Statement for the Record of the House Committee on Veterans' Affairs Hearing on

"Overcoming PTSD: Assessing VA's Efforts to Promote Wellness and Healing"

Submitted on behalf of the Coalition to Heal Invisible Wounds

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Chairman Roe, Ranking Member Walz and members of the Committee,

On behalf of the Coalition to Heal Invisible Wounds, thank you for this opportunity to provide written testimony on the effectiveness of care for post-traumatic stress disorder (PTSD) within the current system of health care services and benefits of the Department of Veterans' Affairs (VA).

In this testimony, we introduce the Coalition and its objectives and outline initial steps at the VA to begin addressing these objectives through, in the words of VA, "radically collaborative science."

I. Introduction

The Coalition to Heal Invisible Wounds was founded in February 2017 to connect leading public and private scientific investigators of new PTSD and traumatic brain injury (TBI) treatments with policymakers working to improve care for Veterans.[1] Coalition members support innovators at all stages of the therapy development life-cycle, from initial research to late-stage clinical trials. The Coalition aims to spur strategic federal institution support to create better treatment and care for veterans suffering from PTSD and TBI. The Coalition seeks to work with the VA and the Department of Defense (DOD) on immediate improvements to public-private partnerships for:

- Developing and validating PTSD and TBI biomarkers and diagnostics;
- Providing research access to PTSD and TBI datasets;
- Providing institution-wide support for PTSD clinical trials;
- Improving messaging of relevant policies and practice guidelines; and,
- Providing up-to-date education around clinical trial endpoints and drug therapy options.

The Coalition also seeks renewed investment in VA-funded PTSD research and an expansion in the types of research supported. Through strategic collaboration between the public and private sectors, the Coalition believes that our nation can improve treatment of Servicemembers and Veterans suffering from PTSD.

[1] The Coalition's members are Cohen Veterans Bioscience (co-chair), Otsuka America Pharmaceutical Inc. (co-chair), and Tonix Pharmaceuticals. The Coalition was founded as the Veteran's Post-Traumatic Science and Policy Coalition.

II. Institutional Hurdles to Next Generation Research Partnerships

Private researchers in both the non-profit and for-profit sectors seek to partner with the VA to leverage extensive VA resources to unlock new medical therapies, but they have faced major institutional barriers. Examples of these barriers include the following:

1. The VA has world-class PTSD datasets and biological samples. However, while the VA has a two-year old policy encouraging public-private partnerships, VA sites often are not aware of it and the VA, in general, does not share biological samples, such as blood draws, with external researchers. When undertaking analyses itself, it can take the VA more than six months to process just small batches of samples, which are analyzed with older technology and assays preventing the combined analysis of all data and severely limiting cooperation with other organizations. Recently, several VA researchers were enthusiastic partners in a global PTSD research initiative. Despite their best efforts, the need to execute multiple agreements and then have the VA samples run on different platforms from the rest of the consortium and then analyzed by separate statisticians ultimately led to significant delays in results and higher costs.

2. The VA has an extensive patient population and facility network, but it provides little support for non-VA clinical trials. One recent multi-center Phase II clinical trial in Veterans for a potential PTSD medication sought to recruit participants from three VA facilities. While the non-VA sites participated on schedule, the VA facilities were slow to secure the necessary approvals. One received approval at the very end of the study, which was too late for meaningful participation, and another failed to obtain approval entirely.

3. The VA creates unnecessary hurdles to providers of external funding. The VA requires external entities seeking to support multi-site VA research to do so through a network of non-profit centers, each affiliated with an individual VA facility. Each center has different contracting procedures and personnel, and requires the funder to sign different contracts. While the VA has a central ethics review committee (IRB) that enables more efficient and consistent start-up VA clinical trials, this central IRB is not able to serve as the ethical reviewer for VA sites participating in clinical trials sponsored by other entities. These serve as significant disincentives, as they add costs and major delays.

III. Understanding the National Mental Health Crisis

Too many of our nation's Servicemembers and Veterans suffer and have suffered from PTSD and the lasting effects of TBI. The prevalence of PTSD ranges from about ten percent of Gulf War Veterans, up to 20 percent of those who have served in Operations Iraqi Freedom and Enduring Freedom, and as high as 30 percent of Vietnam Veterans. A staggering 20 Veterans commit suicide per day, more than 7,400 in 2014. Since 2011, there have been more deaths each year than the total number of combat casualties of the Iraq and Afghanistan wars. One in ten VA health care users have been diagnosed with PTSD, which includes one in four treatment-seeking veterans of the recent wars in Iraq and Afghanistan, according to the VA Working Group described below. Of those, too few receive effective care.

In June 2016, the VA commissioned an internal PTSD Psychopharmacology Working Group to review "the status of the current pharmacotherapy options and… drug development." Through the Working Group, the VA sought to define a central component of the problem, the "critical lack of advancement in the psychopharmacologic treatment of PTSD." In March 2017, the Working Group concluded that "The urgent need to find effective pharmacologic treatments for PTSD should be considered a national mental health priority," as published in the Journal of Biological Psychiatry. [2]

Both the pharmacy shelves and pipeline for research and development of PTSD treatments are thin. Despite the "high prevalence and costly impact" of PTSD in military personnel and Veterans, "most patients are treated with medications or combinations for which there is little empirical guidance regarding benefits and risks," and there is "no visible horizon for advancements in medications that treat symptoms or enhance outcomes in persons with a diagnosis of PTSD."

This hearing provides the Committee an important opportunity to understand how the Working Group reached these conclusions and to identify options for addressing these critical challenges.

First, there is a crisis of efficacy in PTSD treatment. Drug therapies are frequently a component of PTSD treatment— in Fiscal Year 2015 "70% of VA patients with a diagnosis of PTSD were prescribed an antidepressant"—but evidence suggests that "available medications are often ineffective in usual clinical practice."

The Working Group found that "most patients are treated with medications or combinations for which there is little empirical guidance regarding benefits and risks." For example, sertraline, an antidepressant and one of only two drugs approved by FDA to treat PTSD, was prescribed to over 30 percent of VA patients in Fiscal Year 2013 following an initial PTSD diagnosis, but failed to show efficacy in Veterans in two studies. This has led VA doctors to try different off-label drug combinations, or polypharmacy, "for the vast majority of patients treated." To address this problem, the Working Group called for "studies that would serve to provide critical basic information about the optimal treatment of PTSD" in order to begin to close the efficacy gap.

Second, the research pipeline is thin. There are only two medications approved for treating PTSD, both antidepressants, and the last one to secure the PTSD indication did so in 2001. The Working Group found that "the past decade of investments from VA and other federal funding agencies in research on medical treatment of military personnel and veterans with PTSD have yet to bear fruit in the form of new validated pharmacotherapies for PTSD." Federal research dollars are not going to the evaluation of pharmacotherapies for PTSD, just three of 21 active federal grants related to human PTSD research. Few dollars are flowing from the private sector, as well. The Working Group found that in the last decade, "the pharmaceutical industry has completed four Phase II clinical trials and one Phase III clinical trial testing the efficacy of new agents for the treatment of PTSD." Indeed, "few PTSD psychopharmacology experts are submitting clinical trial applications." To address this problem, the Working Group endorsed "novel collaborations between government, industry, and academia."

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[2] John H. Krystal et al., *It Is Time to Address the Crisis in the Pharmacotherapy of Posttraumatic Stress Disorder: A Consensus Statement of the PTSD Psychopharmacology Working Group*, J. Biological Psychiatry (2017) http://www.biologicalpsychiatryjournal.com/article/S0006-3223(17)31362-8/abstract

Third, we need more basic scientific research concurrent to new clinical trials. There are many targets for new drug therapies, according to PTSD psychopharmacology experts, but we need to expand the pipeline further. The Working Group noted that "our understanding of the pathophysiology of PTSD is limited." Indeed, PTSD is not a single entity with a single biological mechanism. There are in effect many PTSDs, and each of them likely has a different pathological mechanism for which different treatment will likely be needed. Through more investment "in translational neuroscience studies" related to PTSD, such as the pathophysiology of PTSD, we can define these mechanisms and better define patients by their specific pathology or endophenotype.

The Working Group's action plan emphasized the shared nature of the work ahead. "Federal, industry, scientific, and clinical communities [should] cooperatively address the state of affairs." Importantly, the Working Group called for more clinical trials conducted in Veterans and "an ongoing effort for the VA and other funding organizations to engage companies on a proactive basis to encourage medication development for PTSD and to develop efficient mechanisms for partnering (financial support, infrastructure support)." Together, we can provide Veterans PTSD clinical practices truly guided by evidence-based PTSD pharmacotherapy research.

IV. Recommendations for Action

The VA has begun to convert the feedback of the Working Group into action. We ask that the Committee support this and further steps in the coming months.

In May, the VA and Coalition member Cohen Veterans Bioscience announced a public-private partnership alliance, called the Research Alliance for PTSD/TBI Innovation and Discovery Diagnostics (RAPID-Dx), "to enable different institutions to coordinate efforts and integrate data across dozens of labs and leverage synergistic capabilities for a "big data" team-science approach to discover and support development of first-generation validated biomarkers and diagnostics for PTSD and TBI."[3] The partnership will to develop new tools "to consistently and accurately diagnose" PTSD and TBI or assess if treatment is working. The VA framed the partnership as "affirming our commitment to a new type of radically collaborative science defined by data sharing and coordination of efforts toward our shared goal of finding clinically-useful diagnostics and treatments for these invisible wounds of war." Secretary David Shulkin reiterated the view of the Working Group in saying that "we're able to accomplish so much more when we work strategically with our private and public sector partners."

We encourage the VA to work with the Committee to maximize the effectiveness of this new partnership, as well as work of similar initiatives to provide researchers access to PTSD datasets and provide institution-wide support for multi-site PTSD clinical trials.

[3] Cohen Veterans Bioscience, Press Release CVB and the Veterans Health Administration Announce Landmark Partnership to Advance the Diagnosis and Treatment of Trauma-Related Brain Disorders (May 17, 2017), http://www.cohenveteransbioscience.org/2017/05/17/cohen-veterans-bioscience-and-the-veterans-health-administration-announce-landmark-partnership-to-advance-the-diagnosis-and-treatment-of-trauma-related-brain-disorders/

Further, the VA should create a master plan to support external research though a strategic, top down approach. In the plan, the VA should move toward larger, multi-site studies, with a focus on clinical trials and research. Today, grant money is divided across too many different projects, leaving each with too little money to appropriately design and run a clinical trial, and unable to lead to the next step of investigation. The plan should include innovation grants for external research, such as the Industry Innovation Competition, in which the VA spurs activity in the private sector to help solve VA's most pressing challenges.

V. Conclusion

Again, thank you for this opportunity to share our perspective on these important issues. We welcome the VA's renewed efforts to address the challenges facing Veterans with PTSD and TBI, and we feel strongly that more can and must be done to ensure that our nations Veterans receive high-quality and effective treatment.