COMMITTEE ON LEGISLATIVE RESEARCH
OVERSIGHT DIVISION

FISCAL NOTE

L.R. No.: 4258H.01I
Bill No.: HB 1830
Subject: Mental Health; Drugs and Controlled Substances
Type: Original
Date: January 16, 2024

Bill Summary: This proposal creates provisions relating to alternative therapies.

FISCAL SUMMARY

ESTIMATED NET EFFECT ON GENERAL REVENUE FUND				
FUND AFFECTED	FY 2025	FY 2026	FY 2027	Fully Implemented (FY Unknown)
General Revenue	($5,972,715 to $8,572,715)	($18,800,982 to $19,475,982)	($18,815,892 to $19,490,892)	Likely to exceed ($25,466,502 to 26,141,502)
Total Estimated Net Effect on General Revenue	**($5,972,715 to $8,572,715)**	**($18,800,982 to $19,475,982)**	**($18,815,892 to $19,490,892)**	**Likely to exceed ($25,466,502 to $26,141,502)**

ESTIMATED NET EFFECT ON OTHER STATE FUNDS				
FUND AFFECTED	FY 2025	FY 2026	FY 2027	Fully Implemented (FY Unknown)
Total Estimated Net Effect on Other State Funds	**$0**	**$0**	**$0**	**$0**

Numbers within parentheses: () indicate costs or losses.

ESTIMATED NET EFFECT ON FEDERAL FUNDS				
FUND AFFECTED	FY 2025	FY 2026	FY 2027	Fully Implemented (FY Unknown)
Total Estimated Net Effect on <u>All</u> Federal Funds	**$0**	**$0**	**$0**	**$0**

ESTIMATED NET EFFECT ON FULL TIME EQUIVALENT (FTE)				
FUND AFFECTED	FY 2025	FY 2026	FY 2027	Fully Implemented (FY Unknown)
General Revenue	5 FTE	5 FTE	5 FTE	5 FTE
Total Estimated Net Effect on FTE	**5 FTE**	**5 FTE**	**5 FTE**	**5 FTE**

☒ Estimated Net Effect (expenditures or reduced revenues) expected to exceed $250,000 in any of the three fiscal years after implementation of the act or at full implementation of the act.

☐ Estimated Net Effect (savings or increased revenues) expected to exceed $250,000 in any of the three fiscal years after implementation of the act or at full implementation of the act.

ESTIMATED NET EFFECT ON LOCAL FUNDS				
FUND AFFECTED	FY 2025	FY 2026	FY 2027	Fully Implemented (FY Unknown)
Local Government	**$0**	**$0**	**$0**	**$0**

FISCAL ANALYSIS

ASSUMPTION

§§ 191.479, 191.480 and 192.950– Alternate therapies

Officials from the **Department of Health and Senior Services (DHSS)** state §192.950 of the proposed legislation would require the DHSS to conduct clinical trials for alternative therapies in collaboration with a hospital operated by an institute of higher education in Missouri or contract research organizations conducting clinical trials approved by FDA. The following needs to be considered while reviewing the information below:

1. Psychedelic drugs commonly used for the purposes mentioned in the proposed legislation are MDMA, Psilocybin and Ketamine.

2. Section 192.950 states that DHSS shall conduct a study on the efficacy of using alternative medicine and therapies, including the use of Psilocybin. Since other alternative medicines and therapies are also listed, fiscal estimates provided are for the three most common therapies used for this purpose.

3. FDA came up with new draft guidance for psychedelic drugs and the fiscal estimates provided do not include any changes that might arise in the final guidance and costs associated with the assessment abuse potential of drugs, particularly for psychedelics where the abuse potential could be high.

The average cost of phase 1, 2, and 3 clinical trials across therapeutic areas is around $4, $13, and $20 million respectively. Pivotal (phase 3) studies for new drugs approved by the Food and Drug Administration (FDA) of the United States cost a median of $41,117 per patient. These cost estimates across therapeutic areas were reported by Aylin Sertkaya et al., in a report submitted to the U.S. Department of Health and Human Services: https://aspe.hhs.gov/sites/default/files/private/pdf/77166/rpt_erg.pdf (see Table 1)

Table 1: Total Per-Study Costs (in $ Millions), by Phase and Therapeutic Area [a]

Therapeutic Area	Phase 1	Phase 2	Phase 3	*Phase 1, 2, & 3 Subtotal [d]*	FDA NDA/BLA Review Phase [c]	Phase 4	Total [d]
Anti-Infective	$4.2 (5)	$14.2 (6)	$22.8 (5)	*$41.2 (3)*	$2.0	$11.0 (12)	**$54.2 (10)**
Cardiovascular	$2.2 (9)	$7.0 (13)	$25.2 (3)	*$34.4 (10)*	$2.0	$27.8 (4)	**$64.1 (6)**
Central Nervous System	$3.9 (6)	$13.9 (7)	$19.2 (7)	*$37.0 (6)*	$2.0	$14.1 (11)	**$53.1 (11)**
Dermatology	$1.8 (10)	$8.9 (12)	$11.5 (13)	*$22.2 (13)*	$2.0	$25.2 (7)	**$49.3 (12)**
Endocrine	$1.4 (12)	$12.1 (10)	$17.0 (9)	*$30.5 (12)*	$2.0	$26.7 (6)	**$59.1 (7)**
Gastrointestinal	$2.4 (8)	$15.8 (4)	$14.5 (11)	*$32.7 (11)*	$2.0	$21.8 (8)	**$56.4 (8)**
Genitourinary System	$3.1 (7)	$14.6 (5)	$17.5 (8)	*$35.2 (8)*	$2.0	$6.8 (13)	**$44.0 (13)**
Hematology	$1.7 (11)	$19.6 (1)	$15.0 (10)	*$36.3 (7)*	$2.0	$27.0 (5)	**$65.2 (5)**
Immunomodulation	$6.6 (1)	$16.0 (3)	$11.9 (12)	*$34.5 (9)*	$2.0	$19.8 (9)	**$56.2 (9)**
Oncology	$4.5 (4)	$11.2 (11)	$22.1 (6)	*$37.8 (5)*	$2.0	$38.9 (2)	**$78.6 (3)**
Ophthalmology	$5.3 (2)	$13.8 (8)	$30.7 (2)	*$49.8 (2)*	$2.0	$17.6 (10)	**$69.4 (4)**
Pain and Anesthesia	$1.4 (13)	$17.0 (2)	$52.9 (1)	*$71.3 (1)*	$2.0	$32.1 (3)	**$105.4 (2)**
Respiratory System	$5.2 (3)	$12.2 (9)	$23.1 (4)	*$40.5 (4)*	$2.0	$72.9 (1)	**$115.3 (1)**

Since psychedelic drugs such as those mentioned in this legislation (MDMA, Psilocybin and Ketamine) modulate brain cell activity, cost estimates were developed using the study costs for the central nervous system therapeutic area (row #3). Furthermore, this report was developed in 2014 and cost estimates were inflation-adjusted using the consumer price index (CPI) inflation calculator provided by the Bureau of Labor Statistics (BLS) available at: https://data.bls.gov/cgi-bin/cpicalc.pl. For example: four million dollars (estimated cost of a phase 1 trial) in 2014 would be $5,115,853.5 in 2023 – a 28% increase since 2014. This could go up when the legislation actually takes into effect as the CPI calculator will not provide inflation-adjusted estimates for 2024 at this point.

A 2018 study published in the Journal of American Medical Association (JAMA) – Internal Medicine reviewed pivotal clinical trial cost data from 59 therapeutic agents that were approved by the Food and Drug Administration (FDA) from 2015 to 2016 and derived a median cost estimate of $19.0 million (interquartile range, $12.2 million - $33.1 million). However, the cost of pivotal clinical trials varied greatly by the number of participants and the duration of study. The median cost for pivotal clinical trials with a duration of 26 weeks or greater was $51.7 million – closer to the number in the above table from the HHS report. Therefore, central nervous system estimates in the table above adjusted for inflation were used to come up with cost estimates for this proposed legislation.

Clinical trials are a kind of clinical research designed to evaluate and test new interventions such as psychotherapy or medications. Clinical trials are often conducted in four phases, not including the FDA review process –

Phase 1 - Study Participants: 20 to 100 healthy volunteers or people with the disease/condition. Length of Study: Several months, Purpose – Safety and Dosage;

Phase 2: Study Participants: Up to several hundred people with the disease/condition. Length of Study: Several months to 2 years, Purpose - Efficacy and side effects;

Phase 3: Study Participants: 300 to 3,000 volunteers who have the disease or condition. Length of Study: 1 to 4 years Purpose: Efficacy and monitoring of adverse reactions

Phase 4: Post-marketing studies, which are conducted after a treatment is approved for use by the FDA Study Participants: Several thousand volunteers who have the disease/condition, Purpose: Safety and Efficacy.

The proposed legislation is asking for a fiscal estimate for three years; therefore, the budget sheet has estimates only for Phase 1 and Phase 2 clinical trials and not for the more expensive and time intensive Phase 3 and Phase 4 clinical trials.

Phase 1 clinical trial for psilocybin (after inflation adjusted) = $5,115,854;

Phase 2 clinical trial for three drugs (after inflation adjusted) = $17,905,487.

While Phase 3 and Phase 4 clinical costs are not included in the budget sheet, the following is an estimate for those phases for the psilocybin after successful completion of phase 1 and phase 2 at the end of three years:

Phase 3 clinical trial for psilocybin (after inflation adjusted) = $24,556,097

FDA – New Drug Application (NDA) review phase (after inflation adjusted) = $2,557,927 * 3 = $7,673,780

Phase 4 clinical trial for psilocybin (after inflation adjusted) = $17,905,487 * 3 = $53,716,462

The DHSS does not conduct clinical trials nor has any experience conducting clinical trials. While the legislation clearly states that DHSS / Office of Epidemiology (OOE) would collaborate with a hospital operated by an institute of higher education in Missouri or Contract Research Organization (CRO's), OOE would require at least three (3) FTEs to coordinate / oversee clinical trials in collaboration with institutes of higher education. The 4 FTE request is only for the first three years and to set up the clinical trials. Based on literature review of clinical trials, it is estimated that the following minimum staff would be needed for the first three years:

Clinical Study Medical Writer (One FTE @ $74,600 annual salary) – The proposed legislation requires quarterly as well as annual reports on the progress of trials to the legislature. A medical writer would be needed to produce quarterly reports in conjunction with the entities conducting trials.

Clinical Research Physician (One FTE @ $203,682 annual salary) – While the clinical trials will

be conducted in collaboration with institutes of higher education, it is essential for DHSS to hire a clinical research physician so that they can coordinate with the institutes on clinical trial plans and update DHSS / legislature accordingly on the progress and handle any clinical questions / issues from stakeholders / legislators on clinical trials.

Clinical Project Manager (One FTE @ $84,900 annual salary)- While the clinical trials will be conducted in collaboration with institutes of higher education, it is essential for DHSS to hire a clinical project manager as well who will work with the physician to ensure plans/protocols are being implemented in accordance with the terms and conditions set forth for clinical trials, handle unexpected issues that arise during clinical trials and to act as a liaison between DHSS / clinical trial site staff to ensure clinical trials to meet scientific standards and government regulations.

Administrative Support Professional (one FTE @ $47,990 annual salary) – While the clinical trials will be conducted in collaboration with institutes of higher education, it is essential for DHSS to hire an administrative support professional to coordinate the activities of the project manager, medical writer and research physician.

Legal Counsel (unknown up to one FTE @ $82,999 annual salary) – There will be need for research and review of grant/clinical study documents. DHSS does not otherwise conduct clinical trials/studies and the program will need legal guidance as we navigate this new area. The legal counsel need is unknown up to one (1) FTE.

Due to the risks associated with a clinical trial and the complexities of documentation review, specialized outside legal counsel would be needed. Based on the following assumptions: Legal consult team of 1-3 attorneys, estimated billing $300-$500 per hour (due to specialized field), and estimated need of 500 hours (10 hours per week) for the first year for each attorney and 250-500 hours per week for each attorney thereafter. The estimated cost of outside specialized counsel is $150,000 - $750,000 for the first year and $75,000 - $750,000 thereafter.

At the end of three years, and if phase 2 clinical trials are successful, the staffing needs will significantly increase because phase 3 trials are usually conducted at multiple sites in different countries and will likely involve significant DHSS staff involvement/travel to ensure these trials are conducted in compliance with the countries where these trials are conducted with respect to human subject involvement and adverse event reporting. It is not possible to estimate DHSS staffing needed for phase 3 and phase 4 at this time because of the uncertainty associated with phase 2 clinical trials. Only 33% of phase 2 clinical trials move onto a phase 3 clinical trial.

Consideration needs to be given to the following notes with respect to this proposed legislation: The three common psychedelics that are relevant to treating the conditions listed in the legislation are – Ketamine, MDMA and Psilocybin.

In Summary –
The state will effectively spend upwards of 200 million dollars (likely to go up) to conduct trials for three alternative medicines that have already been extensively studied. Of the three:

- One has already been approved by FDA (ketamine)
- A new drug application (NDA) has already been filed with the FDA for the other one – MDMA
- The third one – Psilocybin is already in phase 3 clinical trials on a global scale and based on phase I and phase II studies shows promising results.

Oversight does not have any information to the contrary. Based on an internet search of the average length of time for clinical trials, it is possible for them to go on for 10-15 years. Therefore, for fiscal note purposes Oversight assumes costs could exceed the $53,716,462 provided by DHSS for Phase 4 Clinical Trials. It is unknown in what year the provisions of this proposal would be concluded.

Oversight does not have information to the contrary and therefore, Oversight will reflect the estimates as provided by the DHSS.

Oversight notes the provisions of §191.479.4 allows DHSS to provide grants for $2,000,000, subject to appropriation. For fiscal note purposes, Oversight assumes costs of $0 to ($2,000,000) to the General Revenue Fund for the research grants. **Oversight** notes that the proposal specifies a total of $2,000,000 for grants.

Responses regarding the proposed legislation as a whole

Officials from the **Office of Attorney General (AGO)** assume any additional litigation costs arising from this proposal can be absorbed with existing personnel and resources. However, the AGO may seek additional appropriations if there is a significant increase in litigation.

Oversight does not have any information to the contrary. Therefore, Oversight assumes the AGO will be able to perform any additional duties required by this proposal with current staff and resources and will reflect no fiscal impact to the AGO for fiscal note purposes.

Officials from the **Department of Commerce and Insurance**, the **Department of Mental Health**, the **Department of Public Safety – Missouri Veterans Commission** and the **Office of the State Courts Administrator** each assume the proposal will have no fiscal impact on their respective organizations. **Oversight** does not have any information to the contrary. Therefore, Oversight will reflect a zero impact in the fiscal note for these agencies.

Officials from the **University of Missouri System** did not respond to **Oversight's** request for a statement of fiscal impact.

FISCAL IMPACT – State Government	FY 2025 (10 Mo.)	FY 2026	FY 2027	Fully Implemented (FY Unknown)
GENERAL REVENUE FUND				
Costs – DHSS (§191.479) grants for research on use/efficacy of psilocybin p.5	$0 to ($2,000,000)	$0	$0	$0
Costs – DHSS (§192.950) – clinical trial p.				Likely to exceed...
Personal service	($411,809)	($504,054)	($514,136)	($514,136)
Fringe benefits	($222,196)	($270,466)	($274,374)	($274,374)
Equipment and expense	($72,856)	($45,975)	($46,895)	($46,895)
Legal Consultant	($150,000 to $750,000)	($75,000 to $750,000)	($75,000 to $750,000)	($75,000 to $750,000)
Contracts – Phase 1	($5,115,854)	$0	$0	$0
Contracts – Phase 2	$0	($17,905,487)	($17,905,487)	$0
Contracts – Phase3+	$0	$0	$0	($24,556,097)
Total Costs - DHSS	($5,972,715 to $6,572,715)	($18,800,982 to 19,475,982)	($18,815,892 to $19,490,892)	($25,466,502 to $26,141,502))
FTE Change - DHSS	5 FTE	5 FTE	5 FTE	5 FTE
ESTIMATED NET EFFECT ON THE GENERAL REVENUE FUND	**($5,972,715 to $8,572,715)**	**($18,800,982 to $19,475,982)**	**($18,815,892 to $19,490,892)**	**Likely to exceed ($25,466,502 to $26,141,502)**
Estimated Net FTE Change on the General Revenue Fund	5 FTE	5 FTE	5 FTE	5 FTE

FISCAL IMPACT – Local Government	FY 2025 (10 Mo.)	FY 2026	FY 2027	Fully Implemented (FY Unknown)
	$0	**$0**	**$0**	**$0**

FISCAL IMPACT – Small Business

No direct fiscal impact to small businesses would be expected as a result of this proposal.

FISCAL DESCRIPTION

As specified in this bill, any person who acquires, uses, produces, possesses, transfers, or administers psilocybin for the person's own therapeutic use will not be in violation of state or local law and will not be subject to a civil fine, penalty, or sanction so long as the person meets the certain conditions.

The DHSS must prepare and submit to the Governor, Lieutenant Governor, and the General Assembly annual reports on any information collected by the Department on the implementation and outcomes of the use of psilocybin.

This bill specifies that, a physician will not be subject to criminal or civil liability or sanction under the laws of this State for providing documentation that a person suffers from posttraumatic stress disorder, major depressive disorder, or a substance use disorder or requires end-of-life care, and no State agency or regulatory board shall revoke, fail to renew, or take any other action against a physician's license issued under Chapter 334, RSMo based solely on the physician's provision of documentation that a person suffers from posttraumatic stress disorder, major depressive disorder, or a substance use disorder or requires end-of-life care.

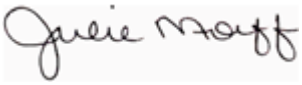
This bill also requires the Department, in collaboration with a hospital operated by the an institution of higher education in this state or contract research organizations conducting trials approved by the United States Food and Drug Administration in Missouri, to conduct a study on the efficacy of using alternative medicines and therapies, including, but not limited to, the use of psilocybin for the treatment of patients suffering from post-traumatic stress disorder, major depressive disorder, substance use disorders, or who require end-of-life care. The bill specifies that such study shall include a clinical trial of psilocybin, as well as a literature review and the submission of various reports. No person participating in the clinical trial shall be subjected to criminal or civil liability or sanction for the participation in the clinical trial, except in cases of gross negligence or willful misconduct.
The Department must maintain the confidentiality of any personally identifiable protected information collected during the clinical trial. A physician will not be subject to criminal or civil

liability or sanction under the laws of this state for referring a patient to the clinical trial under this section, and no state agency or regulatory board shall revoke, fail to renew, or take any other action against a physician's license based solely on the physician's referral of a patient to the clinical trial under this section. (§192.950)

This legislation is not federally mandated, would not duplicate any other program but would require additional capital improvements or rental space.

SOURCES OF INFORMATION

Attorney General's Office
Department of Commerce and Insurance
Department of Health and Senior Services
Department of Mental Health
Department of Public Safety –
Missouri Veterans Commission
Office of the State Courts Administrator



Julie Morff
Director
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Ross Strope
Assistant Director
January 16, 2024