES

Each of the parameters in these equations has been studied to some degree. Some studies are directly relevant to specific parameter values, while others are only tangentially relevant, since they were each written for

different purposes than this equivalency study. Relevant studies are cited numerically and are included in the references section. For these reasons, this study utilizes a range of values that is based on existing research. This range of values is used to determine a point estimate for the equivalency ratio (R), which is the equivalent dose impact of 1 milligram of THC in edible form, in milligrams of THC in smokable form.

Studies related to α_{IN} and α_{EX}

The physical uptake of THC through smoking has been

discussed as part of various marijuana smoking experiments. Numerous studies examine the absorption of THC through smoking cannabis. The results of these studies vary, with one study putting the range of absorption from 2 percent - 56 percent. A study by Perez-Reyes found that absorption varied widely due to various factors, including marijuana potency, the amount of unchanged THC available in the smoke inhaled, amount of THC lost in side-stream smoke, method of smoking (i.e., cigarette or pipe) and the amount of THC passed through the upper respiratory tract. [12] A thorough examination of these studies leads to a more reasonable range of absorption through smoking of 10-25 percent. [5, 2, 10, 8, 7] This value range will be used in this study for calculations related to smoking equivalencies.

Below are relevant excerpts from the medical literature, related to the uptake ratios of inhalation and exhalation for THC absorption:

[12] *"The factor of absorption from smoking varies in terms of THC uptake and the actual amount of THC that is absorbed through smoking of marijuana. The factors that affect uptake ratios of smoking include, (1) the potency of the marijuana smoked; (2) the amount of unchanged THC present in the smoke inhaled (i.e., the amount of THC not destroyed by pyrolysis); (3) the amount of THC lost in side-stream smoke; (4) the method of smoking (cigarette vs. pipe smoking); and (5) the amount of THC trapped in the mucosa of the upper respiratory tract. These identified factors have made exact uptake ratios of THC difficult to determine, and therefore studies to this point have produced a range of THC absorption."*

[2] *"Past studies indicate that smoking cannabis turns approximately 50% of the THC content into smoke, with the remainder lost by heat or from smoke that is not inhaled. Up to 50% of inhaled smoke is exhaled again, and some of the remaining smoke undergoes localized metabolism in the lung. The end result is that the estimated*

bioavailability of a smoked dose of THC is between the range of 0.10 and 0.25."

[10] *"Bioavailability following the smoking route was reported as 2–56%, due in part to intra- and inter-subject variability in smoking dynamics, which contributes to uncertainty in dose delivery. The number, duration, and spacing of puffs, hold time, and inhalation volume, or smoking topography, greatly influences the degree of drug exposure."*

[8] *"The apparent absorption fraction calculated in the current study was in a similar range of previous findings on THC, showing an oral bioavailability of 6 %, and inhalation of 18 % (frequent smokers) or 23 % (heavy smokers)."*

[5] *"A systemic bioavailability of $23 \pm 16\%$ and $27 \pm 10\%$ for heavy users versus $10 \pm 7\%$ and $14 \pm 1\%$ for occasional users of the drug was reported."*

[7] *"Pulmonary bioavailability varies from 10 to 35 percent of an inhaled dose and is determined by the depth of inhalation along with the duration of puffing and breath-holding."*

Studies related to β

The role of the blood brain barrier (BBB) in THC and 11-OH-THC uptake is an important factor in determining equivalencies, as this function limits the flow of THC between the body's blood plasma and the brain, where it creates the psychoactive effects. As previously indicated, where THC is allowed to penetrate the BBB, the rate of penetration is slow. Below is a section from M. Huestis (2007)[10], that highlights the difficulty of THC passing through the BBB:

"Adams and Martin studied the THC dose required to induce pharmacological effects in humans. They determined that 2–22 mg of THC must be present in a cannabis

SECTION I	cigarette to deliver 0.2–4.4 mg of THC, based on 10–25% bioavailability for smoked THC. Only 1% of this dose at peak concentration was found in the brain, indicating that only 2–44 µg of THC penetrates to the brain.” [Section 2.2: Distribution]
SECTION II	The competition between blood plasma concentrations and brain tissue concentrations is described by researchers as hysteresis, an indication that the cognitive effects of THC do not occur immediately when THC blood-plasma levels are elevated, but instead, they occur after the THC has been absorbed by various body tissues (primarily, the brain). The dosing effects are said to occur after the blood level and tissue THC concentrations are equal. The following passage from Cone and Huestis (1993) describes this:
SECTION III	<i>“THC is rapidly absorbed and distributed to tissues; initial changes in blood concentrations are out of phase (hysteresis) with physiological and behavioral changes. Once blood/tissue equilibrium is established, a direct correlation of THC blood concentration and effect is observed.”</i> [Abstract]
SECTION IV	Several studies that were motivated by THC driving impairment purposes have measured the rate of blood plasma clearance. An example is Hartman, et. al. (2015), this team measures the blood plasma clearance for THC after dosing THC using a vaporizing pen. The early clearance of THC was shown to be rapid, with concentration rates falling from a peak of 60 µg/liter 10 minutes after dosing, down to 15 µg/liter 30 minutes after dosing (and 20 minutes after the peak), and then to approximately 8 µg liter 90 minutes after dosing. Small levels of
SECTION V	

THC can be observed up to seven days after dosing.¹³

Based upon the slow BBB permeability, and the relatively rapid blood clearance rate, this study assumes that only a portion, equal to 35 percent, of THC blood plasma levels end up being absorbed by receptors in the brain when smoking. The comparative rate for ingestion will be much higher, as the liver metabolizes THC more slowly, leading to a long, sustained level of blood plasma THC and 11-OH-THC.

Studies related to θ

The process of THC absorption through ingestion is more straightforward. While there can be variation in this value, depending upon the stomach contents, rate of metabolism and a number of other factors [2,13]. Grotenhermen and Schilke et al. find that the rate lies between 6-12 percent absorption, while Borgelt, Franson, Nussbaum, and Wang suggest that the rate is between 5-20 percent, with the rates typically on the lower range of absorption. Given this information, this study assumes 10 percent as a reasonable rate of THC absorption through ingestion. [2, 6, 13] These studies conclude that the absorption rate of THC through oral administration will be typically be less than that of smoking, with metabolism of THC into 11-OH-THC in the liver as a key factor in the low absorption of THC in this process.

¹³ Most of this literature is motivated to identify specific cutoff points to be considered legally “intoxicated” by THC and similar compounds. A non-psychoactive derivative of THC is 11-nor-9-carboxy-THC (THC-COOH), which is the most common trace substance used to detect marijuana use. New research focuses upon THC and 11-OH-THC since allowable levels are now needed, rather than presence alone. Colorado, for example, has a 5 µg/liter “permissible inference” law, as a cutoff value for legal intoxication of marijuana.

A WORKED EXAMPLE

For concreteness, a worked example is provided in Table IV-4. This example compares the uptake ratios for THC derivatives for 100 milligrams of THC that is either inhaled or ingested.

The result from Table IV-4 is that the equivalency ratio, R , equals 5.71, after findings from the medical literature are used to calibrate each of the uptake ratio parameters. This means that one milligram of THC in edible form, is equivalent to 5.71 milligrams of THC that is available in smokable form.

In the example above, which is based upon observations taken from metrc™, marijuana flower, or bud, has

an average potency of 17 percent.¹⁴ This implies that just over 0.5 grams (588 milligrams) of typical marijuana flower in Colorado contains 100 milligrams of THC (or THCa). From the worked example, an equivalent 100 milligrams of THC from an edible product would yield the equivalent effect of 3,361 milligrams (or 3.36 grams) of marijuana in flower form.

Due to each of the pharmacokinetic effects that are presented in this study, 100 milligrams of THC content in a smokable form, yields 7.88 milligrams of THC into the brain itself. In contrast, 100 milligrams of THC content in edible form yields a much higher ratio of 45.0 milligrams.

¹⁴ Based upon 28,023 laboratory test samples reported between October 2014 and May 2015.

Table IV-4. Example of Marijuana Equivalency Between Inhaled and Ingested Uptake Methods

Differential Uptake Equivalency: Inhaled vs. Ingested THC 100 mg Example			
Inhaled THC from Marijuana Flower		Ingested THC from Edible	
THC in Smokable Flower	100	Edible Package: (100 MG)	100
THC Content	17%	Rate of Absorption	10%
% of Content Inhaled	50%	THC absorption (mg)	10
% of Inhaled Air Exhaled	45%	11-OH-THC Conversion	3.5
Gross THC Absorption (mg)	22.5	11-OH-THC / THC Equivalent:	35.00
Blood Cycle De-Rate Factor	35%		
Effective THC Infusion to Brain (mg)	7.88	Effective THC Infusion to Brain (mg)	45.00
Equivalencies			
Flower Weight (mg)	588	Flower Weight Equivalent (mg)	3,361
THC Equivalency Ratio	1	THC Equivalency Ratio	5.71

Source: Author's calculations, combined with published medical research findings and statistical data from metrc™.

Figure IV-5. Conversion Factors between Marijuana Flower Weight and Non-flower Product Units

Conversion Factors		
Edibles (Weight to 10mg Units)		
0.25 Oz of Flower equals:	21	10mg Edible Units
1 Oz of Flower equals:	83	10mg Edible Units
1 Gram of Flower equals:	3	10mg Edible Units
Concentrates (Weight to Weight)		
0.25 Oz of Flower equals:	1.9	Grams Concentrate
1 Oz of Flower equals:	7.7	Grams Concentrate
1 Gram of Flower equals:	0.3	Grams Concentrate
Potency (THC share of weight)	62%	Based upon metrc™ Data

Source: Author's calculations, combined with medical literature findings and metrc™ data.

As discussed earlier, this is caused by a number of factors, including the time-curve of THC and 11-OH-THC blood-plasma levels in the blood and the share of that THC that can pass through the blood brain barrier.

RESULTING EQUIVALENCY TABLES

For policy purposes, Table IV-5 is constructed to compare different quantities of flower to their equivalent edible serving sizes. Concentrates are also included, using the average potency found from laboratory testing in Colorado between October 2014 and May 2015.

The equivalency ratio, *R*, can now be combined with THC content in various products, in order to construct more user-friendly conversion factors between product types. Table IV-5 lists common weights of marijuana flower that are purchased from retail and medical outlets in Colorado. Next to these weights are the number of units, based upon serving size, that are considered “equivalent” from a dosing perspective. For example, the purchase limit for an out-of-state patron at a retail marijuana store is one quarter of one ounce. This purchase limit would correspond to 21 units or servings of THC in edible form. If the edible is packaged in 100 milligram packages, then two 100 milligram packages could be purchased, plus one 10 milligram unit. That would fulfill the patron’s daily limit purchase amount of marijuana.

For enforcement purposes, residents and non-residents alike are allowed to possess up to one ounce of marijuana flower at a given time. This one ounce amount corresponds to 83 units or servings of edible products. It can be packaged in the form of eight 100 mg packages of servings, plus three 10 mg additional individually-wrapped servings.

One gram of smokable marijuana corresponds to three 10 mg servings of edible products.

Of course, any combination of these amounts is also possible. For example, an out of state patron can purchase 1/8 ounce of marijuana flower, and can also purchase 10.5 servings (105 mg) of THC in edible form. Similarly, a resident who is 21 years or older could legally possess ½ ounce of marijuana flower, plus another 41.5 servings of THC in edible form.

For concentrates, the ratio of concentrate THC to flower THC is “one to one,” because both are inhaled. Thus, the conversion factors between smoked concentrates (e.g., “dabbing”) and smoked flower products are based solely upon the THC potency embodied in the weight of

the product itself. In Colorado, the average concentration ratio for wax or shatter type concentrates was 62 percent, based upon data collected between October 2014 and May 2015. Using this ratio, combined with the 17 percent average THC ratio in Colorado marijuana flower, the smoked THC conversion factors can be easily computed. For example, using the concentrate to flower THC ratios above, the result is $62/17 = 3.65$.

For concentrates, the daily limit corresponding to one-quarter ounce of flower, is 1.9 grams of wax or shatter concentrate. Similarly, one ounce of flower equals 7.7 grams of concentrate, and one gram equals 0.3 grams of concentrate.

**OILS, TINCTURES, LOTIONS, AND
LESS COMMON UPTAKE METHODS**

In Colorado, the share of edibles and concentrates in total demand has increased substantially. This demand growth precipitated the need for further regulatory oversight for these products. There also exists a large array of additional uptake methods for consuming marijuana. These include the sublingual approach (using tinctures), dermal (using lotions), and intravenous, among other methods.

These methods are not considered here, because a full investigation into each method is beyond the scope of this report, and because the current demand levels for these methods are relatively low. If the demand shares for these methods grows and becomes more important, then some investigation is warranted.

Market Price Comparison

SECTION I
SECTION II
SECTION III
SECTION IV
SECTION V

There is a third method to consider equivalencies between marijuana products in Colorado’s retail marijuana market. This is the “market price equivalency” method. From an economic viewpoint, this method is considered to be more direct than other methods, because it compares the price per unit of THC across different products, thereby reflecting the price that consumers are willing to pay—on a THC basis—for each product type.

Until now, it was not possible to compare market prices based upon THC content. By using mandated potency tests for flower and concentrates, an average potency rate can be applied, and then compared to edibles, which are marketed with fixed levels of THC content. Prices for marijuana products are easily found on most storefront websites.

Unlike many retail consumption products, the market for marijuana is relatively homogeneous. This is different from tobacco, where consumers identify products by brand name (Marlboro, or Camels). The homogeneity of marijuana suggests that market pricing should be based primarily upon the potency of the drug, rather than by advertising or marketing influences.

Most consumers of marijuana are purchasing the product for its psychoactive properties. To the extent that the product supplies more doses, the supplier can sell the product at a higher price. Therefore, from an economic viewpoint, there should be a positive, and relatively linear, relationship between the psychoactive ingredient provided by marijuana products and the price paid for it. This relationship can be compared across different product types, and used as supporting or detracting evidence for the dosage equivalencies computed in the previous section.

Recent marijuana prices were obtained from various Colorado vendors, and a table of representative prices has been constructed. The product menu in Figure V-6

on the following page displays typical marijuana products and prices for the Colorado recreational market.

How do we know that this product menu is “representative” of other menus along the Front Range? From an economic viewpoint, this menu is “representative” because the market for marijuana is relatively competitive. If this menu were significantly more expensive, or significantly less expensive than other menus, then the company would not sell much product, or they would be selling more product than they can produce in a given period.

Similarly, if the relative pricing between product types were skewed, then buyers would only purchase selected items that are relatively inexpensive, and they would not purchase the items that are relatively more expensive. So, in addition to being “representative” in gross price, the menu here is also representative in relative price—the relationship between prices from this menu will be similar to the offerings from most Colorado retail stores.

The prices listed in Table V-6 are displayed in terms of gross weight – either for marijuana flower or the weight of THC within a non-flower product. Until now, it was not possible to compare different products in Colorado, because there was no common denominator. However, using metrc™ data, this study finds the average potency of most popular marijuana strains to be quite narrow, between 16.5 and 17.7 percent of THCa. Therefore, we can use a midpoint value of 17 percent as the average expected potency in Colorado marijuana flower sold at the retail level.

Using this potency, the menu in Table V-6, listed in dollars per weight or unit, can be converted into a uniform menu, using the weight of THC (or THCa). The most convenient unit of measure is “cents per milligram of THC” ($\text{\$/MG}_{\text{THC}}$).

Figure V-6. Market Pricing for Marijuana Products in Colorado, Priced in Dollars by Weight or by Unit

Representative Recreational Menu Prices — June 15, 2015					
Flower	Price by Weight (\$USD)				
	1 gram	1 eighth	1 quarter	1 half-oz	1 oz
Indica					
Ghost OG	14.03	41.27	82.54	148.58	264.14
Triangle Kush X Ghost OG	14.03	41.27	82.54	148.58	264.14
Sativa					
Glass Slipper	12.38	33.03	66.06	132.12	239.43
Hybrid					
White Master Kush	14.03	41.27	82.54	148.58	264.14
KING CHEM	12.38	33.03	66.06	132.10	239.43
Edibles	THC MG	Price (each)			
Highly Edible	100 mg	24.99			
Incredibles Boulder Bar	100 mg	23.11			
80 mg Dr. J's AM capsules	80 mg	19.81			
Gaia's Garden Garden Drops	80 mg	19.81			
Incredibles Peanut Budda	50 mg	19.81			
40 mg Blue Kudu Chocolate	40 mg	14.00			
Gaia's Garden Single Serving Lollipop	10 mg	6.60			
Gaia's Garden Single Serving Karma Kandy	10 mg	6.60			
Sweetgrass Snickerdoodle Cookie	10 mg	5.00			
Concentrates	THC MG	Price (g)			
O-Pen Vape Cartridge	500 mg	66.00			
Co ₂ Oil		61.92			
Mahatma Shatter		61.92			
TC Labs Shatter (Strain Specific)		55.00			
O-Pen Vape Cartridge	250 mg	46.00			

Source: Marijuana storefront websites, accessed on June 15, 2015.

SECTION I	The price ratios shown in Table V-7 on the following page are notable because they reflect—quite closely—the pharmacokinetic results found earlier. That is, the standard market pricing for edibles, when compared by THC content, has a 3:1 ratio, just as the product equivalency tables would suggest. This means that although the market participants may not have completed their own pharmacokinetic research, they naturally have gravitated toward this result, based simply upon trial and error.
SECTION II	Of course, there are some products at the edge of the pricing structure, where the price ratio for THC is higher than 3:1. For example, the “Single Serving Lollipop” is priced at 66 ¢/MG_{THC}, which results in an 8:1 ratio. This pricing relates mostly to the fact that pricing for very small servings (e.g., single servings) have a lower bound, due to packaging and marketing. The price of a single serving lollipop is \$6.60, mainly due to a lower price bound for marijuana products in general. Products that contain more than a single 10 mg serving of THC are all priced more closely to the 3:1 ratio than the single-serving units.
SECTION III	
SECTION IV	To summarize, the market price method for equivalency supports our earlier pharmacokinetic work. Market forces have led to a pricing structure that reflects a roughly 3:1 ratio between smoked THC products and edible THC products.
SECTION V	

Figure V-7. Comparison of Market Pricing Between Flower and Non-flower Products, Priced in Cents per Milligram of THC Content

Representative Recreational Menu Prices — June 15, 2015					
Flower	Price: Cents per mg THC				
	1 gram	1 eighth	1 quarter	1 half-oz	1 oz
Indica Strains					
Ghost OG	8.25	6.94	6.94	6.24	6.10
Triangle Kush X Ghost OG	8.25	6.94	6.94	6.24	6.10
Sativa Strains					
Glass Slipper	7.28	5.55	5.55	5.55	5.53
Hybrid Strains					
White Master Kush	8.25	6.94	6.94	6.24	6.10
KING CHEM	7.28	5.55	5.55	5.55	5.53
Edibles	Price: Cents per mg THC		Price Ratio: (per 1 g of Ghost OG)		
Highly Edible	100 mg	24.99	3.03		
Incredibles Boulder Bar	100 mg	23.11	2.80		
80 mg Dr. J's AM capsules	80 mg	24.76	3.00		
Gaia's Garden Garden Drops	80 mg	24.76	3.00		
Incredibles Peanut Budda	50 mg	39.62	4.80		
40 mg Blue Kudu Chocolate	40 mg	35.00	4.24		
Gaia's Garden Single Serving Lollipop	10 mg	66.00	8.00		
Gaia's Garden Single Serving Karma Kandy	10 mg	66.00	8.00		
Sweetgrass Snickerdoodle Cookie	10 mg	50.00	6.06		
Concentrates	Price: Cents per mg THC		Price Ratio: (per 1 g of Ghost OG)		
O-Pen Vape Cartridge	500 mg	18.86	2.28		
Co ₂ Oil		9.53	1.15		
Mahatma Shatter		9.53	1.15		
TC Labs Shatter (Strain Specific)		8.46	1.03		
O-Pen Vape Cartridge	250 mg	26.29	3.19		

Note: Conversions based upon average potency for flower and concentrate products in Colorado, determined through required testing of flower and concentrates.

Source: Colorado storefront menus, accessed on June 15, 2015.

References

- 1.) Baggio S, et al. Routes of administration of cannabis used for nonmedical purposes and associations with patterns of drug use. *Journal of Adolescent Health*. 2014;54(2): 235-240.
- 2.) Borgelt LM, Franson K., Nussbaum AM, Wang GS. The Pharmacologic and Clinical Effects of Medical Cannabis. *Pharmacotherapy*. 2013;33(2):195–209.
- 3.) Borns, MM, Traub SJ, Wang, GS, Wiley FJ. Cannabis (marijuana): Acute intoxication. UptoDate.com. <http://www.uptodate.com/contents/cannabis-marijuana-acute-intoxication>
- 4.) Borini, Paulo, Romeu Cardoso Guimarães, and Sabrina Bicalho Borini. "Possible hepatotoxicity of chronic marijuana usage." *Sao Paulo Medical Journal* 122.3 (2004): 110-116.
- 5.) Grotenhermen F. Pharmacokinetics and pharmacodynamics of cannabinoids. *Clin Pharmacokinet* 2003;42:327-360.
- 6.) Grotenhermen F. Clinical Pharmacokinetics of Cannabinoids. *Journal of Cannabis Therapeutics*, Vol. 3(1) 2003;3(1): 3-51.
- 7.) Grotenhermen F, et al. Developing limits for driving under cannabis. *Addiction* 102.12, 2007:1910-1917.
- 8.) Heuberger J, et al. Population pharmacokinetic model of THC integrates oral, intravenous, and pulmonary dosing and characterizes short-and long-term pharmacokinetics. *Clinical pharmacokinetics*. 2015;54(2):209-219.
- 9.) Huestis MA, Henningfield JE, Conet EJ. Blood Cannabinoids I Absorption of THC and Formation of 11-OH-THC and THCCOOH During and After Smoking Marijuana. *Journal of Analytical Toxicology*.1992;16(5):276-282.
- 10.) Huestis MA. Human Cannabinoid Pharmacokinetics. *Chemistry & Biodiversity*. , 2007;(4):1770–1804. doi: 10.1002/cbdv.200790152.
- 11.) Nadulski T, et al. Simultaneous and sensitive analysis of THC, 11-OH-THC, THC-COOH, CBD, and CBN by GC-MS in plasma after oral application of small doses of THC and cannabis extract. *Journal of analytical toxicology*. 2005;29(8):782-789.
- 12.) Perez-Reyes M. Marijuana smoking: factors that influence the bioavailability of tetrahydrocannabinol. *NIDA Res. Monogr* 99. 1990;42-62.
- 13.) Schwilke EW, et al. Δ9-tetrahydrocannabinol (THC), 11-hydroxy-THC, and 11-nor-9-carboxy-THC plasma pharmacokinetics during and after continuous high-dose oral THC. *Clinical chemistry* 2009;55(12): 2180-2189.
- 14.) Law B, Mason PA, Moffat AC, Gleadle RI, King LJ. Forensic aspects of the metabolism and excretion of cannabinoids following oral ingestion of cannabis resin. *Journal of Pharmacy and Pharmacology*. 1984;36(5): 289-294.
- 15.) Cone EJ, Huestis MA. Relating blood concentrations of tetrahydrocannabinol and metabolites to pharmacologic effects and time of marijuana usage. *Ther Drug Monit*. 1993 Dec;15(6):527-32.
- 16.) Nahas GG. Marijuana: toxicity and tolerance. *Medical Aspects of Drug Abuse*. 1975;16-36.
- 17.) Goldstein GW, Betz AL. The blood-brain barrier. *Scientific American*. 1986;255(3):74.
- 18.) Aggarwal SK, Kyashna-Tocha M, Carter GT. Dosing Medical Marijuana: Rational Guidelines on Trial in Washington State. *Medscape General Medicine*.

2007;9(3):52.

19.) Agurell S, Halldin M, Lindgren JE, et al. Pharmacokinetics and metabolism of delta 1-tetrahydrocannabinol and other cannabinoids with emphasis on man. *Pharmacol Rev* 1986;38:21–43.

20.) Brine D, Taylor H, Perez-Reyes M. Metabolism, disposition, and kinetics of delta-9-tetrahydrocannabinol in men and women. *Clinical Pharmacology & Therapeutics*. 34:352–363. doi: 10.1038/clpt.1983.179

21.) Brunet, B., & Mura, P. Cannabis and Drug-Facilitated Crimes. *Toxicological Aspects of Drug-Facilitated Crimes*, 2014;139.

22.) Busto U, Bendayan R, Sellers EM. Clinical Pharmacokinetics of Non-Opiate Abused Drugs. *Clinical Pharmacokinetics*. 1989 Jan;16(1):1-26 <http://link.springer.com/article/10.2165/00003088-198916010-00001>.

23.) Fishedick J, Van Der Kooy F, Verpoorte R. Cannabinoid receptor 1 binding activity and quantitative analysis of Cannabis sativa L. smoke and vapor. *Chemical and Pharmaceutical Bulletin*. 2010;58(2):201-207.

24.) Ginsburg BC. Toward a Comprehensive Model of D9 -Tetrahydrocannabinol Pharmacokinetics Using a Population Pharmacokinetics Approach. *Clin Pharmacokinet*. 2015;54:129–131

25.) Grotenhermen F, Leson G. Reassessing the Drug Potential of Industrial Hemp. 2002;0-48.

26.) Grotenhermen, F. Evaluation of Clinical Data. nova-Institut, Hürth, Germany.

27.) Hazekamp A, Ruhaak R, Zuurman L, van Gerven J, Verpoorte R. Evaluation of a vaporizing device (Volcano®) for the pulmonary administration

of tetrahydrocannabinol. *Journal of pharmaceutical sciences*. 2006;95(6):1308-1317.

28.) Huestis M. Pharmacokinetics and Metabolism of the Plant Cannabinoids, Δ⁹-Tetrahydrocannabinol, Cannabidiol and Cannabinol. *Handbook of Experimental Pharmacology*. 2005;168:657-690

29.) Klumpers LE, et al. Novel Δ⁹-tetrahydrocannabinol formulation Namisol® has beneficial pharmacokinetics and promising pharmacodynamic effects. *British Journal of Clinical Pharmacology*, 2012;74: 42–53. doi: 10.1111/j.1365-2125.2012.04164.x

30.) MacCoun RJ, Mello MM, . Half-Baked — The Retail Promotion of Marijuana Edibles *N Engl J Med*. 2015 Mar;372:989-991 DOI: 10.1056/NEJMp1416014.

31.) McGilveray Pharmacon Inc, and University of Ottawa, Ottawa, Ontario. Pharmacokinetics of cannabinoids. *Pain Research & Management : the Journal of the Canadian Pain Society = Journal de la Societe Canadienne Pour le Traitement de la Douleur*. 2005;(10):15A-22A. <http://europepmc.org/abstract/med/16237477>

32.) Ohlsson A, Lindgren JE, Wahlen A, Agurell S, Hollister LE, Gillespie HK. Plasma delta-9 tetrahydrocannabinol concentrations and clinical effects after oral and intravenous administration and smoking. *Clin Pharmacol Ther*. 1980;28: 409–16.

33.) Ohlsson A, Lindgren, J-E, Wahlén A, Agurell S, Hollister, LE, Gillespie HK. Single dose kinetics of deuterium labeled Δ¹-tetrahydrocannabinol in heavy and light cannabis users. *Biol. Mass Spectrom*. 1982;9: 6–10. doi: 10.1002/bms.1200090103 <http://onlinelibrary.wiley.com/doi/10.1002/bms.1200090103/abstract>

34.) Ohlsson A., Lindgren J-E, Wahlen A, Agurell S, Hollister L E, Gillespie H K. Plasma

delta-9-tetrahydrocannabinol concentrations and clinical effects after oral and intravenous administration and smoking. *Clinical Pharmacology & Therapeutics*. 1980;28:409–416. doi: 10.1038/clpt.1980.181

35.) Zuurman L, Ippel AE, Moin E, van Gerven JM. Biomarkers for the effects of cannabis and THC in healthy volunteers. *Br J Clin Pharmacol*. 2009 Jan;67(1):5-21. doi: 10.1111/j.1365-2125.2008.03329.x.

36.) Cone EJ, Huestis MA. “Relating blood concentrations of tetrahydrocannabinol and metabolites to pharmacologic effects and time of marijuana usage.” *Therapeutic Drug Monitoring*. 1993 Dec. 15(6):527-32.

37.) Musshoff F, Madea B. Review of biologic matrices (urine, blood, hair) as indicators of recent or ongoing cannabis use. *Therapeutic Drug Monitoring*. 2006;28:155-163.

38.) Hartman H.L., et. al., “Controlled Cannabis Vaporizer Administration: Blood and Plasma Cannabinoids with and without Alcohol.” *Clin Chem*. 2015 Jun;61(6):850-69. doi: 10.1373/clinchem.2015.238287. Epub 2015 May 27.

Terms & Acronyms

Butane hash oil (“BHO, dabs, shatter, wax”) — A non-polar hydrocarbon which is used as a solvent in many other industries such as essential oil extraction, butane is especially well-suited for stripping cannabis buds or trim of their cannabinoids, terpenes, and other essential oils while leaving behind the majority of unwanted chlorophyll and plant waxes. In this extraction method, the solvent washes over the plant material and is then purged off from the resulting solution using a variety of techniques and variables such as heat, vacuum and agitation.

Cannabinoid — any of the chemical compounds that are the active principles of marijuana. Cannabinoids include THC, THCa, CBD, CBDa, CBN, and other naturally occurring compounds.

CO₂ extraction — When high pressure is applied to CO₂, it becomes a liquid that is capable of working as a solvent, stripping away cannabinoids and essential oils from plant material. This process is called supercritical extraction and is the most common method of making hash oil using CO₂ instead of a hydrocarbon solvent such as butane. CO₂ extractions can take many of the same textures as BHO, but generally they tend to be more oily and less viscous.

Concentrate — Refers to any product which refines flowers into something more clean and potent. This umbrella term includes any type of hash, solventless (kief), as well as any hash oils (BHO, CO₂ oil, shatter, wax, etc.) and indicates that these products are a concentrated form of cannabis, carrying a much higher potency.

Decarboxylate — The process of converting THCa and CBDa into THC and CBD is an essential part of the process if you wish to consume cannabis orally. Decarboxylation occurs at around 240 degrees Fahrenheit, converting THCa and CBDa into THC and CBD, respectively. Though the acid forms of these cannabinoids have some medicinal benefits, normally decarboxylation is

desired for maximum potency and effect in edibles and other infused products.

Infused product — A marijuana product which is intended to be consumed orally, including but not limited to, any type of food, drink, or pill.

Edibles — Any cannabis product which is consumed orally and digested is considered an edible.

Hydrocarbon extractions — Any extraction process that uses hydrocarbons such as butane or propane.

metrc™ — Marijuana Enforcement Tracking, Reporting and Compliance is the required seed-to-sale tracking system that tracks Retail Marijuana from either the seed or immature plant stage until the Retail Marijuana or Retail Marijuana Product is sold to a customer at a Retail Marijuana Store or is destroyed.

Marijuana Infused Product manufacturer (“MIP”) — An entity licensed to purchase Retail Marijuana; manufacture, prepare, and package Retail Marijuana Product; and sell Retail Marijuana and Retail Marijuana Product only to other Retail Marijuana Products Manufacturing Facilities and Retail Marijuana Stores.

Supercritical extractions — When a substance is heated and pressurized beyond its critical point, it turns into a supercritical fluid capable of working as a solvent to strip away oils and essential compounds. It is used in a variety of industries for botanical extractions with several different types of fluid, but in the cannabis world, it generally refers to CO₂ extractions. Supercritical extraction by nature is not particularly selective in terms of what it extracts, so many CO₂ processors need to utilize a secondary solvent such as ethanol or hexane in order to remove waxes and chlorophyll prior to delivering a finished product.

THC — Tetrahydrocannabinol (THC) is the main cannabinoid found in the cannabis plant and is responsible for the majority of the plant's psychoactive properties. THC has lots of medical benefits including analgesic properties, though perhaps its most defined quality is its tendency to increase appetite. CBD acts as an antagonist to THC, reducing its psychoactive effects.

THCa — Tetrahydrocannabinolic acid (THCa) is the most prominent compound in fresh, undried cannabis. The compound does not have psychoactive effects in its own right, unless it is decarboxylated and converted into THC.

Trim — After harvest, the cannabis plant is generally trimmed of its leaf matter, leaving behind only the buds. Trimming refers to the actual act of removing the leaves, while trim refers to the leftover leaves, which can be used for making concentrates and infused products.

Vacuum purge — After extraction, most concentrates require further refining in order to remove the solvent which is remaining in the product. In order to do this, concentrate makers have utilized vacuum ovens and devices which serve to reduce the atmospheric pressure on the concentrate, which speeds up the process of removing the solvent.