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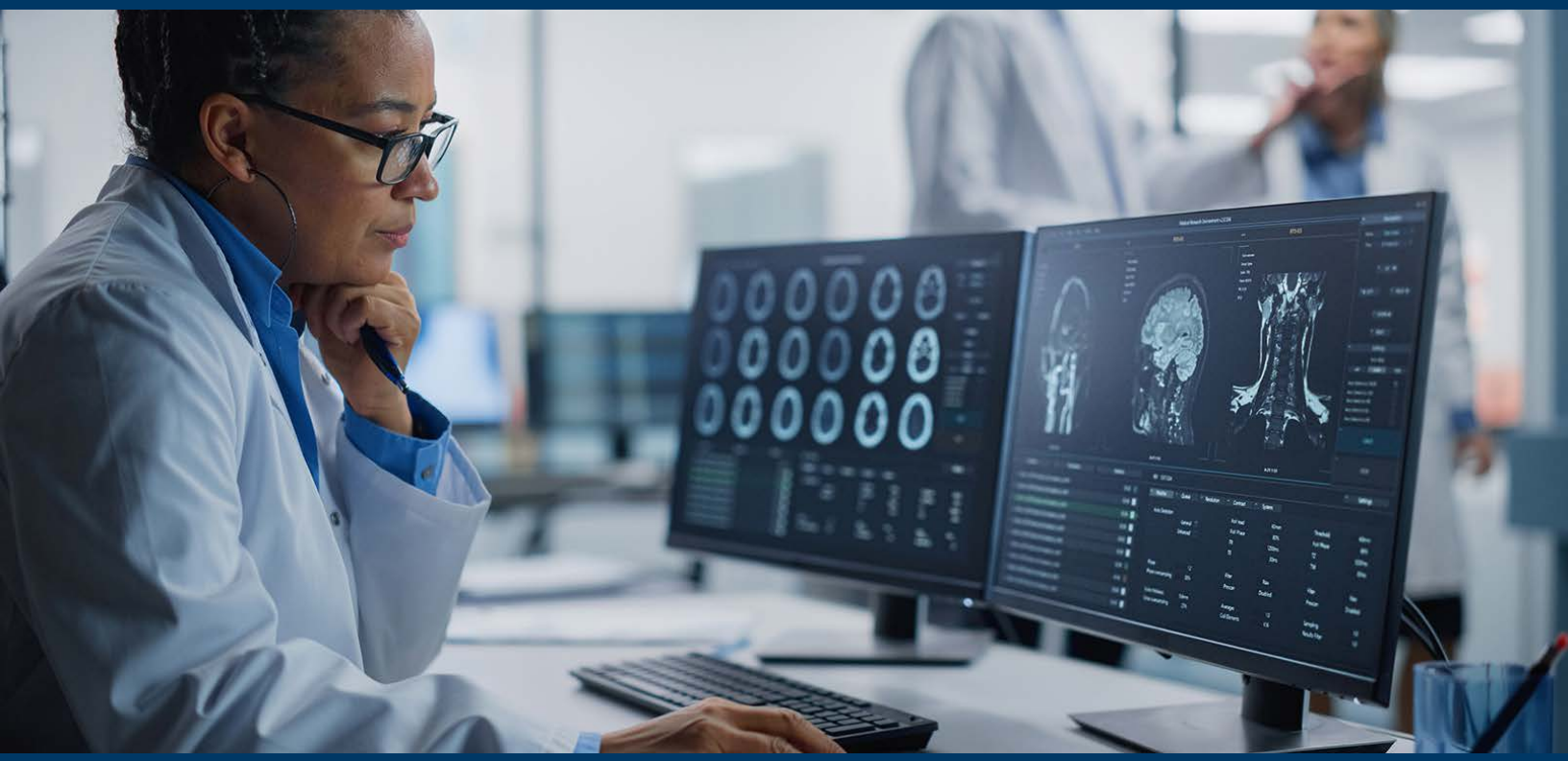

Spinal Cord Injury and Traumatic Brain Injury Research Grant Program 2025 Report

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About the Office of Higher Education

The Minnesota Office of Higher Education is a cabinet-level state agency providing students with financial aid programs and information to help them gain access to postsecondary education. The agency also serves as the state's clearinghouse for data, research and analysis on postsecondary enrollment, financial aid, finance and trends.

The Minnesota State Grant Program is the largest financial aid program administered by the Office of Higher Education, awarding more than $224 million annually in need-based grants to Minnesota residents attending eligible colleges, universities and career schools in Minnesota. The agency oversees other state scholarship programs, tuition reciprocity programs, a student loan program, Minnesota's 529 College Savings Plan, licensing and early college awareness programs for youth.

About This Report

This is a legislative-mandated report. As requested by Minnesota Statutes, section 3.197, this report cost approximately $582.90 to prepare, including staff time.

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Executive Summary

The Spinal Cord Injury and Traumatic Brain Injury (SCI-TBI) Research Grant, established in 2015 by the State of Minnesota, received 33 proposals for fiscal year 2024. Following a competitive review, the SCI-TBI Advisory Council awarded 19 projects totaling $3,000,000.

Introduction

The State of Minnesota established the Spinal Cord Injury and Traumatic Brain Injury (SCI-TBI) Research Grant Program on July 1, 2015, in accordance with Minnesota 2015 Session Law, Chapter 69. This statute directed the Minnesota Office of Higher Education (OHE) Commissioner to establish a grant program for institutions in Minnesota to conduct research that would lead to new and innovative treatments and rehabilitative efforts for the functional improvement of people with spinal cord injuries and traumatic brain injuries. Research areas include, but are not limited to, pharmaceutical, medical devices, brain stimulus, and rehabilitative approaches and techniques. Appendix A provides a copy of the grant program's founding statute.

In July 2018, the Spinal Cord Injury and Traumatic Brain Injury Grant Program was given a Special Revenue Account by Minnesota Management and Budget in order to extend project periods from one to two years to a two-to-five-year timeline. Beginning in FY 2020, new grantees were given two to five years to complete their research projects, with a possibility for an extension based on their progress and the complexity of the research. The timeline extension is crucial for the completion of projects based on the lengthy institutional review board (IRB) review processes. It also accounts for any unexpected challenges that occur naturally with complex research and experimentation. The Special Revenue Account continues to support the program and its grant recipients, as these projects have proven to take several years to complete.

For the 2023-2024 biennium, $3,000,000 was made available for each year from the 2023 Omnibus Higher Education Bill (Minnesota 2021 Session Law, 1st Special Session, Chapter 2[1]) to support the SCI-TBI Grant Program, with a three percent administrative fee. As directed by the program's statute, the Commissioner of the Office of Higher Education, in consultation with the program's Spinal Cord Injury and Traumatic Brain Injury Advisory Council (Advisory Council), allocated 50 percent of the grant funds to research involving spinal cord injuries and 50 percent to research involving traumatic brain injuries throughout the biennium.

Spinal Cord Injury and Traumatic Brain Injury Advisory Council

The 2015 statute language establishing the grant program also required creation of the Spinal Cord and Traumatic Brain Injury Advisory Council. The Commissioner, in consultation with the Advisory Council, has the responsibility of awarding the SCI-TBI grants and developing the program. In 2015, an initial 12-member

[1] https://www.revisor.mn.gov/laws/2021/1/Session+Law/Chapter/2/

Advisory Council was set up using the Open Appointments process of the Minnesota Secretary of State's office. In 2017, the statute language was updated to include two new seats: 1) Veteran with a Traumatic Brain Injury, and 2) Physician Specializing in the Treatment of Spinal Cord Injury. Both seats were filled in 2018, although the Veteran with a Traumatic Brain Injury representative resigned at the end of 2018 due to personal reasons.

Veteran representation is a persistent challenge for maintaining continuity within the Advisory Council. Since the resignation the veteran representative living with a Traumatic Brain Injury in 2018, this seat has remained open despite many attempts to recruit eligible community members. Many veterans who have joined the council do not persist through their first year for personal reasons, mainly related to their health and wellness. A future consideration is to reconfigure those council seats so that veterans with these injuries may send a representative from the Minnesota Department of Veterans Affairs or another an organization representing Veterans in their place or find other meaningful ways to participate on the council without holding a permanent seat.

In 2023, several of the 2022 appointments were also up for renewal. The Commissioner of the Office of Higher Education selected the Advisory Council through the Minnesota Secretary of State's Open Appointments process. The full membership of the Advisory Council at the time of the 2024 Grant Review is shown below:

Table 1: Advisory Council Roster

Member	Representing
Dr. Uzma Samadani	Physician specializing in the treatment of traumatic brain injury
Dr. David Titus	University of Minnesota Medical School
Dr. Peter J. Grahn	Mayo Clinic
Dr. Margaret M. Weightman	Courage Kenny Rehabilitation Center
Dr. Matthew Puderbaugh	Hennepin County Medical Center
Dr. Andrew W. Grande	Neurosurgeon
Mr. Robert Wudlick	Community member living with a spinal cord injury
Mr. Matthew Rodreick, Chair	Family member of a person with a spinal cord injury
Dr. Aleta Steevens	Community member living with a traumatic brain injury
Mr. David Sullivan-Nightengale	Veteran living with a spinal cord injury
OPEN	Veteran who has a traumatic brain injury
Dr. Mark Gormley	Gillette Children's Specialty Healthcare
OPEN	Family member of a person who has a traumatic brain injury
Dr. Ann Parr	Physician specializing in the treatment of spinal cord injury

Fiscal Year 2024 Annual Research Grant

In fiscal year 2024, $3,000,000 was available to award to research projects through the SCI-TBI Annual Research Grant.

Timeline

The timeline for the annual research grant opportunity was as follows:

- March 27, 2024: Request for Proposals available to applicants
- May 22, 2024: Deadline for receipt of intent to submit forms
- May 29, 2024: Deadline for receipt of proposals
- June 25, 2024: Proposal Review Meeting/Project Presentations
- July 5, 2024: Notification of recommendation for grant award
- August-September 2024: Project funding begins with grant contract encumbrance

On May 29, 2024 OHE received a total of 33 proposals (18 TBI and 15 SCI) totaling $7,700,000 in requests. The total request for TBI research projects was $4,093,090.48 and the Advisory Council selected 11 projects to receive awards, totaling $1,455,000.00. Of the $3,573,931.12 in total requests for SCI research, the Advisory Council selected eight projects totaling $1,455,000.00.

Fiscal Year 2024 Awarded Research Grant Summaries

Spinal Cord Injury Research Grants

Use Of Genetically Modified Mesenchymal Stromal Cells or Extracellular Vesicles To Deliver IL-10 Following SCI To Modulate Local And Systemic Inflammation
Mayo Clinic, Receives $190,000

The purpose of this study is to investigate the additive effect of IL-10 enhancement of MSCs on recovery following SCI through local or systemic immunomodulation and determine the optimal infusion protocol. Grantee hypothesizes that reducing inflammation will increase cell survival resulting in functional benefits after SCI. Furthermore, the route of administration would differently enhance regeneration by modulating local inflammation and regenerative processes verses through changes in systemic inflammation and adaptative immunity. The Mayo Clinic is also developing an allogenic MSC bank that will be used to support future clinical investigation using uniform allogenic source for genetically enhanced cells facilitating immediate and early use in SCI.

Principal Investigator: Ahad Siddiqui, siddiqui.ahad@mayo.edu, 507-293-9014

Optimizing Epidural Spinal Cord Stimulation Care: A Comprehensive Approach Integrating PulseShare Utility, Mobile App Development, and Creating an Instructional Guide for Patients and Healthcare Professionals
Minneapolis VA Healthcare System, Receives $190,000

This grant has the following aims:

(1) Users' active participation in iterative surveys on PulseShare will lead to continuous improvement of the platform, resulting in increased user satisfaction and effectiveness in facilitating communication and information sharing among patients, physical therapists, and other healthcare professionals (HCPs).

(2) The development and deployment of a mobile application through PulseShare will enhance the accessibility and usability of the platform, fostering ongoing exchange of insights and data between patients and HCPs. This improved communication channel will facilitate more effective collaboration in optimizing eSCS therapy and improving patient outcomes in spinal cord injury rehabilitation.

(3) Patient engagement in sharing parameter data collected during eSCS placement procedures, post-operative care, and physical therapy appointments will contribute to the expansion of the database on PulseShare. This growth in data will enable meaningful analyses, leading to the development of an instructional manual for eSCS programming that is tailored to patient needs and experiences.

Principal Investigator: Uzma Samadani MD PhD, uzma@samadani.com, 917-388-5740

Reduction Of Oxidative Stress by ROSASINA And Promote Neurological Recovery In The Spinal Cord Injury (SCI)
University of Minnesota, Receives $100,000

Grantee believes ROSASINA can protect the cells from ROS and help people recover better from SCI. ROS is important for keeping the body working normally, but making too many of ROS can harm the cells. Cells make special enzymes to control the amount of ROS. But sometimes, the body makes too many ROS and the enzymes cannot control it, which can damage the cells. Doctors have tried using natural antioxidants, such as vitamins C and E, to control the amount of ROS in patients with SCI. But these antioxidants did not work well for SCI patients. So, they are using a special chemical called "ROSASINA" to stop cells from making too many ROS at the site of injury.

Principal Investigator: Gatikrushna Singh, gsingh@umn.edu, 612-301-6042

Neuromodulation For Recovery Through ECAP Mapping and Personalized Stimulation
University of Minnesota, Receives $325,000

The central hypothesis of this research is that high-resolution, personalized mapping of spinal cord stimulation (SCS) can optimize stimulation parameters, leading to improved motor function restoration in individuals with chronic spinal cord injury (SCI). The study addresses three key questions: How do muscle responses to SCS vary with changes in stimulation location, amplitude, and frequency? Can personalized stimulation patterns effectively restore functional movements? Will these activation maps remain stable over time, ensuring consistent therapeutic benefits and guiding optimal adjustments?

Principal Investigator: David Darrow, darro015@umn.edu, 612-624-6666

Sustained Delivery Of Therapeutic Mrnas For Glial Scar Degradation and Axonal Regeneration
University of Minnesota, Receives $190,000

Grantee hypothesizes that (i) physicochemical properties of MCMs (e.g., dissolution rate and microparticle size) will dictate the transfection efficiency of the complexed mRNA and the duration of biological activity of the

overexpressed proteins, and (ii) overexpressed ChABC and neurotrophic factors (NT-3, NGF, BDGF and GDNF) will be sequestered by MCMs and maintain biological activity for an extended time period to be able to degrade glial scar and induce axonal regrowth, respectively. Objectives of the proposed studies are to (1) establish a well-defined non-viral mRNA delivery system, in which the physicochemical properties of MCMs will be modulated to improve mRNA transfection and extend biological activity of overexpressed proteins, and (2) develop MCM-mediated mRNA delivery in which overexpressed ChABC and neurotrophic factors (NT-3, NGF, BDNF and GDNF) will effectively remove glial scar and promote axon regeneration, respectively.

Principal Investigator: Jae Sung Lee, andjslee@umn.edu, 612-625-1409

Viral-Based Reprogramming Platform for A SCI Therapeutic Approach Of Neurorestoration
University of Minnesota, Receives $190,000

In preliminary studies Grantee has observed improved responses to sensory stimulation in rats with spinal cord injury following the genetic reprogramming of astrocytes to become neurons within the lesioned cavity. The mechanisms underlying the restoration of somatic sensory function in spinal cord injury is at present undetermined. Their hypothesis is that astrocyte reprogramming has led to new connections between neurons to be formed. Recent studies also indicate that activation of neural circuits can lead to enhanced recovery of locomotor function following spinal cord injury. They hypothesize that astrocyte reprogramming combined with activation of motor circuits by way of physical therapy will be synergistic in improving locomotor function.

Principal Investigator: Andrew Grande, grande@umn.edu, 612-624-6666

Investigating the Effect of Purmorphamine on Endogenous Neural Stem Cell by Activating the Sonic Hedgehog Pathway to Promote Regeneration in Rats with Spinal Cord Injury
Mayo Clinic, Receives $80,000

Grantee hypothesizes that PUR-mediated activation of the SMo-Shh pathway will activate eNSC proliferation, and promote neurological recovery after SCI.

Principal Investigator: Mohamad Bydon, MD, bydon.mohamad@mayo.edu, 507-284-4477

Generating Exogenic Spinal Neurons in Homeobox Gene Knockouts for Repair in Spinal Cord Injury
University of Minnesota, Receives $190,000

Grantee hypothesizes that region-specific neurons generated by the process of blastocyst complementation can serve as a source of authentic neurons for transplantation following chronic spinal cord injury and reinstate appropriate neuronal circuits to restore the function of movement and sensory sensation.

Principal Investigator: Walter Low, lowwalt@umn.edu, 612-791-9124

Traumatic Brain Injury Research Grants

Predicting the consequences of chronic effects of neurotrauma in pediatric patients using image processing, machine learning, and MRI
Minneapolis VA Healthcare System, Receives $160,000

Grantee proposes that objective markers of neurostructural damage from the chronic effects of neurotrauma as caused by mild TBI, can be distinguished when compared to age- and sex- matched subjects using radiological analysis of structural head MRI scans in a pediatric population. From this comparative analysis, they aim to develop a computational methodology using image processing and machine learning to better characterize and predict the chronic outcomes of neurotrauma, in hopes to develop early intervention care strategies.

Principal Investigator: Uzma Samadani MD PhD, uzma@samadani.com, 917-388-5740

Development of a Brain Organoid-Derived Exosome Product for the Treatment of Traumatic Brain Injury
University of Minnesota, Receives $75,972

Grantee hypothesizes that exosomes produced by brain organoids, in addition to their direct anti-inflammatory actions may also provide indirect neuroprotective effects by the induction and activation of A2 astrocytes which have been shown to have anti-inflammatory and neuroprotective functions in the brain.7 Thus brain organoid-derived exosomes will provide regenerative factors that will induce reversal and repair of TBI-induced neurodegeneration in the mouse TBI model.

Principal Investigator: Dr. Timothy O'Brien, obrie004@umn.edu, 612-625-8175

Reading after Traumatic Brain Injury: Development of a Guiding Model for Assessment and Treatment
Courage Kenny Rehabilitation Institute, Allina Health, Receives $83,440

Grantee's central question is: What factors are associated with better reading experiences for people with TBI?

Principal Investigator: Katy H. O'Brien, katy.obrien@allina.com, 612-636-1621

Mechanically-induced glymphatic dysfunction as a mechanistic link for TBI and neurodegenerative disease
University of Minnesota, Receives $160,000

Grantee hypothesizes that the extreme forces present during TBI initiate cell processes in vascular smooth muscle cells (artery cells) and astrocytes (brain cells) that lead to alteration of the material properties of both the brain blood vessels and tissue, which subsequently reduces the ability of the glymphatic system to remove waste.

Principal Investigator: Patrick Alford, pwalford@umn.edu, 612-625-4801

Personalized Accelerated Theta Burst Transcranial Magnetic Stimulation in Mild Traumatic Brain Injury
HealthPartners Institute, Receives $160,000

Grant Aim: To develop and test a patient-centered, personalized, and precise targeting with TMS to treat persistent post-concussive symptoms.

Principal Investigator: Bhavani Kashyap, bhavani.x.kashyap@healthpartners.com, 651-495-6358

Reprogramming for Neurorestorative Therapy after Traumatic Brain Injury
University of Minnesota, Receives $160,000

Grantee hypothesizes that using gene therapy to reprogram astrocytes to neurons after a moderate TBI will protect the brain and promote a functional recovery.

Principal Investigator: Andrew Grande, grande@umn.edu, 612-624-6666

Integrating Acute Phase Stem Cell Therapy and Chronic Phase Neurostimulation for PTSD Following Repetitive Mild Traumatic Brain Injury
University of Minnesota, Receives $75,971

The outcome of this pilot study supports previous studies indicating that an increase in avoidance is typically accompanied by an alteration in neuronal communication between critical brain regions such as the medial prefrontal cortex (mPFC), the basolateral amygdala (BLA), and the hippocampus (HPC). This communication occurs via low-frequency (Theta band 4-8 Hz) rhythmic neuronal oscillations, and changes in these rhythmic oscillations in the mPFC, BLA, and HPC are associated with psychiatric disorders. Therefore, Grantee hypothesizes that combining neuroprotection during the critical period immediately after injury (acute phase) and neurostimulation of brain circuitry involved in PTSD during the chronic recovery phase will mitigate mental health illnesses after RmTBI.

Principal Investigator: David J Titus, adaik023@umn.edu, 608-770-2646

Exploring Neuroinflammation and Neural Circuitry Reorganization Associated with Exacerbation of Addiction Behavior in Mild Traumatic Brain Injury
University of Minnesota - College of Veterinary Medicine, Receives $99,617

Grantee hypothesizes that exacerbated neuroinflammation leads to the reorganization of neural circuitry within the medial prefrontal cortex (mPFC), nucleus accumbens (NAc), and ventral tegmental area (VTA) pathways, intensifying addiction behavior.

Principal Investigator: Dr. Maxim Cheeran, cheeran@umn.edu, 612-626-9930

Mitochondrial Transplantation for Repair in Traumatic Brain Injury
University of Minnesota, Receives $160,000

Central Question: Is mitochondrial transplantation an effective form of therapy for treating traumatic brain injury?

Principal Investigator: Walter Low, lowwalt@umn.edu, 612-791-9124

Closed Head TBI In Humanized Mice: Histopathology, Behavior, Cortical Neural Dynamics, And Novel Therapeutics
University of Minnesota, Receives $160,000

To address the issue of human versus mouse susceptibility to mTBI, Grantee will use a new humanized mouse model that replaces three full-length human genes known to cause neuropathological changes in the brain following TBI. They will test the hypothesis that mTBI in these mice will disrupt cerebral cortical functioning, leading to deficits in decision making and memory in mice moving freely in a maze. Finally, they will test the hypothesis that administration of drugs known to inhibit the toxic effects of tau will lead to a marked reduction in tau and APP pathology following mTBI as well as less disruption in brain activity and cognitive performance.

Principal Investigator: Timothy J. Ebner, ebner001@umn.edu, 612-296-5715

Trigeminal Nerve Stimulation to Enhance Brain Clearance After TBI
University of Minnesota, Receives $160,000

Grantee hypothesizes that TNS reduces brain edema after TBI by enhancing glymphatic flow. They seek to directly show that TNS enhances glymphatic transport in the brain after TBI, and they will also identify a nearly-optimal set of TNS parameters.

Principal Investigator: Jeffrey Tithof, tithof@umn.edu, 651-246-4150

Appendix A: Copy of Statute

Laws of Minnesota 2021

136A.901 SPINAL CORD INJURY AND TRAUMATIC BRAIN INJURY RESEARCH GRANT PROGRAM.

Subd 1. Grant program

The commissioner shall establish a grant program to award grants to institutions in Minnesota for research into spinal cord injuries and traumatic brain injuries. Grants shall be awarded to conduct research into new and innovative treatments and rehabilitative efforts for the functional improvement of people with spinal cord and traumatic brain injuries. Research topics may include, but are not limited to, pharmaceutical, medical device, brain stimulus, and rehabilitative approaches and techniques. The commissioner, in consultation with the advisory council established under section 136A.902, shall award 50 percent of the grant funds for research involving spinal cord injuries and 50 percent to research involving traumatic brain injuries. In addition to the amounts appropriated by law, the commissioner may accept additional funds from private and public sources. Amounts received from these sources are appropriated to the commissioner for the purposes of issuing grants under this section.

Subd. 2. Report

By January 15, 2016, and each January 15 thereafter, the commissioner shall submit a report to the chairs and ranking minority members of the senate and house of representatives committees having jurisdiction over the Office of Higher Education, specifying the institutions receiving grants under this section and the purposes for which the grant funds were used.

136A.902 SPINAL CORD AND TRAUMATIC BRAIN INJURY ADVISORY COUNCIL.

Subd 1. Membership

The commissioner shall appoint a 14-member advisory council consisting of:

(1) one member representing the University of Minnesota Medical School;

(2) one member representing the Mayo Medical School;

(3) one member representing the Courage Kenny Rehabilitation Center;

(4) one member representing Hennepin County Medical Center;

(5) one member who is a neurosurgeon;

(6) one member who has a spinal cord injury;

(7) one member who is a family member of a person with a spinal cord injury;

(8) one member who has a traumatic brain injury;

(9) one member who is a veteran who has a spinal cord injury;

(10) one member who is a veteran who has a traumatic brain injury;

(11) one member who is a family member of a person with a traumatic brain injury;

(12) one member who is a physician specializing in the treatment of spinal cord injury;

(13) one member who is a physician specializing in the treatment of traumatic brain injury; and

(14) one member representing Gillette Children's Specialty Healthcare.

Subd. 2. Organization

The advisory council shall be organized and administered under section 15.059, except that subdivision 2 shall not apply. Except as provided in subdivision 4, the commissioner shall appoint council members to two-year terms and appoint one member as chair. The advisory council does not expire.

Subd. 3. First appointments and first meeting

The commissioner shall appoint the first members of the council by September 1, 2015. The chair shall convene the first meeting by November 1, 2015.

Subd. 4. Terms of initial council members

The commissioner shall designate six of the initial council members to serve one-year terms and six to serve two-year terms.

Subd. 5. Conflict of interest

Council members must disclose in a written statement any financial interest in any organization that the council recommends to receive a grant. The written statement must accompany the grant recommendations and must explain the nature of the conflict. The council is not subject to policies developed by the commissioner of administration under section 16B.98.

Subd. 6. Duties.

The advisory council shall:

(1) develop criteria for evaluating and awarding the research grants under section 136A.901;

(2) review research proposals and make recommendations by January 15 of each year to the commissioner for purposes of awarding grants under section 136A.901; and

(3) perform other duties as authorized by the commissioner.

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