# INNOVATIVE TECHNOLOGIES AND TREATMENTS HELPING VETERANS

## HEARING

BEFORE THE

## COMMITTEE ON VETERANS' AFFAIRS U.S. HOUSE OF REPRESENTATIVES

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# CONTENTS

**May 13, 2009**

Page

MATERIAL SUBMITTED FOR THE RECORD

# INNOVATIVE TECHNOLOGIES AND TREATMENTS HELPING VETERANS

**WEDNESDAY, MAY 13, 2009**

U.S. HOUSE OF REPRESENTATIVES,
COMMITTEE ON VETERANS' AFFAIRS,
*Washington, DC.*

The Committee met, pursuant to notice, at 10:00 a.m., in Room 334, Cannon House Office Building, Hon. Bob Filner [Chairman of the Committee] presiding.

Present: Representatives Filner, Mitchell, Hall, Perriello, Teague, Donnelly, McNerney, Walz, and Adler.

## OPENING STATEMENT OF CHAIRMAN FILNER

The CHAIRMAN. Good morning. I apologize for being late. I call this hearing of the House Veterans' Affairs Committee to order.

If the first panel can take their seats while I am just doing a little introduction, that would be great.

I ask unanimous consent that all Members have 5 legislative days in which to revise and extend their remarks. Without objection, so ordered.

I want to thank you all for being here. The purpose of this hearing is very simple. In my job, and I am sure every one of my colleagues has the same experience, we meet constituents who have had contact, have invented, or have manufactured instruments, technologies, or treatments which would seem to have a great benefit for our veterans.

Yet, many have had a frustrating experience of dealing with a bureaucracy that just does not seem to react very quickly to new ideas and new treatments, and people are frustrated. They have things to help, whether it is a device for early detection of oral cancer, for example, or correction of vision for those who are brain injured.

You would think the U.S. Department of Veterans Affairs (VA) would jump on these inventions and, yet, for some reason that is the law of bureaucracies, it is easier to say no.

What I wanted to do today is highlight a series of different medical technologies, treatments, inventions, and discoveries that would seem to me, and to many people that I have talked to, to have great relevance for our veterans. Yet, somehow, they do not seem to have been introduced in to the VA system.

I would ask each of our panelists to summarize the medical situation for a layman as succinctly as possible and talk about some of the frustration you have had with trying to get it introduced into the VA system.

I think people are going to be really startled by some of the things that we can do as a Nation which our veterans can, in fact, increase the quality of their lives and the degree of their health care. Yet, we seem not to have done it and I just want to highlight the fact that there are so many of these around.

I have no special interest in any company per se. I am not trying to get anybody a job or a contract. I just feel it is imperative that the ingenuity of our Nation be more recognized and that the sense that we can do better for our veterans comes out. Somehow, maybe we can change things by having all of you here together showing what we can do as a Nation and hopefully encourage the more quick acceptance of this for treatments.

I thank you for being here. I would welcome panel number one. It is comprised of companies that will discuss a wide range of technologies and treatments that are either ready for use or are currently in development.

[The prepared statement of Chairman Filner appears on p. 36.]

Are you in the same order that I have here? Mr. Bethune, we thank you. You are Chairman and Chief Executive Officer of Zila, Incorporated. Dr. Sidransky is the Director of the Head and Neck Cancer Research Division of Johns Hopkins University School of Medicine joining him. Mr. Beckman is the President and Chief Executive Officer for BrainPort Technologies, Wicab, Incorporated. Mr. Broecker is the President and Chief Executive Officer for Alkermes, Incorporated. Mr. Munroe is the Senior Vice President of Mobile Medical International Corp.. Mr. Stern is the President of TeleMed Network. And, Dr. Scadden is the Founder of Fate Therapeutics, Incorporated.

I would like you to try to summarize the medical knowledge for a layman. Be as dramatic as you would like and give us some sense of what happened when you brought this to the VA's attention, either locally or nationally.

We will start with Mr. Bethune. Thank you.

**STATEMENTS OF DAVID R. BETHUNE, EXECUTIVE CHAIRMAN AND CHIEF EXECUTIVE OFFICER, ZILA, INC., SCOTTSDALE, AZ; DAVID SIDRANSKY, M.D., DIRECTOR, HEAD AND NECK CANCER RESEARCH DIVISION, JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE, AND PROFESSOR OF ONCOLOGY, OTOLARYNGOLOGY–HEAD AND NECK SURGERY, CELLULAR AND MOLECULAR MEDICINE, UROLOGY, GENETICS, AND PATHOLOGY, JOHNS HOPKINS UNIVERSITY AND HOSPITAL, BALTIMORE, MD; ROBERT A. BECKMAN, PRESIDENT AND CHIEF EXECUTIVE OFFICER, BRAINPORT TECHNOLOGIES, WICAB, INC., MIDDLETON, WI; DAVID A. BROECKER, PRESIDENT AND CHIEF EXECUTIVE OFFICER, ALKERMES, INC., CAMBRIDGE, MA; MARK MUNROE, SENIOR VICE PRESIDENT, SALES AND MARKETING, MOBILE MEDICAL INTERNATIONAL CORPORATION, ST. JOHNSBURY, VT; STANLEY STERN, PRESIDENT, TELEMED NETWORK, ROSS, CA; AND DAVID SCADDEN, M.D., SCIENTIFIC FOUNDER, FATE THERAPEUTICS, INC., LA JOLLA, CA**

**STATEMENT OF DAVID R. BETHUNE**

Mr. BETHUNE. Thank you, Mr. Chairman.

I am a proud U.S. Navy veteran and I am Chairman and Chief Executive Officer of Zila, developer and marketer of the innovative ViziLite Plus technology for the early detection of oral cancer and precancerous abnormalities.

Private citizens around the world and even prisoners in our Federal prisons enjoy the life-saving benefits of ViziLite Plus screening.

The VA has repeatedly resisted efforts to understand the great value of ViziLite Plus.

Oral cancer kills one American every hour, but veterans are 2.8 times more likely to get oral cancer than the general public, partly due to the higher rates of smoking, chewing, and drinking.

In 2006, the VA diagnosed 1,704 oral cancers, 5 percent of all U.S. cases. Surviving this disease depends upon detection.

In the VA, their own data shows that 70 percent of oral cancers are diagnosed at late stage when the 5-year survival rate is just 26 percent, which is worse than our general population results.

ViziLite Plus has received FDA clearance to aid in the detection of early stage oral abnormalities including precancer and cancer.

Some clinical studies on oral cancer screening, which when dentists use their unaided eyes and fingertips have shown that up to one-third of serious cancers and lesions are missed.

Supplementing the exam with ViziLite Plus has shown to produce 100 percent screening effectiveness. ViziLite Plus is an adjunctive screening technology similar to the mammogram, PAP smear, or PSA test. They all promote early detection, leading to fewer deaths, enhanced quality of life, and significantly lower health care costs.

The treatment of late-stage oral cancer typically costs $200,000 per patient and while treating a precancerous lesion, it costs less than $1,500.

Zila provides the VA with ViziLite Plus at a deeply discounted $12 per test. Screening all veterans seen in VA facilities yearly would cost about $60 million, a sum that would easily be recouped by the reduction in surgeries, long-term care, suffering and death.

ViziLite Plus is backed by eight published studies, recognized by the American Dental Association through their Dental Procedure Code, adopted by the Federal Bureau of Prisons, used by dentists worldwide, and covered by numerous health insurance plans.

The decision to implement ViziLite Plus exams should be universal in all VA facilities. Congress should urge the Secretary of Veterans Affairs to immediately implement annual ViziLite plus oral cancer screening of all veterans who are seen at VA facilities nationwide. This is the best way to assure the consistent delivery of quality life-saving care to our veterans.

Thank you.

[The prepared statement of Mr. Bethune appears on p. 36.]

The CHAIRMAN. I would now like to introduce Dr. David Sidransky. He is the Director of the Head and Neck Cancer Research Division at Johns Hopkins University, School of Medicine and Professor of Oncology, Otolaryngology-Head and Neck Surgery, Cellular and Molecular Medicine, Urology, Genetics, and Pathology at Johns Hopkins University and Hospital. He is also one of the

world's most cited cancer researchers and author of over 340 peer-reviewed publications.

Dr. Sidransky.

**STATEMENT OF DAVID SIDRANSKY, M.D.**

Dr. SIDRANSKY. Thank you.

The mission is to try and identify and treat oral cancer and its precursors as early as possible. Historically this has a put a premium on the thorough and meticulous initial examination.

However, clinical studies designed to test the effectiveness of visual examination in identifying dysplasia, the earliest cells that turn or can turn into cancer and cancer itself, say otherwise.

In the meta-analysis of six worldwide studies, it was reported that the weighted sensitivity of visual examination in identifying oral cancer and precancerous lesions was under 80 percent.

Visual examination by untrained examiners often misses the earliest more curable lesions. These results demonstrate that disease remained undiagnosed by conventional examination.

By contrast, published studies reporting sensitivity values from ViziLite are consistent. To date, the sensitivity of ViziLite examination in identifying dysplasia and cancer is nearly perfect.

According to published literature, pharmaceutical-grade toluide blue, such as that included in the ViziLite Plus test kit, preferentially stains lesions consistent with severe dysplasia, carcinoma in situ and cancer.

In one study, we find that a TBlue application correlated to a reduction of false positives by more than 50 percent. As such, ViziLite Plus has adequate sensitivity to find the meaningful number of individuals with disease while having sufficient specificity to not falsely identifying individuals without disease as being positive for cancer.

It is within this framework that ViziLite Plus fits into clinical practice. No other medical device has sufficient sensitivity and specificity to meet the requirement of early detection of oral cancer among veterans.

Other dyes and devices cannot precisely identify precancerous lesions and early invasive cancers while excluding healthy patients who need no further intervention.

Indeed ease of use makes ViziLite appropriate for use by all oral disease health care professionals including dentists, periodontists, oral surgeons, otolaryngologists, and even primary care physicians.

In conclusion, ViziLite Plus is an easy-to-use, sensitive, and specific medical device to help both relatively untrained and expert examiners both identify oral lesions in their patients who are in the high risk group for oral cancer.

Additionally, in an aging patient population, this product can bring diagnostic power to physicians outside the dental specialties for greater value and potentially more savings in hospitalization.

Inclusion in VA oral cancer screening protocols would improve screening efficacy for lesions suspicious for both precancer and cancer and ultimately reduce the terrible morbidity and mortality of this disease that our veterans suffer.

Thank you.

[The prepared statement of Dr. Sidransky appears on p. 39.]

The CHAIRMAN. Thank you so much.
Mr. Beckman.

**STATEMENT OF ROBERT A. BECKMAN**

Mr. BECKMAN. Good morning. I am Robert Beckman, the Chief Executive Officer of Wicab, Inc., a medical device company based in Madison, Wisconsin.

I want to thank the Committee for inviting me to present information on two innovative medical devices we are developing. Both devices are available today for further clinical testing that could ultimately lead to unique benefits for some of our wounded or disabled veterans.

We are developing sensory substitution technology invented by Dr. Paul Bach-y-Rita at the University of Wisconsin. Before he passed away, Paul famously said, "We see with our brains and not with our eyes and the brain is not hardwired."

What he meant is that if your eye is not functional, an alternate sensor such as a digital camera can be used. And because the brain is not hardwired, alternative neuro channels such as the tongue can transmit the impulses.

Wicab is developing and testing two unique medical devices based on this invention, one for balance and one for vision.

First the BrainPort vision device, which I brought with me, today consists of a small digital camera with zoom capability. The user controls the intensity of the stimulation on their tongue and the zoom feature. The image is transmitted real time and displayed on the user's tongue through this 20-by-20 array of stainless steel pins.

So our device provides a streaming video image on the tongue for blind people. With the BrainPort vision device, users are able to identify and navigate complex paths, doorways, and objects.

For example, one blind user with two glass eyes was able to successfully shoot a basketball and another used the BrainPort vision device at an indoor rock climbing gym to see the next rock holds and at home with his daughter to play tic-tac-toe.

The BrainPort vision device will not replace the cane or the sight dog, but it will become an important additional tool to improve the safety, mobility, and quality of life for blind users.

Some examples, finding the open seat on a crowded bus or train, identifying the direction to the target building in a confusing parking lot, finding the handle in order to remove a hot pot from the stove.

Wicab recently sponsored clinical testing of the BrainPort vision device at the Atlanta VA. Dr. Michael Williams, the PI, "concluded bottom line the device performs remarkably well for the tasks that we looked at in phase one."

To optimize the device, we need feedback from a much larger pool of users who are blind. We would welcome the opportunity to further test the BrainPort vision device at VA sites. Perhaps those willing soldiers who are blind as a result of a blast injury should be first inline to test this new technology.

Now I would like to turn your attention to the BrainPort balance device. This devise uses an accelerometer mounted within the intra-oral device to sense head position information. An acceler-

ometer is like a digital carpenter's level which senses tilt information as the patient's head moves.

This tilt information is displayed on the patient's tongue in the form of an electrical signal which feels like a bubble moving on their tongue.

We trained patients with chronic balance disorders to maintain their balance by keeping the bubble on the center of their tongue. This training is intuitive. On day one, patients learn to maintain their balance simply by keeping the signal in the center of their tongue. More importantly, within 3 to 5 days after patients start training, they start to experience improved balance even after the device is removed.

Patients perform most of the training at home during two 20-minute sessions per day. This is an important feature because patients with chronic balance disorders cannot easily travel to a clinic.

Early patient results after BrainPort balance device training are very promising. For instance, a traumatic brain injury (TBI) patient in Madison, Wisconsin, has now used our device for 2 and a 1/2 years. His physician, his mother, and the patient all agree that his recent improvement dramatically exceeds the gains he achieved in the first 13 years after his injury.

University of Wisconsin investigators recently analyzed data from 26 stroke patients, all of whom continued to experience significant balance disorders despite extensive vestibular rehabilitation. The results of the training with the BrainPort balance device over 8 weeks were quite promising both statistically and clinically according to the PI, Dr. Mary Beth Badke.

The BrainPort vision device and the BrainPort balance device have both been hindered by limited funding available to run clinical studies necessary to demonstrate the efficacy to the standards of the medical community.

The VA could help accelerate adoption of both devices into standard medical care by prioritizing and sponsoring further clinical studies within the VA system, especially in cases where the overall target populations are relatively small such as people who are blind or have a balance disorder related to a traumatic brain injury. VA funding could make the difference for those deserving veterans.

Mr. Chairman, thank you for inviting me to make this presentation to the Committee Members today.

[The prepared statement of Mr. Beckman appears on p. 41.]

The CHAIRMAN. Thank you so much.

I have to get my list here. Next, we will have, Mr. Broecker.

## STATEMENT OF DAVID A. BROECKER

Mr. BROECKER. Thank you, Chairman Filner. I really appreciate you inviting me here today to address the Committee.

My name is David Broecker and I am the President and Chief Executive Officer of a small biotechnology company in Cambridge, Massachusetts, called Alkermes. At Alkermes, we are dedicated to developing medicines that make a difference in patients' lives.

I am pleased to be with you here today and appreciate the time you have given me to share the story of a breakthrough medicine

that we believe can make a tremendous difference in the lives of numerous veterans suffering from alcohol dependence.

The medicine is call VIVITROL. But before telling you about VIVITROL and how it might benefit veterans, I would first like to highlight the problem of alcohol dependence.

As you are well aware, alcohol dependence is a huge public health problem, especially among people who have served in the military. It is a disease that not only hurts the patient but also affects the lives of family and friends. Unlike other illnesses, most alcohol dependent people do not seek treatment unless confronted by family or friends and many times treatment only occurs after a patient is in some sort of crisis situation.

Nationally, there are approximately 20 million people who abuse or have become dependent on alcohol. Of these, fewer than 10 percent are actually in treatment for their disease.

Today treatment consists almost exclusively of counseling or talk therapy aimed at changing the behaviors of alcohol dependent patients. Fewer than ten percent of these people in treatment are actually offered any sort of addiction medicine in the ongoing treatment of their disease.

Unfortunately, without medication-assisted therapy, the relapse rates of 1 year of treatment are extremely high. Tragically the problem of alcohol dependence is intensified in military personnel, particularly combat personnel who are often subjected to extremely difficult circumstances.

According to estimates from the Substance Abuse and Mental Health Services Administration, approximately 650,000 veterans suffer from alcohol dependence. When you combine the diagnosis of alcohol abuse with alcohol dependence, the number jumps to approximately seven and a half percent of all veterans or nearly 1.9 million people.

Despite these challenges, there are ways to dramatically improve care for our alcohol dependent veterans. Current treatment guidelines issued by the National Institute on Alcohol Abuse and Alcoholism call on providers to consider medically assisted treatment in addition to counseling on an ongoing basis for all patients.

Currently there are only four medicines approved by the FDA for the treatment of alcohol dependence, Antabuse, ReVia, Campral, and our product called VIVITROL.

Unlike the other medicines which must be taken on a daily basis to have a clinically significant effect, VIVITROL is unique in that it is an injection that delivers medicine over an entire month.

For alcohol dependent patients struggling with their addiction and trying to change their behaviors in profound ways, the challenges associated with adhering to daily medications are significant, and this is what often leads to relapse.

These are fragile patients, particularly in the early stages of treatment. This is why VIVITROL represents a breakthrough in the treatment of this disease.

With VIVITROL, patients receive medicine for an entire month allowing them to focus on changing their behavior through counseling and other psychosocial support.

VIVITROL was developed in conjunction with support from the National Institutes of Health (NIH) and was approved by the FDA

in 2006 for the treatment of alcohol dependence. It was shown in a large, multi-center, placebo-controlled study to dramatically reduce drinking among dependent patients. It has also been shown to prolong abstinence and prevent relapse, especially among severely dependent patients.

Since launch, we have heard numerous stories that tell us that this medicine does indeed make a difference in patients' lives.

In addition, we know of large managed care organizations that have done their own assessments and concluded that VIVITROL works well and reduces the utilization of other health care services within their system.

Our belief is that veterans would benefit significantly from widespread adoption of VIVITROL within the VA for the treatment of alcohol dependence.

The utilizations of medicines in general, and VIVITROL in particular, within the VA has been extremely limited. I believe there are several reasons for this.

First, the current VA/U.S. Department of Defense (DoD) guidelines for the use of medically assisted treatment for alcohol dependence were written in 2001. VIVITROL was launched after these guidelines were developed. These guidelines need to be updated and disseminated throughout the VA.

Second, metrics and targets need to be established and tracked for the screening and treatment of alcohol dependence. Make the metrics simple so that no one can argue with them. I believe that the systems are in place to do this.

And, finally, make the treatment of alcohol dependence within the VA, and with our current service personnel, a real priority. The benefits for patients and their families will be dramatic.

And we look forward to working collaboratively to see that these goals are achieved.

Again, I would like to thank the Committee for letting me share the story of Alkermes and VIVITROL and, at the appropriate time, I would like to answer any questions you might have.

[The prepared statement of Mr. Broecker appears on p. 50.]

The CHAIRMAN. Thank you.

Mr. Munroe.

**STATEMENT OF MARK MUNROE**

Mr. MUNROE. Good morning. First I want to thank Chairman Filner and the Committee for allowing me to testify here today on behalf of my employer, Mobile Medical International Corp. of St. Johnsbury, Vermont.

My name is Mark Munroe, Senior Vice President of Mobile Medical. My sole purpose here today is to explain how Mobile Medical is using an innovative approach to help Veterans Health Administration (VHA) medical centers provide top-flight surgical care, keep VA surgeons engaged with their patients, and save a significant amount of time and money associated with the refurbishment of VA operating rooms.

It is important to note that this is not a new concept. We have been engaged with the private sector over 14 years and our solutions with VA medical centers for more than 3.

Mobile Medical is an international company that develops and manufactures commercial and military mobile surgical hospitals which meet all U.S. health care standards. These mobile health care solutions are rapidly deployable, fully integrated, self-contained, and present innovative solutions for today's health care delivery needs.

To illustrate the versatility of this technology in various markets, please note that Mobile Medical has responded to a Federal Emergency Management Agency (FEMA) request to support the University of Texas medical branch in Galveston after Hurricane Ike.

We provide on-site surgery at a maximum security prison in North Carolina with a Mobile Medical staffed unit and have delivered eye care and surgical care units to Armenia, Saudi Arabia, Oman, and Iraq.

As a point of reference, about 6 weeks ago, Mobile Medical was featured on the international television program Little People, Big World where Iraqi dwarf children were shown receiving care on the mobile unit in southern Iraq.

Our flagship product, the mobile surgery unit, can be driven to any VA hospital location and upon deployment, triples in size to become a mobile surgical hospital that meets all U.S. health care standards.

These standards include those required for State licensure, Medicare certification, and Joint Commission on the Accreditation of Health care Organizations. Mobile Medical units meet all three of these standards.

Mobile Medical has provided mobile surgical capability to private, nonprofit, and university medical centers for over 12 years from California to Virginia, and beyond. This service has most often been provided on a rental basis and contract periods last anywhere from 6 months to several years.

The primary reasons hospitals opt for this mobile solution are that it eliminates the cost of contracting out surgical cases to other hospitals and saves additional resources by trimming months from the duration of the project.

Over the past 18 months, Mobile Medical has successfully brought this cost-saving innovation to VA medical centers which are undergoing hospital operating room renovations.

Our conservative estimates indicate that VA medical centers can save on average $12,000 per surgical case by maintaining control of their cases rather than contracting them out to local or regional hospitals. This approach also assures VA management that VA surgeons are handling the cases and maintaining their skills.

Mobile Medical has successfully utilized this approach at the VA medical center in White River Junction, Vermont, and has a unit actively working on endoscopic cases at the VA medical center in Martinsburg, West Virginia.

Mobile Medical is preparing to provide several units to cover a major operating room renovation project at the Miami VA and is currently working on similar opportunities at VA facilities in New Orleans, Kansas City, San Diego, Clarksburg, and Fayetteville.

Many facility leaders have indicated interest in utilizing our units for the purpose I have described in a streamlined contractual process administered by the VA headquarters.

In order to address these concerns, Mobile Medical submitted an unsolicited proposal to VA's National Acquisition Center in 2008. This submission proposed a pilot project using three mobile surgery units over 3 years, saving $90 million. Those savings are summarized in the attached two page executive summary I have provided. This request was ultimately denied.

Mobile Medical estimates that a more robust project using 20 mobile surgery units for currently scheduled operating room projects could result in a total cost avoidance of nearly $700 million over a 5-year period. We have also attached a document that supports that information as well.

Mobile Medical continues to attempt a dialog with the National Acquisition Center (NAC) in order to emphasize the significance of the cost savings this approach offers. The benefits of keeping patients and staff inside the VA system for their surgeries and the difficulties VA medical center contracting officers face as they attempt to fashion appropriate contract vehicles for this service.

Mobile Medical stands ready to provide the VA and the veterans it serves with cost-effective solutions for complex health care delivery concerns. We would be happy to provide private sector references as well as VA references if so desired.

Thank you for taking the time to learn about our innovative work. It has been a pleasure being here today.

[The prepared statement of Mr. Munroe appears on p. 55.]

The CHAIRMAN. Thank you so much.

Mr. Stern.

**STATEMENT OF STANLEY STERN**

Mr. STERN. Chairman Filner, Members of the Committee, thank you for the opportunity to testify today on behalf of TeleMed Network.

My name is Stanley Stern. I am the President of TeleMed Network.

Our team has the singular goal to reduce the shocking rate of veteran suicides. As you know, suicide is a solitary and misguided act. Our technology addresses this issue directly, confronting isolation with connectivity to both the VA and other veterans, especially those who are isolated because of geography or health status.

Further, our technology can provide direct and indirect guidance to avert these misguided decisions. Our technology team is led by Ed Yoon, the former Engineer of the Year for Microsoft, and Dr. Mervyn Silverman, an internationally recognized leader in the fight against AIDS, provides public health guidance.

Our technology provides veterans with video teleconferencing capability in their home. Teleconferencing is not new, but it is expensive and complicated to install, costing boardrooms hundreds of thousands of dollars per room, a cost that can be justified, but cannot be done on a large scale.

Our TeleMed Internet Endpoint known as a TIE costs less than $1,000. It is designed to scale. It is small, three pounds, portable, mailable, and provides a brilliant videoconferencing image on a veteran's home television display.

The TIE and its secure network are mutually optimized for video. There is no installation. It is plug and play. Just plug it into the

TV, connect it to the Internet, and turn it on. In order to scale, it has to be simple.

Let me explain how being visually connected benefits a veteran. First, with just one touch on a wireless keyboard, a veteran sees and speaks with a VA health care service provider whenever he or she needs help. The health care worker immediately appears full screen and the call can be initiated by the VA or the veteran.

A second button connects the veteran to a 24/7 group therapy session. The caller can participate or simply observe his peers speaking about issues he also confronts. It is an ever-accessible confirmation that he is not alone and that there are solutions available.

With this technology, these benefits can be available without an appointment, without travel, and, most important, without stigma because these conversations do not need to be part of a medical record. They just need to help the veteran.

TIE provides many other communication benefits. After an 18-month deployment, close friends are dispersed across the country. TIEs allow veterans to see and converse with each other again.

For example, squad or platoon meetings every Tuesday night. Local veterans can meet on Wednesday nights and there can be various interest group meetings as well. TIE connects vets from their homes to their veteran peers and professionals at the VA. It directly confronts isolation and misguided decisions.

Help is the least accessible for our rural veterans who must often drive hours to receive care. Inaccessibility compounds the medical problem and many choose just not to get the needed attention.

Our focus remains suicide prevention, but a TIE unit is also an excellent vehicle for medical checkups, evaluation, counseling, and eliminating the driving, the waiting, and the mileage expense to the VA.

The TIE can benefit spouses left at home who will be able to communicate with each other for support and learn from the successes of those who have already had these experiences themselves.

Accessible marriage counseling is just another benefit. Job training, classes, even interviews will be available to provide new directions, possibilities, and hope for returning veterans.

The network also creates cost-saving efficiencies. An available health care provider in Nevada can answer an urgent call from busy New York.

TIE is a conduit that connects the VA to its veterans, allowing the VA to provide its best Post Traumatic Stress Disorder (PTSD) remedies 24/7 to a veteran's home.

Our technology provides the quality, simplicity, and cost that allow these advantages to be scalable, benefiting both rural and urban veterans.

We will measure these improvements with independent research that will quantitatively demonstrate reduced suicide rates and intentions, improved medical benefits and access, and lower costs all within 1 year.

Mr. Chairman, that completes my statement. I will be happy to answer any questions. Thank you.

[The prepared statement of Mr. Stern appears on p. 56.]

The CHAIRMAN. Thank you.

Dr. Scadden.

**STATEMENT OF DAVID SCADDEN, M.D.**

Dr. SCADDEN. Mr. Chairman, Members of the Committee, thank you very much for the opportunity to speak with you today.

I am here as a representative and scientific founder of Fate Therapeutics which is a new biotech company started in San Diego, California.

My day job is as a physician. I am a hematologist/oncologist. I run the Center for Regenerative Medicine at the Massachusetts General Hospital. I am the Jordan Professor of Medicine at Harvard where I co-founded and co-direct the Harvard Stem Cell Institute and the Department for Stem Cell and Regenerative Biology.

Fate Therapeutics is a company that is dedicated to taking advantage of the explosive new information about stem cell biology as a way to induce regeneration and thereby reduce disability.

The technology of stem cells is something that has become available now as a modality by which we can approach problems of chronic disability as a means to try to reverse, not simply forestall, the development of disease.

Stem cells that we are approaching are really of two types. The first is the adult stem cell population that resides in all of us, that is in most of our tissues. And our approach is to identify compounds that have the capacity to turn these cells on as a means to enhance the body's ability to repair itself.

We have identified drugs that are capable of doing this, and are entering into clinical trials to do so, and have, as a number of different opportunities, ways in which we can take advantage of learning about the stem cells that, for example, make up our musculoskeletal system and turn them on with medications as a way to improve the outcome of blast injury to limbs, an important aspect of veteran care.

In addition, another stem cell technology that we focus on is the ability to take cells from any one of us simply by plucking a hair, exposing them to particular compounds in a laboratory, and reversing the history of those cells so that they become essentially an embryonic-like cell.

They are clearly not derived from an embryo. They can be derived from any of us, but they have the full capability of being able to serve as a source of any cell type.

The advantage of this cell is that it then becomes essentially an identical reproduction of the cells that we all have and, therefore, it could be potentially used as a tool kit for each of us as a way to potentially replace injured tissue. That would be accomplished without the potential for immunologic rejection.

These cells also have the capacity to be used as a model for the development of new medications. Again, an emphasis of our company is to try to design ways in which we can identify molecules that could be used as a way to enhance regeneration, to induce an ability to restore function of damaged tissues.

So we are an early stage company that has focused on the two different types of stem cells using essentially the strength of the pharmaceutical approach to now develop strategies to improve the ability of regenerative capabilities in settings that are particularly

relevant for veterans including those of limb injury, with blasts to musculoskeletal tissues, as well as neurologic regeneration in the setting of hearing loss and visual loss.

So our company is one that tries to take advantage of the necessary need for the innovations in the academic setting, coupled with the commercial enterprise, and we hope with government partnership.

Thank you for your attention.

[The prepared statement of Dr. Scadden appears on p. 59.]

The CHAIRMAN. Thank you so much.

In a conversation with the Secretary of the Department of Veterans Affairs, I asked him to send somebody to this hearing. Is there a representative from the VA here? Thank you so much, we have a representative. I appreciate you being here.

Both the Secretary, in his use of the word transformative, and the Deputy Secretary's understanding of innovation bode well for the future, but we wanted to make sure people were all aware of this.

Mr. Mitchell, do you have any questions?

Mr. MITCHELL. Thank you, Mr. Chairman. I would like to ask a couple questions of Mr. Bethune.

What makes the use of ViziLite Plus by the VA such a high priority?

Mr. BETHUNE. Well, I would ask Dr. Sidransky to answer that if you do not mind.

Dr. SIDRANSKY. Yes. The bottom line is that veterans are at great risk for oral cancer. And while we all accept screening for various types of cancer like cervical cancer, colon cancer, et cetera, we sometimes neglect this important disease which is really a plague for veterans.

By using this technology, lesions that are curable, resectable, and would impact these veterans. It would be available to them, and that is the main reason to really approach and use this technology with the veterans.

Mr. MITCHELL. I have one other question of Mr. Bethune.

In your prepared testimony, you argue that this Committee should call upon the VA's headquarters to implement ViziLite Plus exams across the VA system despite objections raised by senior VA dental officers. However, you also mention six facilities in the VA system are already using ViziLite.

What feedback have you received from those VA offices who have decided to utilize your product and does it square with the assessments of the senior VA officials?

Mr. BETHUNE. Congressman, I believe that they do agree that it is a very worthwhile test to be performed routinely. We have——

The CHAIRMAN. I am sorry. Can you put the microphone in front of you?

Mr. BETHUNE. Yes. Those that we have contacted and talked to about this product found it very important to implement.

Our problem is as a very small company, we do not have the resources to call on all of the many VA hospitals and clinics around the United States and it would take us years to have each of these institutions look at this technology and then make the decision. That is why we are urging the head of the VA here, General

Shinseki, to look at it as a universal program for all of the VA hospitals.

Mr. MITCHELL. But the feedback you have gotten from the six VA hospitals so far has been very positive?

Mr. BETHUNE. Pretty much so, yes, sir.

Mr. MITCHELL. Thank you, Mr. Chairman.

The CHAIRMAN. Thank you, Mr. Mitchell.

Mr. McNerney.

Mr. MCNERNEY. Thank you, Mr. Chairman.

Well, I have to say I found all of your testimony very exciting. And this is the kind of thing I want to see happen.

Mr. Bethune, the ViziLite Plus, how intrusive is it to administer this test? Is it just a swab or how is the test administered?

Mr. BETHUNE. We have a person out here. Dr. Balanoff is a practicing dentist and he uses this routinely in his practice.

Dr. Balanoff, could you answer that question, please?

Dr. BALANOFF. Yes. It is a very simple test. You have a patient rinse with an acetic acid rinse——

The CHAIRMAN. Sir, we have a microphone at the end of the dais. If you could use that one? Thank you.

Dr. BALANOFF [continuing]. You have the patient rinse with an acetic acid rinse which has kind of a vinegar taste to it. And the most important thing is to use a light. And this light will identify all abnormalities. And this is really important for the general dentist, which is going to be screening the VA population.

So it is just a very simple, easy test that takes less than 2 minutes to do and is noninvasive and is 100 percent accurate to all leukoplakias, white lesions, inside the mouth.

And then the follow-up to that would be if you found something abnormal to use the blue, the tolonium chloride that we have as part of our kit and, again, noninvasive.

Mr. MCNERNEY. So you rinse out the mouth and then look at it with a light or something?

Dr. BALANOFF. That is correct. That light is a special wavelength. White light which will allow the dentist to find something abnormal and then once they find something abnormal to refer it off to the appropriate specialist. And what this light does, it is an adjunctive test, which just makes it easier.

It would be kind of equivalent to going to a medical doctor and not allowing the medical doctor to use a stethoscope or a blood pressure cuff. You want something adjunctive to help you diagnose the health of the patient and that is what the light does.

Mr. MCNERNEY. All right. Thank you. Thank you.

Mr. Beckman, the BrainPort vision device, this sounds very—how intrusive is the device that is on the tongue? Are you able to eat? Do you have to remove it for different activities or how intrusive is this?

Mr. BECKMAN. Well, for vision, the device does rest on top of the tongue. And so, yes, indeed, in its current form, you would have to remove the device when you were eating, talking, et cetera.

However, with additional funding, there are no technological barriers to making this device totally wireless so that the intra-oral device could be mounted on the upper palate. And blind people using wireless technology would be able to use the device without

anybody even knowing that they actually have the technology available to them.

Mr. MCNERNEY. Well, that is pretty exciting. I am kind of thrilled by the technical aspect of this rather than the administrative aspect, if you cannot tell.

Mr. Broecker, the drug that you are talking about, how does it work? Does it make you nauseous when you have alcohol or how does it work?

Mr. BROECKER. No. You know, one of the very first medicines that was developed was a drug called Antabuse and that is the one that if you take it and you drink alcohol, it makes you sick.

Our drug, VIVITROL, is a monthly injection. And what is thought is that this diminishes the cravings that occur in alcohol dependent patients by blocking your opiate receptors. And so that is how the drug works.

Mr. MCNERNEY. Are there any side effects?

Mr. BROECKER. Some minor nausea, but that quickly goes away after a couple days.

Mr. MCNERNEY. And do you have to continue the usage of VIVITROL for a long period of time or is a couple months sufficient?

Mr. BROECKER. Well, in the studies that we have done, we have monitored patients over a 6-month period of time. So the clinical studies we have done have been over 6 months of time. However, we do know of patients that have been on it for, you know, 2, 3 years.

But it is very important that, you know, the patient not only get the drug but they are engaged in an active counseling, you know, a program to deal with the behavioral aspects of alcohol dependence. So the medicine addresses the biological urge and craving to drink while the counseling addresses the behavioral change that is required.

Mr. MCNERNEY. Well, thanks.

Again, I want to thank the panel for their testimony and for the Chairman for the insight to bring this panel together.

The CHAIRMAN. Thank you.

Mr. Walz.

Mr. WALZ. Thank you, Mr. Chairman.

And thank you to each of you for coming in and, as my colleague from California said, sharing with us some very exciting and innovative technology.

Obviously the goal of this Committee and I would say the goal of all Americans is to provide for the highest quality of life for our veterans after they serve our Nation. It is an honorable goal and also if it is done right, and we have heard many of you say this, it is not only doing morally the right thing, it is going to save us money in the long run.

So my question to you, and I am with Mr. McNerney, I like the technology side, too, but I also know that it is not the technology that stops this from happening, it is bureaucracy that stops it from happening in many cases.

So that is the part I want to talk about a little bit, about acquisition reform and contracting reform because we heard the President

talk last week, just in cost overruns at DoD, if we do this right in acquisition reform, we can save up to $300 billion.

I do not think people realize what we are talking about. That is the entire pay of our entire military and the health care for their families for 2 and 1/2 years in cost overruns, not cutting weapon system, just cost overruns.

So my issue on this is, I wanted to ask each of you, we all understand that the reason we have a lot of these things in place is to prevent fraud, waste, and abuse. Obviously it is not totally doing that, at least from an efficiency standpoint in DoD. The same might be true of the VA. Those procedures were never put into place to stop innovative and life-saving technologies from getting to our veterans.

So I would like each of you to just take, you know, a few seconds or whatever. What has been your experience? And some of you, you are obviously coming from the private sector, too, so you are dealing with private institutions.

I say this because I always ask all of my questions against a backdrop that I represent the Mayo Clinic and I ask them how does it work for you as opposed to the VA. And we all agree the VA does many, many, many things as well as anybody in the world in terms of the care.

This is the part I want to understand: are we nimble enough to innovate or are we behind the curve in that? So why don't each of you just give your input as you see this. Are we inhibiting it and not really protecting the taxpayer dollars in the right way?

So if we just start with Mr. Beckman and go around, that would be great.

Mr. BECKMAN. Neither the BrainPort balance device nor the BrainPort vision device are cleared by the Food and Drug Administration (FDA) at this time. So we are not in the process of attempting to commercialize or market our devices to the VA.

On the other hand, I think that the VA could take a leadership role, especially when you consider that people with traumatic brain injury represent a very small population overall and within the military. And, second, people that are blind, especially people that are totally blind with no better than light perception are also a very small population.

So, again, it would, I think, make sense for the Veterans Affairs to take a leadership role so that the people, for instance, who have been blinded or who have suffered traumatic brain injury as a result of the most recent conflicts would be the first in position to be able to test these technologies rather than being the last.

Mr. BROECKER. When it comes to alcohol dependence, as I mentioned in my testimony, the latest guidelines that have been adopted by the VA were in 2001. And, since that time, not only has our drug been approved by the FDA, but there has been another drug called Campral that has been approved by the FDA.

So, as it relates to adoption of innovative treatments for a disease like alcohol dependence, these guidelines need, you know, continued to be updated and then disseminated within the VA system.

My understanding is that there were recent guidelines that were developed last spring that still have not been disseminated. So, I think something that they need to do is clearly, you know, the ex-

pert groups and the key opinion leaders within the VA should see to it that these things get adopted and get put into practice within the VA system.

I think the other thing is, you get the results you measure. And, I know that the VA is a big, complex system, but if you could, develop very simple measures that could be adopted across the VA about things like alcohol dependence or, the variety of the diseases that are represented up here with all the various technologies and hold the people accountable for implementing some of these new technologies.

And then the final thing I would say is, make funding available. If there are certain funding pools that could be allocated to the adoption of certain technologies, as you mentioned about, sight and things like that, there is no better testing ground than the VA for some of these innovative therapies.

Mr. MUNROE. Congressman, we are in a little bit of a different category here with Mobile Medical in that we currently work with the VA. We are on an innovative technology track, which is answering a question that exists today and that is that with the current state of the VA facilities and the need for operating room renovation, the facilities really have two options when it comes to doing that.

The first is they close their operating rooms altogether and they send their patients outside into the private health care sector. When you do that, you lose all control. And certainly from a cost perspective, now you are in the commercial setting paying commercial rates. You are not in the existing setting which is really health care at cost.

The second option that they have is they can close a portion of their operating rooms and essentially phase a renovation project. If they do that, two major things happen. One is the construction and renovation of that project doubles and sometimes triples in length, i.e., it triples in cost.

The second thing that happens is you are always concerned about infection control. And we have seen some of that very recently in the VA setting because when you are doing construction in an operating room theater on one side of a wall and you are treating a patient on another side of a wall, I am sure some of the surgeons here could say, you know, that is not the most conducive environment.

Additionally you have staff that now have to work different shifts, overtime, double time in order to cover that type of schedule.

So to answer your question of the bureaucracy component of this, just today we received an e-mail from one of the VA facilities that says our renovation project is approved. It is part of the stimulus bill. We forgot how we are going to treat our patients when we close our operating rooms.

We did not put that on the front end of our project plan. We just said we need to fix the hardware, the operating room. So now the contracting officer has to scramble and they have to scramble to take operating dollars to solve that problem. That issue is apparent at every VA facility I go to and visit when they talk to us about operating room renovations.

So as you can see in some of the numbers we have presented, our objective and our goal with our unsolicited proposal was to show the VA that the request is there. The contracting officers, the chiefs of surgery, have the need for this solution. The projects are scheduled. The facilities need to be renovated.

If there was a pool of units such as ours that they could now say, okay, this project now receives two, three, four mobile surgery units, all that bureaucracy goes away because now they have access to the tool that they need, no different than having access to the drug that they need or anything else to help the veterans in that setting.

Mr. WALZ. I appreciate it. I went over my time. I will wait if we get a chance to come back around again to let the four of you take that on too.

So, Mr. Chairman, I yield back.

The CHAIRMAN. Mr. Walz, why don't we just try to finish?

Mr. WALZ. Thank you, Mr. Chairman. I appreciate that.

Mr. Stern, go ahead.

Mr. STERN. Well, I will be brief. In our case, this is a dramatic reduction in cost for communication and communicating with veterans about their real psychological needs early will truncate many years of therapy thereafter. So it has to stand up to the cost benefits and I am sure that it does.

That said, for many of the technologies we have heard about today, there is also a social benefit that often transcends the economic parts. And I think that somehow, even though it cannot be quantitative, has to be measured.

Dr. SCADDEN. I will just say that in the setting of rehabilitation, the VA is clearly very strong, but its emphasis is largely on device and engineering-based approaches.

And one of the things that I think stem cell biology represents is a way to try to take advantage of cellular components that may enhance the ability of such devices to be functional.

And to have the VA be involved in bringing together teams of individuals who have the perspective and expertise that the VA system represents coupled with those who have the expertise in cell biology, I think, could actually be a very productive area of developing new approaches to rehabilitation regeneration.

Mr. BETHUNE. Yes, sir, Congressman. Our product, ViziLite Plus, has been approved by the FDA. It has been awarded a special government award contract for use in any Government Federal facility. So there is no impediment for this product to be used.

The impediment, I believe, is that we do not have a universal requirement that this be administered around all of the VAs. It is a decentralized decision now being made where the local VA can make the decision.

And most of the VAs, you asked this morning, Congressman Mitchell, about what do they think about this product is that many of them say, well, we do not have the funds earmarked for this product.

So many VAs report that they don't have available money to spend, although they tell me they do have the funding for other projects, but they do not have a special earmark fund for ViziLite Plus to administer this oral cancer screening exam.

Mr. WALZ. Thank you, Mr. Chairman.

The CHAIRMAN. Thank you, Mr. Walz.

Mr. Donnelly.

Mr. DONNELLY. Thank you, Mr. Chairman.

Dr. Scadden, this area of stem cells is really interesting. What can it be rewound to do? There are a couple of specifics that you mentioned, but what is the overall feel that is out there?

Dr. SCADDEN. So right now we have the ability to take a cell that is defined as being something like a skin cell or a blood cell and essentially have it be able to forget all of its history. It no longer identifies itself as such and it can become any one of the different cell fates. There are over 200 cell types that make up our body.

So the potential is to be able to now say, well, maybe from this population of cells that we derived from here, we could now make a cell population that makes insulin and that could be used for individuals with diabetes or we could make things like muscle and potentially have it be useful in that context.

So I think the range of possibilities is quite enormous. The technology is obviously very, very early and the question of how to do it in a way that gets predictable outcomes, that is safe, all of these things are still in need of development.

But it is, I think, something that we should frankly be driving full speed ahead because this is really a very transformative technology and the ability to potentially reverse, not just forestall, the outcome of injury and disease.

Mr. DONNELLY. So while you talk in the documents we received about three specific applications, the applications are basically limitless?

Dr. SCADDEN. Yeah. I mean, we do not know now whether or not we will be able to create all of the different cell types of the body, but certainly this potential is something that when tested has been possible to achieve. And I think a lot of it is more technical than it is in biologic terms.

Mr. DONNELLY. And this is simply just one of our skin cells from our hand?

Dr. SCADDEN. Right. So what is done now is either biopsy from the arm, for example, you can literally pluck a hair, you can take a blood sample.

Mr. DONNELLY. Thank you.

Thank you, Mr. Chairman.

The CHAIRMAN. Mr. Hall.

Mr. HALL. Thank you, Mr. Chairman.

And thank you to all of our panelists. I am sorry to have missed the first part of the testimony, but I have a couple questions.

Mr. Beckman, I wonder if you could tell us why BrainPort devices are not implantable and is that something that could change?

Mr. BECKMAN. I think one of the key advantages of the BrainPort device is the fact that it is not implantable. In fact, it is a portable device where there is no need to implant the technology.

Other technologies for vision such as retinal implants are being developed, but I think the fact that they involve surgery, that they are invasive means that those technologies will likely not be avail-

able for probably 10 years or more. Our technology is available today.

Mr. HALL. I understand that. And I can see the advantages to either, or both. But cochlear implants, for instance, have been and are being used by large numbers of people with some success.

Is it because of the location in the brain of the nerves that one would need to get at, the nerve centers one would need to get at, that it is more difficult or is this something that you see happening in the future?

Mr. BECKMAN. That goes back to my testimony. One of Dr. Paul Bach-y-Rita's main hypotheses is that the brain is not hardwired. So, in other words, you can use an alternate sensor and also an alternate path to send that signal to the brain.

And we have demonstrated that, for instance, people who are blind who perform a certain task with our device and while they are performing that task, they are analyzed with PET imaging, we have demonstrated that those people process the visual information in the visual cortex of their brain.

On the other hand, people who are sighted that perform the exact same task process that same information in the somatoesensory region of their brain. So, in other words, the brain is masterful in the way that it can process the information in the appropriate area.

Mr. HALL. And it can change, it can switch and adapt from one pathway to another?

Mr. BECKMAN. Yes.

Mr. HALL. What is the typical training, you may have said this in response to a question before I got here, what is the typical training time for someone to be able to use, to adapt to the BrainPort?

Mr. BECKMAN. I think that is also an amazing part about this technology. We train blind people, literally in hours they start to recognize symbols, pathways, doorways, et cetera. We have not so far had anybody except for one blind person, Eric Weihenmayer, use the device for more than 10 hours.

We have videos on our Web site that show some of the benefits. All of those people are performing the tasks with less than 10 hours of training.

And I think what is most interesting is what will happen when we get this technology into the hands of many, many adults, letting them take it home, use it on their own, explore the potential benefits of the technology on their own. That is where we will start to really discover what the advantages and possibilities are for this technology.

Mr. HALL. Thank you.

Regarding the use of, I believe it is Mobile Medical and TeleMed, well, certainly, you know, having just come back from Afghanistan and Iraq as many of us did on our so-called break at the end of last month, we are all very much in favor of and encouraged by the work that you are doing to make the treatment of our wounded servicemen and women faster and more effective. And we realize the conundrum of battlefield medicine saving more lives but then leaving more grievously wounded people for us to treat when they get home.

I read something here, I believe it was Mr. Stern, the TeleMed testimony, about remote computer provided sessions for group therapy counseling, et cetera.

What are the limitations of that? I mean, there are inherent, I believe there are inherent limits to what a soldier will diagnose him or herself with or how—the interpersonal reaction between therapists and patient or a room full of participants face to face is different. There is body language. Well, it is harder to just get up and walk out the door. It is easier to log off. How do you address that or can you address that problem?

Mr. STERN. Yes, Congressman.

Mr. HALL. Would you push your microphone there, please. Thank you.

Mr. STERN. How is it now?

Mr. HALL. That is fine. Thank you.

Mr. STERN. The idea behind a group session is, there are a number of types. I only had 5 minutes to explain there and so I welcome the question.

There is absolutely room for private group therapy session where somebody can be there as an individual or anonymously. That is all right, too, because the stigma is a big part of this.

But I think the thing that will benefit most people is having the ability for, with the knowledge of those participating, with their full knowledge, having others observe them passively.

You know, it is not unlike what we see in talk radio where you will have a psychologist or a doctor explaining a problem to one person who knows they are being heard nationally, but many of us just listen in the car and listen and think, well, that relates to me. I have had those problems and I like hearing that solution.

But we would not have gone to a psychologist or a doctor to get that solution. This offers that benefit, but it has to always be very clear. You need to know if it is public or private and it is easy to do both.

I hope that answers your question, sir.

Mr. HALL. It does. Thank you.

I yield back, Mr. Chairman.

The CHAIRMAN. Mr. Perriello?

Mr. PERRIELLO. Just quickly. Thank you very much, Mr. Chairman, for holding this hearing.

I think this intersection of innovative technologies and treatment of our veterans is a very exciting area and obviously in many ways, the VA system itself is in a great position to deal with this given the issues that we face. But we also know so many independent private-sector groups are at the cutting edge of this.

So not only helping us to understand where the technology is and where it can go, but also addressing some of these issues of the dynamic relationship between the VA system itself and independent companies is very important.

So I enjoyed reading your statements even though I missed many of them here. I really just want to say how important this is as an issue and something we want to push on.

There are not many questions I have. I just wanted quickly to understand a little bit more from you, Mr. Bethune, about what some of the real world experiences have been with doctors and

health care providers with the ViziLite Plus innovative technology. It is just something I wanted to understand a little more about how that has played out in the real world applications.

Mr. BETHUNE. Well, thank you for that question. I have a person here in the audience who would be great for that question, Dr. Joel Epstein. He is Professor of Oral Medicine and also Oral Cancer at the University of Illinois. So he might be able to answer that question more.

Dr. EPSTEIN. Thank you for your question. It is nice to be here with you.

The real world utilization requires increasing education for utilization of detection adjuncts based upon the principle that early detection of any cancer is critical. It is critical more from the standpoint of diagnosis and preventing reducing the morbidity of more intensive therapy that is required for advanced disease management.

In addition, there are the cost savings in terms of quality of life impact which is dramatic for head, neck and oral cancer and from the standpoint of cost of care.

Early detection that is being promoted on an ongoing basis in the community and to a large degree the dental community because currently we see earlier stage disease being diagnosed by dental providers rather than medical providers. This relates in part to the way in which patients present.

For example, if it is weight loss or voice changes occur, those patients may present at a late stage to a physician's office rather than a dentist's office.

But certainly, all health care providers should be involved in early detection procedures and this can and has been shown to enhance the early detection of oral cancers.

Mr. PERRIELLO. Let me ask one other question that is hypothetical. It came up anecdotally talking to some of the doctors, but more the troops when I was over in Afghanistan, was this issue about whether we are sufficiently prescreening folks. And it was all anecdotal in terms of a propensity for PTSD.

And there was no evidence, and I am not claiming that there is such a thing, but do we think that down the road, there may be some way to look at this from the front end of being able to identify more accurately potential predisposition in some of these directions before we send people into conflict or is that really something that will continue to play out as sort of myth among folks at the battlefront but not real medicine?

Dr. SIDRANSKY. Hi. Yeah. So this probably goes away from the area of expertise of the people that are here. I am actually also a geneticist.

And I think that in general, that is the way the medicine is going, but it will be a period of time. We will understand more the makeup of individuals as well as some of the risk factors perhaps with questionnaires and other things that they fill out.

And I think for any type of disease, whether it be cancer, posttraumatic stress or anything else, I think there will be an interaction between the genetic information that the veteran comes with as well as some of the environment that can be related and the questionnaire is some sort of intake.

And I think it can. I think for many of these diseases that interaction, if you can actually take it out and implement some way of actually looking at it, we will be able to identify some of these individuals, to identify them as being potentially at risk or basically, you know, for therapy or something else or actually not able to be able to participant because of that.

We are not quite there yet, I think, for a lot of the mental and the psychiatric issues, but I think there is a lot of movement in that direction.

Mr. STERN. And I agree with Dr. Sidransky on this point, that this is solvable. And right now it is being done in a very crude way, I am afraid.

I mean, I know an anecdote that was told to me by the person in charge of suicide prevention at the Palo Alto VA. She was telling me the story of a sergeant who on the day they were being deployed had questions about one of his troops and his behaviors and really did not know how to diagnose it.

And it was happening at that level and clearly it could be done before that by professionals, not the sergeant ready to board the plane, but by professionals before that, as long as you have the communication ability or some other mode to get people in and diagnose them. So I think it is very solvable.

The CHAIRMAN. We need to go for votes. We have been called for votes and we are going to have to take a recess for about 15 minutes. I will dismiss the first panel after I just ask some quick questions.

I want to thank you all, I think everybody who has heard you was blown away by the excitement of what new technology can really do. You represent just a slice of what is happening in America with new innovations.

I am confident that our new Administration will be more open on the various levels you talked about, not only in testing, but if you need a centralized decision, for example, or more openness.

I had a long talk with Secretary Shinseki and Mr. Gould, the Deputy Secretary, and they are very aware of how an agency needs to have a way to innovate. I think we are going to have a much more flexible, nimble VA to make use of some of the innovations very much more quickly. We will be testing that by your experiences.

I just again want to make it clear for the record, you see that none of our Republican colleagues are here. They decided that somehow special interests were invited, somehow that we were promoting this or that company. That was not the intention. We are trying to take a cross-section of what is available. Nobody here is pushing for a contract, just a sense of ideas that are available and how we might respond as an institution.

I just want to make sure, since this always comes up, that none of the witnesses have ever given me or anybody else up here a campaign contribution.

This is a hearing to talk about the excitement and the possibilities of new innovations. I see someone who might want to say a few words, from the Blinded Veterans Association, of what this might mean for someone who is blind.

The opening up of fields of vision for people who have eye injuries, or brain injuries is exciting. It is a tool where people can read, with a non-invasive technology that has been shown to us and, yet, the VA does not have it for some reason.

I want to thank you all for helping us generate that excitement and to make sure the new Administration understands that we have to look at this in a much more nimble fashion.

We have the second biggest bureaucracy in the government, but it has to move faster because it affects our patients' care and their quality of life. Every one of you talked about how we could save hundreds of millions, if not billions, of dollars. This is not rocket science to say if it works, let us use it.

Just one quick question. Mr. Munroe, you talked about the mobile surgical unit to help when there are problems, for example, refurbishing a VA facility.

How about access into rural areas? That is one of the biggest problems faced by the VA. I assume we can adapt this and take that to the veterans in rural areas as opposed to forcing them to go 200, 300, 400, 500 miles.

Mr. MUNROE. Mr. Chairman, understanding one thing. The genesis of Mobile Medical was exactly that, was that there are patients in the private sector and in the VA setting that spend hours traveling for procedures and having a mobile solution that can go to a community, draw from that pool while it is there, and then travel to another community is exactly the reason that the mobile surgery unit was created in the first place.

The CHAIRMAN. Thank you.

Mr. MUNROE. You are welcome.

The CHAIRMAN. Again, we have to run for some votes. We will be back in 15 minutes. I will dismiss the first panel. Ask the second panel to approach the witness table.

Again, thank you so much for sharing these innovations. Some of this is proprietary, but I really appreciate you sharing with us the excitement and to demonstrate the kinds of changes that we can make to better serve our veterans. We will start panel two in 15 minutes.

[Recess.]

The CHAIRMAN. I apologize again for the interruption, we have no control over when votes are held. We thank you for your patience and look forward to panel number two. I hope that in your presentation you answer the question that Mr. Walz asked, which is, "What do you need from the VA to make this a reality for the veterans we are responsible for?"

I appreciate your being here. Dr. Howard Federoff is the Executive Vice President for Health Sciences at Georgetown University, Dr. Nelson Handal is the Founder and Medical Director of Harmonex, Inc., Clinicom, and James Schoeneck is the Chief Executive Officer of Braincells Inc.

Dr. Federoff.

**STATEMENTS OF HOWARD J. FEDEROFF, M.D., PH.D., EXECUTIVE VICE PRESIDENT FOR HEALTH SCIENCES, EXECUTIVE DEAN OF THE SCHOOL OF MEDICINE, GEORGETOWN UNIVERSITY MEDICAL CENTER, WASHINGTON, DC; NELSON M. HANDAL, M.D., FAPA, FOUNDER, CHAIRMAN, AND MEDICAL DIRECTOR, HARMONEX, INC., CLINICOM, ATLANTA, GA, BOARD CERTIFIED CHILD, ADOLESCENT AND ADULT PSYCHIATRIST, AND FELLOW, AMERICAN PSYCHIATRIC ASSOCIATION; AND JAMES A. SCHOENECK, CHIEF EXECUTIVE OFFICER, BRAINCELLS INC., SAN DIEGO, CA**

**STATEMENT OF HOWARD J. FEDEROFF, M.D., PH.D.**

Dr. FEDEROFF. Good afternoon Chairman Filner and Members of the Committee, thank you for holding this hearing, for the work you are doing on behalf of America's brave veterans, and for allowing me to testify this morning.

I will be focusing on innovative work that from my perspective is critically important to addressing the long-term implications of traumatic brain injury both to ensure that we are serving the long-term needs of returning veterans who have experienced TBI and also to do so in ways that are wise for the Department of Veterans Affairs Health Care Programs.

The Defense in Veterans Brain Injury Center makes the point on its Web site that America's armed forces are sustaining a tax from explosions or blasts almost daily in Iraq and Afghanistan. It also notes that screenings at Walter Reed have found that 32 percent of servicemembers evacuated from theater had traumatic brain injury. Those statistics obscure the reality.

Also referenced on that Web page that sometimes in the setting of mild traumatic brain injury there may be no outward sign of injury. Over 90 percent of combat-related TBIs are close brain injuries.

Indeed, TBI has been termed the silent epidemic. While 1.4 million Americans suffer from TBI from a variety of sources each year, many of these injuries with potential long-term consequences are not reported. Even in mild cases of trauma the central nervous system can suffer permanent, often debilitating damage.

There can be no dispute that our military is moving aggressively to respond as best as they can to the flood of very visible and tragic traumatic brain injuries that our men and women in uniform are experiencing in these 21st century conflicts.

Just as the nature of these injuries has changed from shell shock suffered by those serving in earlier conflicts, medical science has made significant strides. But we owe it to those who are serving and those who have served our Nation in uniform to act on the important realization that notwithstanding the attention they are receiving, there are all too many who have suffered mild to moderate traumatic brain injuries that pose serious but hidden threats to their long-term well-being. We need to act.

Developing methodologies for more rapid and accurate diagnosis of traumatic brain injury and its associated risk determine the most effective approaches to triaging patients with traumatic brain injury.

Pursue the rational design and screening of new therapies, including novel drug discovery and development targeting the prevention or minimizing of cognitive impairments which can impact learning capabilities, the ability to hold down a job, and to predispose to post-traumatic stress disorders.

Years of neurologic research has taught us a great deal about the human brain, and therefore there is information that is relevant to TBI victims.

First the plasticity of the human brain permits unique recuperative responses to trauma. We must fully understand these responses to better understand when to intervene and when to allow the body to heal itself.

Second research to date indicates that unlike in the case of stroke in at least some forms of TBI there is a longer timeframe from the time of injury for possible therapeutic intervention before permanent loss of brain function.

And third, research in other areas. Alzheimer and Parkinson's disease makes clear that blood in its circulating cells may serve as an important window into the human brain helping us to better understand the impact of neurologic disease and injury.

For example, understanding the neuropathology of brain inflammation through the analysis of blood based proteins and distinct populations of white blood cells called leukocytes may help us to determine the extent to which the brain has been injured and the degree to which the body is responding and possibly recovering.

These observations are generally invisible, absent a molecular analysis of the blood of an injured person, but they potentially hold the key to effective and timely interventions.

Recently the Department of Defense, through its Neurotoxin Exposure Treatment Program, NETRP, has awarded a 5-year grant to Georgetown University Medical Center neuroscientists to perform systematic and extensive biomolecular profiling of brain tissues and peripheral blood to identify and validate robust and sensitive and specific markers for traumatic brain injury. These signatures can be read from the blood, and early on may aid in the diagnosis of a variety and severity of brain injuries and guide therapeutic responses.

Indeed this research I am confident will inform the rational design of new drugs and therapies to prevent both short-term and lasting brain damage.

Our work will be carried out in conjunction with the Seattle based Institute of Systems Biology and researches at the University of Rochester.

As someone who believes in the tremendous benefits of possible collaboration, I am pleased that we are working with the Uniform Services Universities of the Health Sciences as they pursue their direction from Congress to focus on TBI, as well as the National Institute for Nursing Research, the National Institute of Neurologic Disorders and Stroke, and the Washington Hospital Center.

Our research for the Department of Defense will rely critically on first the civilian-sector TBI patients for our initial studies in recognition of the reality that we will be able to recruit these individuals without delays that are inherent in working with patients injured in combat.

However, I am following up with the recommendations from Chairman Filner that we reach out to the DC VA Medical Center to pursue approaches to ensure longitudinal follow up between the care received in these cases from the military and the ongoing Department of Veterans military care.

Given the ongoing work of traumatic brain injury at the Washington VA Medical Center, as well as over 30 Georgetown Medical Center faculty who hold appointments there, I am confident that we will actively engage the Washington VA Medical Center in this research to provide the best possible care for traumatic brain injury patients now relying on the Department of Veterans Affair for medical services. Ongoing monitoring of their conditions and well documented longitudinal follow up will be critical, it will likewise enrich our research.

Members of the Committee know very well that the vast majority of military personnel who are returning from the field have experienced TBI are very young. God willing, they have long lives ahead, therefore it is incumbent upon us to ensure that we are aggressive in this kind of research endeavor that looks beyond the immediate consequences of even mild TBI. With this type of research we can address the silent epidemic before it takes a toll on the long-term quality of life of those serving our country.

I urge the Department of Veterans Affairs, in close concert with the Department of Defense and Department of Health and Human Services, to remain vigilant in pursuing the identification of both these biomolecular signatures and of effective therapeutic responses to traumatic brain injury.

Again, thank you for giving me this opportunity.

[The prepared statement of Dr. Federoff appears on p. 68.]

The CHAIRMAN. Thank you. Dr. Handal?

**STATEMENT OF NELSON M. HANDAL, M.D., FAPA**

Dr. HANDAL. Mr. Chairman, Members of the Committee, thank you for the opportunity to share information about innovative treatments and technologies that are serving to enhance quality of care, especially in our area of mental health. I am a board certified psychiatrist.

As you know, information, and the way it is used, is at the core of psychiatrist assessment and diagnosis. Typically patients requiring mental health care are interviewed in what is commonly referred to as a traditional face-to-face psychiatric interview. Practicing medical health clinicians know that too often time constraints, volume and complexity of the information, limited access to care, and other factors, if not properly identified and addressed, end up limiting the accuracy of their face-to-face interview.

The key question is how to gather information comprehensively in a reasonable amount of time utilizing an easy to use tool that generates a valuable report to facilitate disposition and the clinician's initial face-to-face interview?

Our organization, Harmonex, is the developer of a patient self-administered and computer-based assessment tool known as CliniCom. CliniCom is comprehensive, easy to use, and allows the clinician to verify suggested diagnosis. The technology resides in a secure platform that comprehensively screens for 56 mental ill-

nesses and traumatic brain injury. CliniCom also includes a powerful suicide alert. CliniCom is based on the DSM–IV standard and incorporates clinical research and widely accepted community standards of care.

CliniCom is being used successfully across our Nation at private outpatient clinics and hospital settings alike. The technology can be equipped to run in most clinical environments using tablets, desktops, and kiosks. CliniCom evokes the appropriate question sets based on the user type and the patient's age. It does not replace the mental health professional, it simply allows them to significantly enhance the face-to-face interview, its outcomes, and quality of care.

CliniCom does not forget to ask pertinent mental health questions each and every time. It gathers complete medical, social, and family histories and can also identify concerns associated with suicide, violence, and traumatic events. CliniCom will also quantify severity of symptoms and severity of conditions automatically. It allows for secure and uniform documentation by organizing clinical information in the standard history and physical format.

Once patients complete the assessment, clinicians can devote much of their interview toward building rapport, validating the clinical report, and helping patients understand the nature of their condition. It is very difficult to gather all of this information during a single traditional face-to-face psychiatric interview. Our technology can gather clinically relevant and necessary information in a reasonable and quantifiable manner.

The clinical decisionmaking process overall is significantly enhanced by allowing CliniCom to identify individuals that may have co-morbid conditions, meaning the presence of one or more disorders or diseases in addition to a primary disease or disorder. An example would be an individual with depression, in addition to PTSD and substance abuse. With CliniCom clinicians can better ensure that both primary and comorbid problems are identified simultaneously, leaving no stone unturned.

A recent independent survey of 1,109 CliniCom users identified that 92 percent of users reported that CliniCom was very easy to use. In addition, survey results indicate that 87 percent of the users found CliniCom to be very easy to understand, while 88 percent found it to be very thorough. Seventy percent of users completed the assessment in 60 minutes or less. This is a function of the severity of their case.

While CliniCom has served to enhance care to the private sector, we have confidence that the technology can also serve to enhance care within military mental health. CliniCom has unique characteristics that make it well suited for use both as pre—and post-deployment screening tool and also as a comprehensive mental health assessment tool.

By implementing a technology like CliniCom, DoD and the VA can use these valuable clinical resource to help mitigate the overarching issues of stigma and access to care, an issue that every member of our armed forces is given a complete comprehensive and responsible mental health assessment.

In summary, CliniCom is a unique information gathering tool designed to assess mental health conditions, TBI, and suicidality. The

technology is comprehensive, easy to use, and its conclusions can be easily verified by mental health professionals.

In addition, what is learned from these cases can be used to conduct research that could lead to even greater advantages in mental health care. Truly modernizing the way we help people of all walks of life, who today suffer from mental illness.

We are grateful to the Members of this Committee for the work you do on behalf of our veterans and soldiers. Thank you for your time and the opportunity to introduce to you CliniCom. We look forward to answering your questions and are prepared to help in any way we can.

[The prepared statement of Dr. Handal appears on p. 69.]

The CHAIRMAN. Thank you very much. Mr. Schoeneck?

**STATEMENT OF JAMES A. SCHOENECK**

Mr. SCHOENECK. Chairman Filner and Members of the Committee, thank you for your opportunity and the honor of being able to appear before this distinguished Committee today. And I wish to commend you for your attention to the compelling issues surrounding military post-traumatic stress disorder or PTSD.

I have served as Chief Executive Officer of BrainCells since 2005 and have worked on successful drugs in both the biotech and pharmaceutical industry for almost 30 years. BrainCells is a San Diego based biotech founded on the discovery made only 10 years ago that new nerve cells grow in certain parts of the human brain. In fact, new neuron production, a process known as neurogenesis, is a requirement for the normal emotional responses that mentally healthy people take for granted.

By way of ground breaking studies from our founding scientists from Columbia University and the Salk Institute, we have demonstrated that stress can arrest the formation of these new cells resulting in immeasurably shrunken site within the brain called the hippocampus.

We now have the first physical understanding of the biologic processes that are involved in psychiatric diseases. Image studies performed on PTSD patients confirm that they also suffer abnormal changes in the hippocampus. And although these methods are not yet available to diagnose and study progress of all clinical PTSD patients, they may some day soon be available.

Importantly, BrainCells has designed a drug screening platform to search for new classes of drugs that will help this nerve cell growth function return to normal, restoring neurogenesis with the intention of improving emotional integration with fewer side effects. BrainCells believes that its compounds provide alternatives to the traditional anti-depressant and anti-anxiety drugs by directly increasing neurogenesis.

Expanded screening and treatment for PTSD and depression and new efforts to reduce the stigma surrounding mental illness among servicemembers are to be commended. But since October 2001, approximately 1.6 million U.S. troops have been deployed for Operations Enduring Freedom and Iraqi Freedom, and according to last year's Rand Study, one in seven servicemembers is returned from deployments with symptoms of PTSD.

PTSD can be regarded parenthetically as a chronic wounding of the brain just as traumatic brain injury bruises the brain. Violence, divorce, domestic abuse have skyrocketed among returnees and suicide rates in the military now exceed those in the civilian population; unheard of as a historic suicide rate has always been much lower among soldiers, sailors, Marines, and airmen.

PTSD is classified as an anxiety disorder with symptoms of chronic anxiety and fear that serve no purpose. It is often accompanied by typical or atypical depression. Non-drug treatment is regarded as the first line option for PTSD and is routinely incorporated in the management plans for patients. Many do not achieve a response from this non-drug therapy.

The selective serotonin reuptake inhibitors, or SSRIs, are used as first line pharmacological treatments. These are familiar classes of anti-depressants like Prozac and Paxil. Response rates for these medications rarely exceed 20 to 30 percent of PTSD patients. In fact, this class of drug routinely causes side effects like insomnia, weight gain, and most significantly for young returnees, sexual dysfunction. This is because of the increased serotonin resulting from the medication that can affect many parts of the brain and the body, many of which do not need to extra serotonin.

Less than 40 percent of servicemembers diagnosed with PTSD receive mental health care, and some of those voluntarily forego treatment or compliance because of sexual functional effects or those worries. Many soldiers use alcohol and illegal drugs to deal with the symptoms rather than take their SSRIs.

Combat veterans are now thought to suffer a more severe form of PTSDs than civilian victims of trauma. Military stress is generally associated with greater depression, more anger, irritability, more aggression, and a far greater tendency toward suicide or violence as illustrated by the deaths in Iraq this week. Additional studies are needed, but experts are moving to the conclusion that military PTSD is both different from civilian trauma and also it is more difficult to treat.

Methods used to treat civilian PTSD are at times inadequate to address military syndromes. It is disturbing to realize that we still have thousands of Vietnam veterans in the full throws of chronic PTSD and simultaneously we are being advised by the military that currently deployed troops are experiencing severe problems in record numbers, and if left untreated PTSD is a lifetime disorder.

Probably because of the nature of this unique physiological insult, combats for PTSD is different than the mental syndrome that civilians suffer. It has its own symptoms that require medications designed and tested for military and veteran populations.

It is unlikely that the civilian pharmaceutical industry can or will invest resources to address this as it is a specialized orphan-like condition that suffers from anxiety, depression, memory, and memory processing disorders.

The investors at BrainCells, for example, anticipate that we will use our resources to develop drugs for large civilian populations, like major depressive disorder. This market may provide investors with their anticipated return on the investment in exchange for the high financial risks taken in drug development.

Unless the government provides collaboration incentives and funding directly to biotech and pharmaceutical industry to deliver to the FDA-approved drugs labeled for military post-traumatic stress disorder, clinicians will be left with a combination of existing drugs tested and approved for people with a different medical condition.

Members of our military who voluntarily protect our Nation from harm are deserving of well funded pharmaceuticals that are directly and specifically directed to the disease of military PTSD.

Congress has generously funded significant amounts into the research of determining the organic causes and best practices for treating PTSD, but its yet to fully engage those of us who are singularly and professionally dedicated to identifying and testing safe new compounds.

Members of the Committee are undoubtedly aware of the myriad of ways that private enterprise can be provided incentives as exemplified by orphan drug laws that offer tax credits and patent extensions to illnesses affected by small populations. Tragically, military PTSD has already exceeded the statutory 200,000 patients that define orphan drug laws, but surely our war fighters are deserving of the best that our creative laboratories can provide.

In closing, I wish to summarize the following thoughts and recommendations.

PTSD is a disease that dramatically impacts the lives of our troops and returning veterans and their families. There are wonderful new developments in the field of neuropharmacology that could make a huge difference to sufferers of PTSD with fewer side effects. We must respond with a sense of urgency around testing new classes of drugs to treat the patients with military PTSD. Our collective goal should be to have new medications for the veterans of these conflicts, not the next. And a public private pathway to drug development is necessary, including regulatory and financial incentives for orphan-like drug development, including supporting clinical trials.

Thank you once again for the opportunity to speak before the Committee.

[The prepared statement of Mr. Schoeneck appears on p. 71.]

The CHAIRMAN. I thank you all and appreciate all the thought that has gone into this.

If I can just go back. Mr. Schoeneck, have you brought up these suggestions directly with the VA or have you been in contact with the VA Central Office?

Mr. SCHOENECK. We have not talked directly with the VA Central Office. We have previously spoken more with the DoD than with the VA around these problems.

The CHAIRMAN. You want direct support, either money or some of the other incentives you talked about for research into these areas?

Mr. SCHOENECK. That is correct, that is correct.

The CHAIRMAN. Just for the layman here, I know it in general, but give me a more specific definition of the orphan-drug incentive. What is an orphan-drug incentive?

Mr. SCHOENECK. When you are designated as an orphan drug you get 7 years of market exclusivity on the back end of the ap-

proval for the drug. And particularly if we are using drugs that may have already exhausted some of their normal patent life that becomes very important in terms of having a time that the risk for the investment can be paid back for those that have taken that risk.

The CHAIRMAN. What is the criteria?

Mr. SCHOENECK. It is 200,000.

The CHAIRMAN. Is it a small population?

Mr. SCHOENECK. Yes, small populations that are 200,000 or less.

The CHAIRMAN. So that number needs to be revisited as one of the things you are suggesting.

Mr. SCHOENECK. Exactly.

The CHAIRMAN. Is the VA research process big enough? Is there enough money? Is it open enough? Are you aware of what is available now and how they go about that?

Mr. SCHOENECK. The dollars that are available now tend to be more toward treatment or exploring treatments with existing medications, not things that are novel and in development. And the drug development process and the requirements that are there from the FDA, which should be there in terms of protecting the safety of Americans, those are not things in general that the VA pays for. Those are generally paid for by some outside source or by a more specific funding source.

The CHAIRMAN. Does NIH do any of this?

Mr. SCHOENECK. The NIH, to my knowledge, is not doing anything directly on PTSD. There is a Congressionally directed consortium that is working on PTSD, but they are looking more at the currently available compounds and how they may be able to be used together rather than looking at things that are truly novel.

The CHAIRMAN. Could the VA use the NIH as an agent to make sure there is specific granting authority or amounts of money available for things that the VA wants? Is that a model that we could use?

Mr. SCHOENECK. I think it is possible. I would have to think about it more, but I think it is possible.

The CHAIRMAN. If the NIH system works, and I don't know if it does, but let us assume it does, some of the money from VA could be put in NIH or NIH money could be targeted to the areas of research that the VA needs as opposed to forming a bureaucracy within the VA to deal with it. If you think it is a good idea, let me know.

Dr. Handal, have you dealt with the VA in trying to get CliniCom used or have you dealt with the Department of Defense?

Dr. HANDAL. I have talked with several people.

The CHAIRMAN. I assume this is a computer program?

Dr. HANDAL. Yes. It is software that has been developed over the past 5 years, and we have implemented the technology in 13 States.

The issue with DoD or the VA is, I think, the same as what we heard this morning. It is very difficult, I think, for—specially for innovative technologies to, you know, have some audience, and that is why I really appreciate the opportunity today.

The CHAIRMAN. Are the people you deal with afraid that it is not proven or that they are going to buy something that is not worth it or proves to be wrong or what is the problem?

Dr. HANDAL. No. I think everybody gets very, very interested and very excited about it. I think part of it is the bureaucracy.

Now you were mentioning, you know, the fact that there are ways to probably get application, and those ways we have tried, many of those ways, and still I think we have had difficulty. I would like to have Ms. Sharon Allred, she is our Chief Executive Officer, and maybe she can give you a little bit more information about how that pathway went.

The CHAIRMAN. If you can just use that microphone there? Whom do you go to in the VA and what occurs when you get there? Give me a sense of what is going on.

Ms. ALLRED. Well we have tried a lot of local approaches working with chief of psychiatry at Walter Reed and we have worked with Fort Rucker and several of the places where we have actually gone to where the psychiatrists themselves and the medical professionals believe very strongly in what we have developed and built. But when you start trying to put it into place, then you start hitting some of the red tape type issues. You know, they have to get approval and they can't necessarily get approval at the local level, and they have to, you know, it has to be a top down type process.

You know, we have tried to look for solicitations and other things that actually deal directly with this, but again those are very difficult to find. And as we were talking with the gentlemen here earlier that represent the VA, a lot of times it is just difficulty in trying to find who the right person to talk to within the VA that handles the type of technology that we are dealing with.

We are tried, true, and proven in the private sector. We have definitely done our research on the security. We have actually had it analyzed by personnel from the military. So we feel like we are ahead of the curve, we are just not exactly sure how to get directly into the right people.

The CHAIRMAN. Okay, thank you.

Ms. ALLRED. Uh-huh.

The CHAIRMAN. You need a little revolutionary cadre on the side that is working constantly at subversive activities. Of course, I will chair that.

I am only being half facetious. Any big bureaucracy needs to institutionalize a way to undermine it to institutionalize change. That is to find ways that somehow don't get through the normal processes.

As I said, I had a long conversation with the Secretary and the Deputy Secretary, and they seem to understand that. As the Deputy Secretary said, you want to have openness, but you have to have some constraint on it as well.

There has been FDA approval of a lot of innovations we have heard and there has been other peer reviewed innovations. It seems to me that risk is minimized with all these other things that are going on.

We have, as everybody pointed out, many cases of PTSD and TBI. We need all the help we can get and I will look at anything. Particularly with PTSD as you point out—as everybody has pointed

out—it would be good to have pre-deployment and post-deployment data to see what kinds of differences there are. If you have a tool to do that, I don't know why we don't use it.

The numbers are so high, and I think that the numbers that we have used here tend to underestimate it. As policy makers, we should say prove to me you don't have TBI or PTSD before you leave, rather than us having to prove you have it. Make a mandatory physical evaluation for everybody. Whether you are using something like CliniCom or, a personal interview with a psychiatrist or other medical professional. We don't do that. We have all these self-administered questionnaires that are gained, and they are not comprehensive any way.

We are letting servicemembers who can explode at any time, and it is up to us to minimize that. You all have given us some ways to help them. It seems that the military and the VA should be looking at all these innovations. By not doing so, we get two statistics. Half of the homeless on the street tonight are Vietnam veterans, because we did not look at PTSD, and the suicide rate of Vietnam veterans now outnumber those killed on the battlefield.

We have done something wrong there. We can't keep repeating that mistake, and yet it seems that we are. We have far less numbers in Iraq and Afghanistan, but the percentages are as high or higher in all the things we don't want to happen.

As we proceed as a Committee and as a VA with new leadership, what is the first thing each of you would like to see happen? What is the key thing that you would like—a new VA, a transformed VA, an innovated VA, how could it help what you all are thinking? If each of you would take a turn at that? Give me one thing.

Dr. FEDEROFF. In the current context being able to engage the spectrum of health care professionals in longitudinal follow up. Particularly now that it is clear that there is some elements of blast-related head injury that distinguishes itself from other forms of head injury.

Without that natural history work and a commitment to support it long term, some of the answers that are needed will not be known, and it may well be the case in citing the Vietnam example that some of those answers may not be known for decades. But commitment long term for follow up—careful follow up is, I think, warranted.

The CHAIRMAN. And, the VA is about the only institution that can do that?

Dr. FEDEROFF. Yes.

The CHAIRMAN. Or, can provide you with the subjects for such research?

Dr. FEDEROFF. Correct.

The CHAIRMAN. Yes.

Dr. HANDAL. One idea would be the creation of an office for innovative technology, and that would basically be where people who develop technology, especially in health care, would approach that office and present to them whatever claims they have, and then that office probably should be responsible for carrying this information through the VA and DoD, and then replying back to whoever is interested in working with the VA.

I think it sounds to me, and I am not a businessman in the true sense, I am a physician, but it really sounds to me that there are so many ways that you can try to approach the VA and the DoD, but there really is no one door where you can go and say okay I have this technology and I want you to look at it and talk to me about it and I can describe it and then you can carry it forward and see who is interested in the VA.

And we can claim for instance that we have a hospital in our area that could use it. The director for instance of the program, with the Behavioral Health Program, Dr. Barry Frankhauser, he told me I want to use it. And he wanted to use it at that particular military hospital. And you know, it was very difficult to convince other people to do it, despite the fact that they thought it was a very appropriate thing to do.

The CHAIRMAN. Yes, you are getting back to my revolutionary cadre of subversives. I put it a little differently than you.

Of course, setting up that office will go through a bureaucratic process which will take 7 years and which will only be staffed by those who have given adherence to the bureaucracy.

You have to almost institutionalize a revolutionary part of your—I mean, how does IBM or how does Microsoft innovate? They are big bureaucracies. Our new Deputy Secretary of the VA comes from IBM, so I think he can give us some help on that. How do those big bureaucracies constantly innovate? There is probably a secret little room with a lot of young geeks in jeans, who are thinking things through all the time to undermine Microsoft, then they adopt them, and then they make another $500 billion. It seems to me we have to do that if you want to carry back that message somewhere. Of course, that will go through your bureaucratic process and may never get to the Secretary.

I am sorry, am I pronouncing your name right by the way?

Mr. SCHOENECK. Schoeneck.

The CHAIRMAN. Schoeneck. Okay, thank you.

Mr. SCHOENECK. So I think just two brief things. One is access to VA populations with PTSD and funding to look at and examine truly novel medications in this area.

We have been stuck in the same cycle of medications coming off of the Prozac-like spins for the last 25 years and it is time for this population to have an opportunity to get something truly novel that might be able to treat the disease in a different way.

I think the other one is to potentially think about an orphan-drug exception that designates military PTSD as an orphan drug. You would definitely get the attention of more an industry by doing that.

The CHAIRMAN. So just by doing that, that makes incentive to——

Mr. SCHOENECK. Absolutely.

The CHAIRMAN. Well, I appreciate all of your thoughts. We look forward to working with you in the future. We will follow up on all this and hope that we can make the quality of life for our veterans a lot better, quicker and cheaper.

Thank you so much. This hearing is adjourned.

[Whereupon, at 12:40 p.m., the Committee was adjourned.]

# A P P E N D I X

### Prepared Statement of Hon. Bob Filner, Chairman, Full Committee on Veterans' Affairs

I would like to thank everyone for attending this hearing today. The purpose of today's hearing is to be made aware of, and learn about, the innovative technologies and treatments which are currently available or are in development to help veterans.

We will hear from companies that have devoted many resources into researching the unique maladies that affect veterans of all conflicts.

While I applaud the VA for being the leader in research and treatment of such conditions as Traumatic Brain Injury and Post Traumatic Stress Disorder, it is important that our veterans have access to other ground-breaking treatment modalities which have been developed in the private sector.

As the Chairman of the Veterans' Affairs Committee, I have learned about many exciting developments in technology and treatments that can help our deserving veterans. However, it has come to my attention that the developers of these new technologies and treatments face many barriers. For example, it is a challenge to add a new treatment tool to the VA's supply schedule and there is yet another obstacle of the VA not making active use of the treatment tool on the supply schedule.

In the end, this affects veterans who cannot access the best technologies and treatments that are available in the market. Just as our veterans bravely risked their lives for our country, it is our duty to ensure that they have access to the latest and the most effective treatments.

### Prepared Statement of Hon. Harry E. Mitchell

Thank you, Mr. Chairman, for calling this hearing. We live in the most innovative country in the world and at a time of unprecedented technological advancement. I am pleased that we will have the opportunity to review a number of cutting-edge products and treatments that can help save lives—and improve the quality of life—of many of our veterans.

Before I yield back my time, I'd like to thank David Bethune—the Chairman of Scottsdale's Zila, Inc.—for appearing before the Committee today. Zila develops and markets the ViziLite Plus Technology, which provides a method for detecting oral cancer. This product is already in use at a number of VA facilities, and I look forward to learning about its results at the VA.

Thanks also to Vomaris Innovations—who produces a bio-electric wound care product in Chandler, Arizona—for submitting testimony to the Committee. And finally, thank you to the rest of our panelists. I look forward to hearing about new tools and methods we may use in the care of America's veterans. I yield back.

### Prepared Statement of David R. Bethune, Executive Chairman and Chief Executive Officer, Zila, Inc., Scottsdale, AZ

Thank you, Mr. Chairman and Members of the Committee, for inviting us to participate in today's important hearing on Innovative Technology and Treatments Helping Veterans. I am David R. Bethune, a proud navy Veteran and Chairman and Chief Executive Officer of Zila, Inc., the developer and marketer of the ViziLite Plus technology for the early detection of oral abnormalities that could lead to cancer.

It has been said that without change, there is no innovation. With respect to the Department of Veterans Affairs, I would modify that: Without change, our Nation's Veterans will not enjoy the life-saving benefits of innovation.

Innovation has already brought an effective, fast and low-cost screening technology to dental offices throughout America and the world. And yet our Veterans,

who are among the most in need and most deserving of this technology, are being denied its benefits. In this respect, our Veterans receive inferior care to the inmates in our Federal prisons. Why? Because the VA has not added a 5-minute procedure to routine dental check-ups, that could save lives, improve the quality of life, and prevent costly surgeries and long-term care.

**The Tragedy of Oral Cancer**

Oral cancer is a killer. Yet while it claims one American life every hour, it flies under the radar for most Americans. In times past, oral cancer was thought to be a disease of old men who had smoked all their lives. Today, with oral cancer rates increasing among women, and striking both women and men in their 20's and 30's, we know that virtually everyone is at risk. Tobacco and alcohol are confirmed causes, and now, thanks to Johns Hopkins research, it is becoming clear that the HPV virus, long known as the primary cause of cervical cancer, is emerging as a leading cause of mouth cancer. Seventy-5 percent of all people carry the HPV virus at some point in their lives, and it is easily spread to the mouth through oral sex.

Oral cancer is the eighth most common type of cancer among males in the United States. 34,000 new cases are reported yearly, and regrettably, most are discovered at later stages, when the outlook is most grim. This helps explain the surprisingly high death rate associated with this disease. The tragedy is that because oral cancer occurs in the mouth, which is totally accessible to the eyes of dentists and physicians, it should be one of the most avoidable and manageable forms of cancer.

Based on available statistics, Veterans are especially susceptible to oral cancer. In 2006, 1,704 cases of oral cancer were diagnosed within the VA. That's 5 percent of all annual cases in the U.S. Given that the VA treats about 5.5 million patients per year, Veterans are almost 3 times more likely to be diagnosed with oral cancer than are members of the general public. And now we know that the conflicts in Iraq and Afghanistan are producing another generation of tobacco-using Veterans. A survey of Marines and sailors show they are using tobacco at more than twice the rate of other Americans—64 percent vs. 30 percent.[1] If there was any doubt that oral cancer is a real and growing threat for vets, this should put it to rest.

As with most other types of cancer, chances of surviving this disease depend largely on how early it is detected. In the VA system, the record for detection and survival is dismal. Seventy percent of VA oral cancers are diagnosed at late stage, when the 5-year survival rate is just 26 percent. Early stage detection occurs only 30 percent of the time; those lucky patients have an 82 percent 5-year rate of survival. The goal, however, should be detection of pre-cancerous tissue—cells on the pathway to cancer. Identifying these abnormalities offers the best chance of avoiding the often horrific or fatal consequences of oral cancer itself. *And this—the early detection of oral abnormalities that could lead to cancer—is exactly what ViziLite Plus was cleared by the FDA to do.*

The hardworking and highly professional dentists of the VA should not be faulted for these poor cancer detection statistics; after all, their record closely aligns with that of the historical record of dentists who serve the public. A primary reason that so many cancers go undetected for so long is that the conventional examination method is far from perfect. Dentists have long been taught to use their trained eyes and fingertips to conduct a conventional visual exam. Yet studies to date of the conventional visual exam have demonstrated that it is only effective in identifying suspicious lesions about two-thirds of the time; in other words, **it misses suspicious lesions one-third of the time.** *When you supplement the conventional visual exam with ViziLite Plus, you increase screening effectiveness to 100 percent.*

**Adjunctive Screening Technology Makes Sense: Fewer Deaths, Enhanced Quality of Life, Lower Health care Costs**

ViziLite Plus falls into a category of medical devices called adjunctive screening technologies. It is similar in function to (although less expensive than) the mammogram for breast cancer; the Pap smear for cervical cancer; and the PSA test for prostate cancer. The rationale for adjunctive screening technologies comes down to this: They promote early detection, which leads to fewer deaths, enhanced quality of life, and significantly lower health care costs.

There is ample evidence that adjunctive screening technologies save lives. From 1972–1992, breast cancer deaths declined 45 percent with mammograms. From 1950–1990, the Pap smear helped reduce cervical cancer deaths by over 70 percent. And from 1993–2002, prostate cancer deaths declined 18 percent, thanks to the PSA test.

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[1] Tobacco use in Iraq vets—http://www.medpagetoday.com/MeetingCoverage/CHEST/11520 accessed 5/4/09.

It's hard to put a valuation on the dramatic reduction in pain and suffering that is achieved through early detection, especially with oral cancer. When a pre-cancerous lesion is identified, it and the threat of imminent cancer can be eliminated in a quick out-patient procedure. That contrasts with gross surgical removal of large segments of the tongue, cheek or jaw bone for patients with late-detected mouth cancer. With such extensive surgery, and accompanying radiation and chemotherapy, quality of life plummets as simple, everyday tasks like talking, eating and sleeping are made near-impossible.

As for cost savings, we have solid evidence that early detection of oral cancer dramatically reduces the need for expensive surgery, chemotherapy and long-term care. Analysis by the Delta Dental insurance company shows that treatment of late stage oral cancer typically exceeds $200,000 per patient, while treatment of pre-cancerous lesions costs only $500–$1,500. For patients, early detection means a faster return to the workplace, which reduces lost wages and improves productivity.

Even in these challenging economic times, the VA can afford wide-scale implementation of ViziLite-assisted oral cancer screening exams. Zila Pharmaceuticals has contracted to provide ViziLite Plus to the government at a deeply discounted price of approximately $12 per test. If the VA were to provide a potentially life-saving ViziLite Plus exam to every Veteran receiving VA services (5.5 million in 2007), the cost would total only $66 million—a meager amount compared to the agency's $41.2 billion budget[2], and a sum that would be totally eclipsed in cost by the reduction in surgeries and long-term care.

The military should also provide ViziLite Plus-assisted oral cancer exams to all personnel undergoing medical exams as they end their active duty.

**Adjunctive Technology for Oral Cancer Screening is Widely Utilized**

ViziLite Plus screening is gaining wide acceptance as an adjunctive technology, advancing the standard of care. This is confirmed by: American Dental Association recognition (through their dental procedure code); adoption by the Federal Bureau of Prisons; acceptance by dentists; approval for reimbursement coverage by numerous commercial health insurance carriers; and contractual inclusion in the Federal Supply Schedule.

Recognizing the need for an adjunctive screening technology to fight oral cancer, the American Dental Association in 2005 created a new procedure code for this type of screening. ViziLite clinical evidence was the sole data supporting the ADA's decision to create the Code, which facilitates insurance billing.

The Federal Bureau of Prisons (BOP) has embraced ViziLite Plus. The BOP strongly encourages every Federal prison facility to incorporate ViziLite into their care protocols, both for new prisoners at intake and for those already incarcerated. The BOP recognizes the economic benefits of early detection and treatment, and ultimately, the importance of being fiscally responsible with moneys provided to it.

Dentists across the United States and the world are incorporating ViziLite Plus into their oral cancer screening protocols. Patients are benefiting from the technology in Canada, the UK, France, Germany, Spain, Portugal and beyond.

A growing number of health insurance carriers provide coverage for the ViziLite Plus screening exam. These include Guardian, UnitedHealth care Dental, Humana Dental, Northeast Delta Dental, Essex Dental Benefits, SafeGuard and many self-insured employer and union groups. Altogether, some 24 million people are enrolled in plans that offer ViziLite Plus coverage.

ViziLite Plus is available to all VA facilities through a Federal Supply Schedule (FSS) contract (V797P–3158M) administered by the VA National Acquisition Center (VA NAC).

**Zila's Experience Encouraging Use of ViziLite Plus in the Veteran's Administration**

ViziLite Plus has been or is currently being utilized at six facilities out of the entire national VA system. Other than these facilities the VA has been slow in their response to our wanting to describe the system and its potential benefits to the Veteran. Given the ability of all facilities to readily purchase ViziLite Plus through the Federal Supply Schedule contract, I strongly recommend that this technology be made available to all that visit the VA clinics.

One of the unique aspects of oral cancer is that screening and detection are typically performed by a dental professional, while treatment is administered by a medical professional. As a result, a simple budgetary fact may be undercutting care: The VA's dental budget bears the cost of using innovative technology to help identify

[2] VA budget—http://www.whitehouse.gov/omb/budget/fy2009/Veterans.html accessed 5/4/09.

oral cancer, but the economic benefit of early detection is shifted to the medical budget.

To underscore this, our company has had far greater success in securing coverage for ViziLite Plus from those national insurance carriers that provide both dental as well as medical coverage, because they take a comprehensive look at costs and have come to the conclusion that ViziLite Plus saves money.

Some dentists say, "Your technology is not proven," or "We'll consider using ViziLite Plus when it has matured." Rejecting innovation this way endangers lives. The ViziLite technology has been cleared by FDA and thoroughly vetted by scientists, regulators and private practitioners. Eight peer reviewed papers have been published demonstrating the efficacy of ViziLite and ViziLite Plus. This extensive research supports sensitivity of 100 percent—where oral cancer was present, ViziLite Plus detected it every time. A clinical study published in the journal Oral Oncology (using a high-risk patient population similar to that served by the VA) demonstrated a reduction of false positives by 55 percent—suggesting the potential of reducing unnecessary biopsies by half.

We have been told by senior VA dental officers, "My dentists don't have time to do a ViziLite exam," and "We don't have the budget to purchase it." The exam takes only 5 minutes, so that should not be an issue. The cost savings of early detection vs. late detection have already been explained.

Innovative technologies like ViziLite Plus are sometimes resisted by professionals who are set in their ways. VA leaders need to break through such resistance and bring this important and economical technology to our Veterans. Allow me to emphasize: *The decision to implement ViziLite Plus exams should not be left to individual VA hospitals; it should be directed by VA's headquarters here in Washington.*

Without ViziLite Plus screening, cancers could grow, metastasize and wind up costing the VA extraordinary amounts of money, and could subject Veterans to gross physical distress, for no good reason.

This Committee should urge the Secretary of Veterans Affairs to immediately implement annual ViziLite Plus oral cancer screening of all Veterans who are seen at VA facilities nationwide. This is the best way to assure the consistent delivery of quality life-saving care to our Veterans.

In accepting the nomination to be Secretary of Veterans Affairs, General Eric Shinseki said, "I can think of no higher responsibility than ensuring that the men and women who have served our Nation in uniform are treated with the care and respect that they have earned." Mr. Chairman, our Veterans deserve state-of-the-art innovative technologies like ViziLite Plus.

On behalf of all the employees of Zila, Inc., I thank you and the Committee for your concern about this important matter, and I urge you to exercise continuing close oversight of this issue going forward.

Thank you.

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**Prepared Statement of David Sidransky, M.D., Director, Head and Neck Cancer Research Division, Johns Hopkins University School of Medicine, and Professor of Oncology, Otolaryngology–Head and Neck Surgery, Cellular and Molecular Medicine, Urology, Genetics, and Pathology, Johns Hopkins University and Hospital, Baltimore, MD**

Mr. Chairman and Members of the Committee, I am Dr. David Sidransky, M.D.:

Oral cancer (squamous cell carcinoma of the head and neck, SCCHN) remains a significant cause of morbidity and mortality among Americans. While the death rate for many other cancers has improved, the mortality from advanced head and neck cancer has not changed in decades. Although 90 percent of patients with SCCHN are often diagnosed over the age of 40, the diagnosis of SCCHN is often delayed at all ages and the even with the best treatment, death in advanced cases of oral cancer does not spare any age group. Specific risk factors have been linked to the development of this cancer, including the use of tobacco products and excessive alcohol intake. However, about 25 percent of those diagnosed do not share any of these behaviors. A portion of these cancers are also associated with a virus, called the human papilloma virus or HPV. These cancers often strike the young in our society and their treatment leads to severe deformity, impairment of swallowing and drinking, and death. There is little hope of this society abandoning the major behavioral risks, specifically smoking or drinking. Moreover, HPV infection will not be controlled for decades even with the advent of new vaccines. Thus, oral cancer will continue to cause significant morbidity and mortality in our population.

Most cancers, including SCCHN develop over a long period of time and arise from early precursor lesions. Most cancers in the oral cavity are not found at this pre-

cursor stage and are already invasive at the time of diagnosis. Clinical outcomes in advanced cancers depend on the histological type of cancer, the size of the tumor at presentation, spread to local draining lymph nodes and how aggressively the tumor is attacking the body and spreading throughout other organs as metastases. When cancers are small and have not spread the chances of cure are much higher. Thus, morbidity and mortality can be impacted by effective identification of cancer at early enough stages to be more easily cured, or at least halted, and by use of effective therapeutic modalities to remove or kill the cancer cells. Today, these interventional options depend on surgery to remove as much of a tumor as possible, and then radiation therapy or chemotherapy to attempt to prevent the smaller tumor foci from seeding distant locations and enabling metastatic disease. These latter approaches are fairly burdensome interventions, which are most effective before cancer cells spread to multiple, more distant sites in the body.

Doctors have now known for decades that early detection is the best chance to impact the death rate from this disease (50–60 percent over 5 years). A cancer that is caught early enough is often curable. The problem is that patients with oral cancer do not present to their health care professional with readily visible signs or symptoms of their cancer until the disease has advanced to a late stage. Thus, clinicians strive to identify and treat individuals with SCCHN as early as possible. This puts a premium on identification tools that can be easily integrated into clinical practice, that are relatively non-invasive and also inexpensive, so they can be applied to large populations. Perhaps most importantly, early detection tools must have adequate sensitivity to find a meaningful number of such individuals while having sufficient specificity to not falsely identify individuals without disease as being positive for cancer.

In a meta-analysis of six worldwide studies it was reported that the weighted sensitivity of visual examination in identifying oral cancer and precancerous lesions was 79.6 percent. Visual examination by untrained examiners often misses the earliest more curable lesions. These results demonstrate that disease remained undiagnosed by conventional examination. By contrast, published studies reporting sensitivity values for ViziLite are consistent. To date, the sensitivity of ViziLite examination in identifying dysplasia and cancer is reported as 100 percent.

According to published literature, pharmaceutical-grade toluidine blue, such as that included in the ViziLite Plus test kit, preferentially stains lesions consistent with severe dysplasia, carcinoma in situ and cancer. In one study we find that a TBlue application correlated to a reduction in False Positives by 55 percent. As such, ViziLite Plus has adequate sensitivity to find a meaningful number of individuals with disease while having sufficient specificity to not falsely identify individuals without disease as being positive for cancer.

It is within this framework—early identification in high-risk populations; use of accessible, inexpensive yet effective diagnostics; demonstrated clinically relevant diagnostic sensitivity and acceptable specificity—that the ViziLite Plus by Zila finds its niche. No other medical device has sufficient sensitivity and specificity to meet the requirement of early detection in oral cancer. Other dyes and device can not precisely identify precancerous lesions and early invasive cancers while excluding healthy patients that need no further intervention. Indeed, the ease of use of the ViziLite product makes it appropriate for use by dentists, periodontists, oral surgeons, otolaryngologists, and primary-care physicians.

Considering the demographics of the U.S. military, past and present, one can see that risk factors such as alcohol consumption, cigarette smoking and advancing age imply that military members and veterans of military service are lat elevated risk of developing SCCHN whether they are young or old. Clearly, having a product that can be used to screen for oral cancer by any number of physician or dental specialists as well as generalists, makes this a valuable and necessary tool in the early diagnosis of oral cancer among military Veterans.

The FDA has cleared this combination device with an indication for use to assist in the evaluation of oral mucosal lesions for patients at increased risk for oral cancer. This is the intended use of the product, which has been studied in clinical trials in the United States and abroad and data reviewed by FDA. Interestingly, research and clinical studies by oral surgeons and dental research scientists has shown is that this product is capable of much more. While it is not proper for any FDA-regulated company to make references to claims for which the product is not cleared, it is interesting to note the publications regarding the tolonium chloride component of ViziLite Plus.

There is a great deal published in the literature which suggests that the identification of oral premalignant lesions by this product, in conjunction with use of ViziLite, may identify lesions that are a greater risk to the patient, perhaps by virtue of identifying specific changes in the DNA of the tumor cells that indicate a

more aggressive cancer. The tolonium chloride dye has demonstrated relatively high values for sensitivity and specificity. Thus, arrays of intriguing molecular studies have shown that the lesions that tolonium chloride (TBlue) detects are those that will become or are already aggressive cancers.

Probably at least partially because of the strength of the literature in support of tolonium chloride (TBlue) and the use of chemiluminescence (ViziLite), the ViziLite Plus system was selected to assist in the identification of precancerous lesions in a national Institutes of Health-funded, Phase II study of Cetuximab (Erbitux®, ImClone Systems Inc.) in upper aerodigestive precancer. Its inclusion is to identify those patients meeting the eligibility requirements of molecular changes consistent with oral lesion likely to progress to cancer. Because of unique characteristics, ViziLite use in this trial also allows the physician to clearly mark the boundaries of the lesion to determine the efficacy of the tested drug.

In conclusion, ViziLite Plus is an easy to use, sensitive and specific medical device to help both relatively untrained and expert examiners to identify oral lesions in their patients, who by virtue of their lifestyle choices regarding tobacco smoking and alcohol use, are in a high risk group for oral cancer. Additionally, in an aging patient population similarly at high risk of developing this cancer, use of this product can bring diagnostic power to physicians outside the dental specialties for greater value and potentially more savings in hospitalization. It is anticipated that inclusion into oral cancer screening protocols within the VA clinics would help to improve screening efficacy for lesions suspicious for precancer and cancer, and ultimately reduce the morbidity and mortality of this disease.

**Prepared Statement of Robert A. Beckman, President and Chief Executive Officer, Brainport Technologies, Wicab, Inc., Middleton, WI**

***Purpose of this Testimony***

The BrainPort vision device and the BrainPort balance device represent novel technologies with the potential to address certain needs of soldiers who have suffered vision loss due to eye trauma or balance disorders related to traumatic brain injuries, as well as those veterans who experience chronic balance disorders after a stroke. Both devices are available today for further clinical testing. VA participation and sponsorship of such studies would accelerate the introduction of these devices into standard rehabilitation practices.

***Background on Sensory Substitution***

Sensory substitution is based on the premise that the input sensors for the human senses can be augmented or substituted by alternate sensors. Cochlear implants are an early example of sensory substitution. Miniature electrical components attached to an external microphone are implanted in people who are totally deaf. With training, people learn to interpret the electrical impulses as sound, which enables them to hear. Wicab, Inc., founded by the late Dr. Paul Bach-y-Rita, is developing sensory substitution technology for patients with chronic balance disorders and people who are blind or vision impaired. Unlike cochlear implants, BrainPort devices are not implantable. Instead, the electrical signals are effectively transmitted from the sensor to the brain through the tongue. The tongue is a uniquely qualified target for electrical impulses because of 1) the density and sensitivity of nerve fibers 2) the suitability of the tongue's chemical environment to receive and maintain contact and 3) the rapid transfer of information from the tongue to the brain.

For people with balance disorders, the BrainPort balance device uses an accelerometer to provide accurate head position information. For people who are blind or vision impaired, the BrainPort vision device uses a digital camera to provide visual images. In both cases, the sensory information is provided via a substitute channel, an electrical impulse on the surface of the tongue.

***BRAINPORT VISION DEVICE***
***Description of Vision Device Technology***

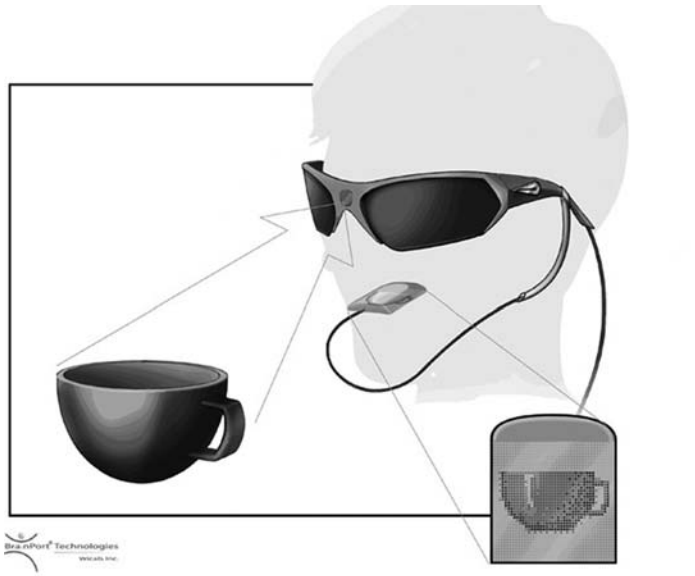
The BrainPort vision device provides information to blind individuals via a neurostimulating array placed on the tongue. This unique device provides immediate benefits to its blind users in areas of safety, mobility, and recreation and opens a new world of sensory experience and exploration.

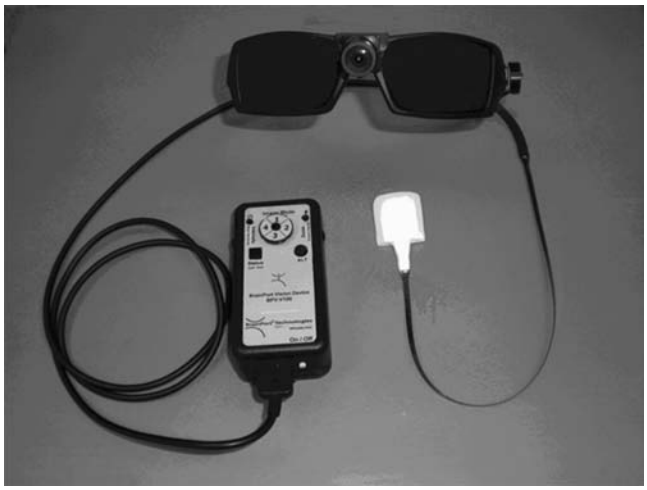
The BrainPort vision device operates by acquiring an image stream from a camera, similar to a camcorder. Like a camcorder, the moving images are sent to a display, which, in this case, is the electrode array on the tongue. The image stream is displayed on the tongue by converting light information to electrical stimulation, which feels like microscopic bubbles to the user. With minimal training, users learn

to interpret the images on their tongue as information about the scene in front of them.

The BrainPort vision device includes an imaging system capable of working both indoors and outdoors, with a field of view spanning 3–75 degrees (magnified versus wide angle views). The tongue array contains 400 electrodes and is connected to the controller via a flexible cable. The control system is approximately the size of a PDA and runs for about 3 hours per charge, with swappable batteries.

An artist's concept of the tongue array (or Intra-Oral Device, IOD) and camera mounting is shown below alongside the device. The IOD is attached to a flexible boom by a thin wire. The camera unit is mounted on a pair of eyeglasses frames. The user controls and the power supply are connected to a belt-worn, pager-style, controller.





***Who would benefit from the BrainPort Vision Device?***

According to the American Federation for the Blind, there are 1.3 million people in the U.S. who are legally blind, of which 20 percent, or 260,000 have no better than light perception. Considering the current resolution of the tongue display, the BrainPort vision device is most applicable to this subset of people who are blind, with no better than light perception. The BrainPort vision device is not intended as a replacement for the guide dog or the cane. However, blind users can use the BrainPort vision device independently—at home, at work, and in public spaces indoors and out as a tool for improved safety, mobility and object recognition. Secondary benefits include applying the technology toward specific hobbies and recreational situations. These benefits enable greater independence at home, school and in business, greatly improving quality of life.

The following list of product benefits was compiled from survey responses gathered from blind individuals who have used and know the capabilities of BrainPort technology.

**Safety**

Navigating difficult environments, such as parking lots, traffic circles, complex intersections
Recognizing quiet moving objects like hybrid cars or bicycles
Crossing the street and staying within the lines of a crosswalk
Avoiding unexpected overhead obstacles like tree branches, low signs, doorways, and holiday decorations

**Mobility**

Finding doorways, hall intersections, lobby or restaurant in an office or hotel
Finding continuous sidewalks, sidewalk intersections and curbs
Finding and navigating to buildings in school or business campus environment
Avoiding obstacles on sidewalks and in hallways
Finding stairwells and recognizing if they go up or down

**Object Recognition**

Spot reading signs, mail, book titles, etc
Locating people
Locating known objects such as shoes, cane, coffee mug, keys
Discriminating between empty and occupied chairs on a bus or in a conference room
Finding the trash can, the restroom, kitchen
Orienting oneself in a new environment, finding where objects are within a room
Recognizing graphics: web pages, mathematical graphs, photos
Signing documents such as checks and legal documents

**Recreation**

Playing off-the-shelf board and card games
Walking in the woods
Finding a wayward basketball
Running a road race
Cross-country skiing
Rock climbing
Computer games

***Current Status of Vision Device Product Development***

The development of the BrainPort vision device to its current state has been enabled by funding provided from the National Eye Institute and DARPA. The technology has evolved dramatically as a result of this funding and accomplishments by our engineering and neuroscience teams. Four years ago, the vision device required a desktop computer, employed a camera that had no zoom capability, a limited field of view and was only functional indoors. Today the device for the first time is small, versatile and user-friendly enough to enable blind users to explore the capabilities of the device both indoors and outdoors, without active supervision.

Although the BrainPort vision device is not yet commercially available, Wicab plans to file for FDA clearance shortly. Nevertheless, the BrainPort vision device is nowhere near optimized. The current resolution on the tongue is limited by the density of the electrical tactors on the tongue array. The current density is 20 times 20 pixels, effectively 20 DPI resolution. Wicab projects users would experience increased perception by increasing the resolution, up to a limit of approximately 150 DPI. With technology adapted from high definition television displays, this improved resolution is feasible today, but would cost approximately $1 million to implement. Wireless technology could eliminate the current requirement for cables running

from the control unit to the user's mouth—another advance that is feasible today, but expensive to implement.

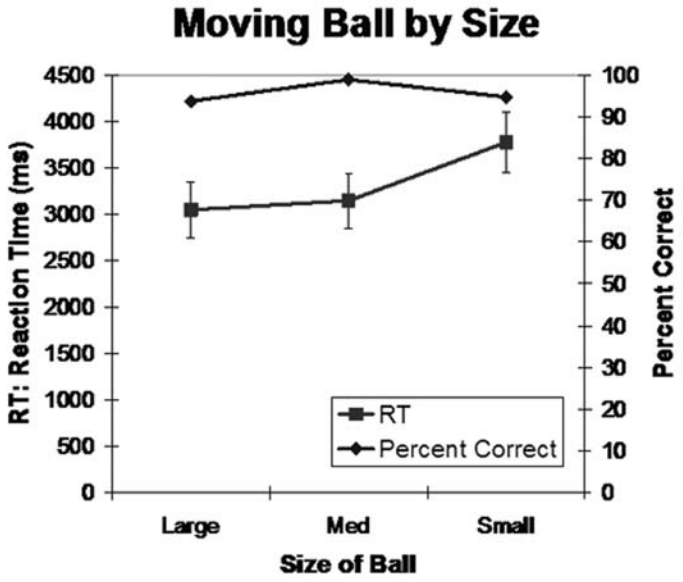
Beyond the physical aspects of BrainPort device design, there are more effective methods for information transfer (luminance or otherwise) through the tongue. These techniques include: *Advanced Image Processing* (pattern recognition, image stabilization, optical flow, etc); *Context aware computing*—adaptive algorithms to automatically adjust for visual task, reading a book versus walking down the street, for example; *Proactive guidance*—providing attentive signaling to important items in a scene (a 'do not walk' sign is flashing); *Directed guidance*—to allow a blind user to query about items in a scene—'are my shoes in this room' (and highlight everything in the scene that looks like a shoe); and *Information Stream Synergy*—Integration of image data with external data, to overlay or interleave data from multiple sensors or data sources (the Internet, for example), with the image data.

***BrainPort Vision Device Preliminary Clinical Results***

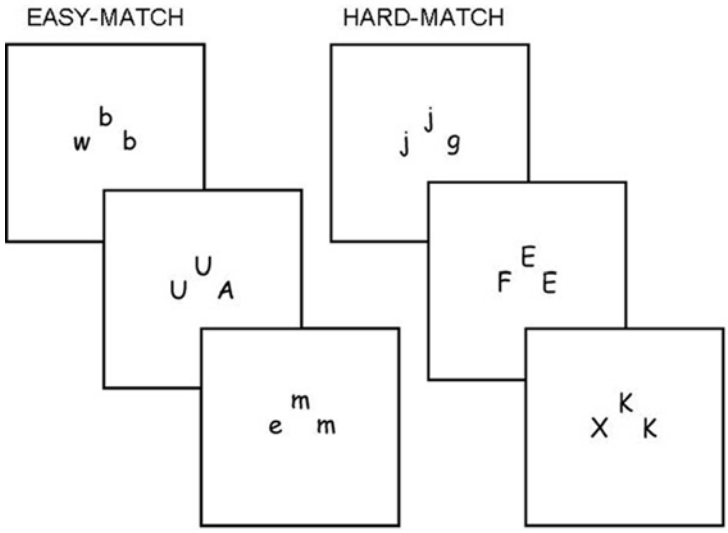
Over the past 2 years, Wicab has developed clinical tests to understand the capabilities of blind individuals while using the BrainPort device, and to develop product features based upon user performance and requests. Two years ago, the BrainPort vision device consisted of a 100-pixel tongue display and a narrow fixed field of view webcam. During testing, we noticed that subjects moved closer or farther away from an object for recognition. Based on this observation and suggestions from users, we incorporated user controlled zoom magnification. With this feature, users could magnify small characteristics (like letters on a page) or reduce large objects like buildings for appropriate recognition. In mobile situations, we noticed that users made repeated head movements to gather enough information to avoid obstacles, make turns, judge distance, etc. We found that expanding the camera's effective field of view enabled more comfortable use and better judgment of distance. In the last year, we have improved the resolution of the tongue display, from 100 pixels to 611 pixels. User feedback and performance confirms that more resolution provides crisper and clearer information to the user, especially when conveying curves and diagonal line features. Moreover, it enables object identification without reducing the field of view due to magnification.

During studies with the 100-pixel tongue display, 10 participants accurately reported the orientation of a 10-inch line presented on a wall 2 feet in front of them, approximately 80 percent of the time. Participants also accurately sorted cards with squares and circles of varying sizes into their respective categories, again >80 percent correct performance. From a distance of 5 feet and utilizing the BrainPort zoom magnification features, participants could report the orientation of the 'gap' in a rotating letter C, a controlled visual acuity test with a mean "acuity" of 20/135. To test orientation and mobility with the device, participants were placed in a large room, 15–20 feet away from a wall that displayed a variety of shapes. Participants could accurately identify shapes from a distance, using zoom, as well as navigate to the targeted shape (85 percent and 95 percent success rates, respectively). These high success rates demonstrate that with as little as 100 points of information, the BrainPort device enabled both identification of key features and the formation of a spatial reference for that information.

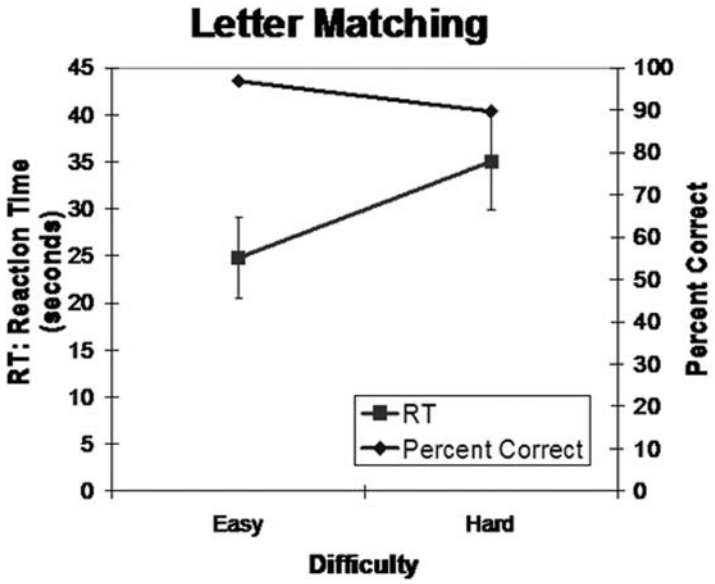
The next experiments represent more recent work with five subjects and a higher resolution tongue display of 611-pixel, identifying moving balls. One hundred four-alternative forced choice (4AFC) trials were presented on a LCD computer display. In each trial, a filled in circle/ball of three different sizes (small, medium and large) traveled in one of four directions (up, down, left, right). The subjects were to indicate with a button press on a numeric keypad which direction they perceived the motion of the circle or ball. As the graph below illustrates, all subject performed with greater than 90 percent accuracy within 3–4 seconds of trial presentation. This indicates that in the absence of other sensory input, participants using the BrainPort are quite sensitive to motion.




Another computerized experiment focused on object recognition, specifically letter matching. Fifty two-alternative forced choice (2AFC) letter stimuli were presented to all participants with a high resolution LCD video display system. Participants were instructed to respond, as quickly and accurately as possible, which of two letters matched the target item above the pair. Difficulty was manipulated by making the incorrect foil either visually similar to the correct answer in the hard condition, or dissimilar in the easy condition.



As the graph below illustrates, all subjects responded with greater than 90 percent accuracy, regardless of difficulty level within 25–35 seconds. Participants responded faster to "easy" letter matches than for the "difficult" matching, while maintaining accuracy. With practice and experience, we expect response times would decrease.




Wicab is also conducting clinical studies of the BrainPort vision device at the Atlanta VA under the direction of Dr. Michael Williams. According to a recent preliminary report, Dr. Williams concluded "Bottom line, the device performs remarkably well for the tasks we looked at in Phase I, and substantially enhances subjects' ability to accurately identify a variety of shapes at varying distances, **this is statistically significant at the .001 level, and not a random or chance finding.**"

***Recommendations***

The BrainPort vision device is now available for the next phase of clinical testing. One of the populations that may benefit from participating in these studies are soldiers who are blind, including those soldiers that lost their vision due to a traumatic injury. Wicab is very interested in obtaining further user feedback regarding the overall usefulness of the device in performing everyday tasks.

***BRAINPORT BALANCE DEVICE***

The BrainPort balance device provides change in head position information to the brain through electrical impulses directed to the tongue. The device consists of: (1) an intraoral device, which contains an accelerometer for sensing head tilt and an electrode array for transmitting the signal to the tongue; and (2) a control unit, which contains the micro controller, signal processors, memory, battery, user controls and associated driver electronics. The signal on the tongue moves in relation to the patient's head position. Patients are trained to maintain their balance while standing with their eyes closed by focusing on keeping the signal in the center of their tongue. As the patient feels the stimulus move on their tongue, they can adjust their body to move the stimulation toward the center of the tongue.

Training protocols typically require the patient to use the device during two 20-minute sessions each day. **Within a few days, most subjects learn to use the signal on their tongue to help maintain their balance and, more importantly, start to experience retention of the therapeutic effect, improved balance, after the training session ends.** Preliminary clinical data has demonstrated impressive results in treating the symptoms in a wide range of subjects with central or peripheral vestibular balance disorders.

***Who would benefit from the BrainPort Balance Device***

The prevalence of balance and/or vestibular disorders is significant:

- At least half of the overall U.S. population is affected by a balance or vestibular disorder sometime during their lives.
- Vestibular disorders (or dizziness) affect about 20 percent of the general population. Prevalence increases with age: approximately 1/4 to 1/3 of the elderly complain of some form of dizziness, and by age 75 this proportion approaches 50 percent.
- Approximately 12.5 million Americans over the age of 65 and 6 million under age 65 experience balance or dizziness problems that significantly interfere with their lives.
- Fifty percent of falls suffered by the elderly are associated with vestibular problems.
- The annual cost of medical care for U.S. patients with balance disorders exceeds $1 billion.
- Each year, over 700,000 people suffer a new or recurring stroke in the U.S.
- About 5.7 million U.S. stroke survivors are alive today, many of them with permanent stroke-related disabilities.
- **Over 70 percent of military individuals involved in blast injuries have a resultant balance disorder.**

The conventional treatment for individuals with vestibular dysfunction is vestibular rehabilitation. Vestibular rehabilitation is effective for many vestibular disorders, however, approximately **30 percent of all vestibular patients do not derive meaningful benefit from vestibular rehabilitation; instead, they rely solely on compensatory strategies.** Furthermore, most vestibular disorders are not amenable to surgical treatment. Pharmacological management of these conditions with vestibular suppressants often retards the recovery process or is associated with adverse side effects such as drowsiness. Consequently, many people are left to manage their lives with inadequate therapeutic intervention. These people represent the target market for the BrainPort balance device.

Chronic balance disorders can dramatically alter a person's ability to engage in daily activities, greatly diminishing their quality of life. Because both vestibular and visual cues for postural control are compromised, patients with chronic balance dis-

orders are often at greater risk of falling, and must rely on constant vigilance and restricted physical activity to avoid instability and falls.

Preliminary patient results indicate the BrainPort balance device will be useful in treating a broad population of patients that suffer balance disorders related to vestibular dysfunction. Target etiologies are both unilateral and bilateral vestibular dysfunction, including such specific vestibular disorders as ototoxicity, vestibular neuritis, and perilymphatic fistula, as well as a wide variety of disorders that affect vestibular function, such as balance deficits due to stroke or brain injury.

***Current Status of Device Development and Regulatory Process***

The development of the BrainPort balance device and preliminary clinical studies have been funded by the National Institute of Deafness and other Communicative Disorders and private investors. Wicab received the CE Mark for the balance device in January 2006, and has commenced limited commercial activities in Europe, Canada, Brazil and Russia. Wicab expects initial sales will be modest, because most people in these countries rely on government reimbursement to cover the cost of medical devices such as the BrainPort balance device.

Wicab is currently conducting a controlled clinical study in an effort to secure FDA 510(k) clearance. Wicab anticipates study completion by March 2010.

Medical devices intended for commercialization in the United States must be designed under established Design Control procedures that meet the FDA Quality System Regulations. Wicab quality system includes design controls, supplier controls, manufacturing and post-market surveillance in accordance with FDA's QSR and the European standard ISO 13485. The BrainPort balance device also complies with national standards such as Underwriters Laboratory and the EU Medical Device Directive.

***BrainPort Balance Device Preliminary Clinical Results***
***Peripheral and Central Vestibular Dysfunction Study***

Wicab studied the benefits of training with the BrainPort balance device in 112 subjects with vestibular dysfunction at 17 clinical sites. Etiologies of the subjects include peripheral vestibular dysfunction (bilateral vestibular dysfunction, unilateral vestibular dysfunction, post acoustic neuroma resection), central vestibular dysfunction (stroke, brain injury and age related changes), and mixed etiologies. These prospective studies designed to measure short-term and long-term balance-related changes that resulted from training with the BrainPort balance device. The BrainPort device training procedure was consistent across all sites.

Subjects received clinical training for 3–5 consecutive days (2 1-hour sessions each day) with the BrainPort balance device. Subjects then continued training at home for two 20-minute sessions each day for the duration of the study and were assessed at the end of the at-home period. Subjects did not use the BrainPort device during the assessments.

Changes in balance were measured using clinically accepted standardized outcome measures including Computerized Dynamic Posturography Sensory Organization Test, Dynamic Gait Index, Activities-specific Balance Confidence Scale and the Dizziness Handicap Inventory.

Subjects showed statistically significant improvement in all measures. Almost all of the study subjects had received prior conventional rehabilitation and had reached a plateau. This improvement is in addition to that reached by traditional rehabilitation.

***Atlanta VA Pilot Traumatic Brain Injury Study Summary***

Patients with traumatic brain injury (TBI) frequently have problems with balance and walking due to problems of integration of sensory inputs. Under sponsorship from Wicab, the Atlanta VAMC Rehab R&D Center is conducting a study to investigate the effects of the BrainPort balance device with patients with a traumatic brain injury and balance deficits.

Standard physical therapy tests of balance and walking, including Computerized Posturography testing, and Dynamic Gait Index are used to measure of fall risk. After completing the testing, subject are trained to use the device while trying to maintain balance while standing with eyes closed and feet in a challenging position (such as together or heel-to-toe) and on altered surfaces, such as a foam cushion. Training occurs over 5 days. Subjects then take the device home to use twice daily for 20 minutes. Subjects return to the Atlanta VAMC for follow up testing to see if balance and walking improve after a 12-week period of home training.

This project is still in the very early stages. Measures of balance confidence, computerized posturography and fall risk improved in the three subjects trained thus far. These data, while preliminary, suggests a positive effect of the BrainPort balance device on balance in individuals with TBI.

***Traumatic Brain Injury Case Study***

One of the patients participating in a study with the device is a 39-year-old male who sustained a severe traumatic brain injury due to a motor vehicle accident in 1993. Following his accident, he completed the full range of conventional rehabilitation including inpatient and outpatient physical therapy, occupational therapy and speech therapy. His balance and walking improved to where he could walk using a walker, but required supervision to navigate outside of his home and occasionally fell when walking or trying to do an activity. His cognitive function improved to the point where he was able to live independently and work part-time, but he felt like his head was never quite clear. He continued to have difficulty with balance, walking, and daily activities due to ataxia and impaired motor control on his right side, caused by damage to the left midbrain and cerebellum. After extensive rehabilitation, he had reached a plateau in his recovery. In 2006, 13 years after his injury, he began using the BrainPort balance device.

He has been training with the BrainPort balance device consistently for the past 2½ years. After the initial week of clinic training sessions, the majority of his training is completed in his home. He returns to the clinic for modifications to his training approximately every 3 months. He has demonstrated ongoing improvements in his balance since enrolling in the BrainPort study. His score on a standardized balance confidence scale improved from 74 percent confidence to 94 percent confidence at 1 year, where it remains. Though he continues to use his walker, he demonstrates a much more upright posture with decreased dependence on the walker. He no longer falls and does not require supervision to walk in the community. He is transitioning to walking with a quad cane, which is much less cumbersome for daily use. He is able to walk longer distances both with and without his assistive devices. When he has a loss of balance, he is able to regain his equilibrium independently. He reports that he is more confident in his balance, and his activities do not require as much effort, which results in an increase in his energy level. The patient, his mother and his doctor attribute the improvements in his posture, standing balance, ataxia, and gait over the last 2½; years to training with the BrainPort balance device.

***Stroke Pilot Study Summary***

A pilot study with 26 patients who have a balance problem due to stroke was conducted at 5 clinical sites. Participants learned to use the BrainPort device over a 5 day (10 hours total) clinic training period. Following clinic training, each participant continued their training in their home, independently for 8 weeks. Participants were assessed at baseline and at 8 weeks to compare their balance and mobility before and after training.

Training with the BrainPort device for 8 weeks, seven of which were at home, yielded statistically significant (p values less than .05) improvements on the Dynamic Gait Index (DGI), Berg Balance Scale (BBS) and the Timed Up and Go Test (TUG), three valid objective measures used to assess balance and ambulation. With the BBS, this statistically significant change was over two times the minimal criteria established for clinically significant improvement. For the TUG, the degree of improvement also exceeded the minimal difference for clinical significance.

Consistent with these objective findings, participants showed statistically significant improvement on the Activities-Specific Balance Confidence Scale, a self-report measure. This improvement was over two times the minimal criteria established for clinically significant improvement. Similarly, on the Stroke Impact Scale, patients demonstrated statistically significant improvement on their ratings of mobility, activities of daily living, social participation and overall rating of stroke recovery. Importantly, no statistically significant changes were obtained with measures of memory, communication and emotions, all subjective measures that were ***not*** anticipated to be affected by BrainPort training.

Taken together, these data provide both objective and participant endorsement of the BrainPort device in the treatment of balance, mobility and function among individuals with stroke.

Early studies with the BrainPort balance device demonstrate the potential for helping patients with stroke and traumatic brain injury improve their balance and motor control. Ultimately, the device could become a key component of a comprehensive rehabilitation program.

***Recommendations***

The medical community requires rigorously planned controlled clinical data prior to adopting new technologies such as the BrainPort balance device. Wicab is sponsoring such a study in patients with peripheral vestibular dysfunction. Based on the early promising results in traumatic brain injury, we would welcome the opportunity to work with soldiers who have a balance disorder related to a blast injury

to incorporate BrainPort balance training as a part of their rehabilitation regimen. VA leadership is appropriate, given the relatively small patient population with traumatic brain injuries, which hinders funding by commercial entities. Finally, the preliminary results in stroke warrant the initiation of a controlled clinical study in that target patient population, and Wicab would similarly welcome VA participation in this patient study.

## Prepared Statement of David A. Broecker, President and Chief Executive Officer, Alkermes, Inc., Cambridge, MA

Mr. Chairman, Ranking Member Buyer and Members of the Committee, thank you for inviting me to testify here today on behalf of Alkermes.

**Overview**

Alkermes is pleased to have the opportunity to submit testimony on innovative technologies and treatments for veterans. Given the personal sacrifice that our brave servicemen and women have made, we believe that it is important to give them access to the best medicines and treatments currently available to help them get the care they need to live happy, healthy and productive lives. Using innovative drug delivery technology, Alkermes has developed a unique medicine for the treatment of alcohol dependence, called VIVITROL® (naltrexone for extended-release injectable suspension). VIVITROL is a breakthrough medicine that, when combined with counseling, has the potential to greatly reduce the human and financial toll associated with alcohol dependence.

**Alkermes**

Alkermes is a small biotechnology company located in Cambridge, Massachusetts. As a company, we are committed to developing medicines that make a difference in patients' lives. Our products, which use novel molecules and innovative drug delivery technologies, target the unmet medical needs of patients suffering from diseases like schizophrenia, bipolar disorder, addiction and diabetes. We approach the drug development process with patients as our top priority, beginning with a thorough understanding of the challenges they face on a day-to-day basis. Our products are designed with patient needs and behaviors in mind, with the goal of dramatically improving therapeutic outcomes.

**Substance Use Disorders Among OEF/OIF Veterans**

Alcohol dependence is a major problem among military veterans. In 2003, a survey conducted by the Substance Abuse and Mental Health Services Administration (SAMHSA) estimated the veteran population in the United States to be 25 million, or roughly 11.5 percent of the entire non-institutionalized civilian population.[1] Approximately 7.5 percent, or nearly 1.9 million, of these veterans reported drinking heavily in the month prior to being surveyed (compared to 6.5 percent of comparable nonveterans). SAMHSA estimated that approximately 650,000 veterans (2.6 percent) were alcohol dependent. By 2006, the VA's own data showed that only 175,268 veterans were actually receiving treatment for their alcohol abuse or alcohol dependence within the VA system.[2] In addition to post-traumatic stress disorder (PTSD), alcohol abuse and alcohol dependence are consistently among the most prevalent psychological disorders in male veterans of the Vietnam era.[3] In female veterans of Vietnam, alcohol abuse and dependence are second only to depression and generalized anxiety.

Since the start of Operations Enduring Freedom (OEF) and Iraqi Freedom (OIF), over 1.8 million American military personnel have been deployed, with nearly a third coming from the National Guard and Reserves.[4]

In 2006, the New Jersey Department of Military and Veterans Affairs, in conjunction with the University of Medicine and Dentistry of New Jersey and the Bloustein Center for Survey Research at Rutgers University, surveyed New Jersey National Guard members who had returned from Iraq within the past year. The results of

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[1] U.S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, *National Survey on Drug Use and Health*, November 10, 2005.

[2] U.S. Department of Veterans Affairs, *Health Services for VA Substance Use Disorder Patients* Comparison of Utilization in Fiscal Years 2005, 2004, 2003, and 2002, June 2006.

[3] U.S. Department of Veterans Affairs, National Center for Posttraumatic Stress Disorder, *Findings from the National Vietnam Veterans' Readjustment Study*, available at http://www.ncptsd.va.gov/ncmain/ncdocs/fact__shts/fs__nvvrs.html?opm=1&rr=rr45&srt=d&echorr=true.

[4] Legal residence/home address for servicemembers currently deployed as of December 31, 2008. (2009) Defense manpower data center. Retrieved April 8, 2009 from: dva.state.wi.us/WebForms/Data__Factsheets/ResDistribution__Dec08.pdf

the study were striking—37 percent of those surveyed reported problem drinking in the year following their deployment. Even more troubling, 55.3 percent of the veterans with PTSD reported problem drinking.[5]

In a study published in the *Journal of the American Medical Association*, Hoge et al. of the Walter Reed Military Research Institute administered anonymous surveys and assessed 2,530 U.S. combat duty personnel before their deployment to Iraq and 3,671 troops three to 4 months after their return from combat duty in Iraq or Afghanistan. Over 35 percent of Marines reported experiencing at least one symptom of alcohol dependence (drinking more than intended) after deployment, and over 29 percent reported that they felt they needed to cut down on their drinking.[6]

To put the seriousness of these alcohol problems in perspective, Hoge et al. found substantially lower rates for depression (7.1 percent), anxiety (6.6 percent) and PTSD (12.2 percent). Only PTSD showed a comparable rate of increase (pre-deployment to post-deployment)—an expected finding given that over 90 percent of the combat duty personnel had been directly involved in gun battle and/or handling the bodies of fellow servicemen and women, killed in the line of duty.[7]

The incidence of alcohol dependence symptoms appears to be the most common problem facing returning combat duty personnel. Alcohol dependence exacerbates other psychiatric and medical problems and undermines treatment. Combat duty personnel may be particularly likely to use alcohol to self-medicate their psychiatric problems, resulting in worsened overall mental health and alcohol dependence. The strong reluctance to seek professional help may be a particularly important factor contributing to the misuse and ultimate dependence on alcohol.

While the incidence of mental health and alcohol problems within a few months of returning from combat is high, alcohol problems in particular often take years to manifest. For this reason it is important to consider research from past military conflicts. Specifically, the National Vietnam Veterans Adjustment Survey found 40 percent of male veterans reported lifetime alcohol problems post-deployment. In 2000, the Department of Defense's Alcohol Abuse and Tobacco Use Reduction Committee reported that, even prior to the start of the conflict, 21 percent of servicemembers admitted to drinking heavily, costing the Department of Defense more than $600 million each year in terms of medical care and lost productivity.[8]

A February 2007 report by the American Psychological Association on the mental health needs of returning veterans found a variety of barriers are preventing military personnel from accessing much needed mental health and alcohol treatment. The report cited stigma and a lack of availability of services as the primary reasons why personnel and their families are not accessing care.[9] Shortages of trained uniformed personnel, high burn out rates among providers and difficulties in referring military personnel to civilian providers often mean long waits for care. Moreover, in other reports and testimony before this Committee, providers have reported significant recent decreases in the availability of inpatient beds for alcohol dependence treatment. During these high service utilization periods, medication assisted treatment for alcohol dependence may improve VA care delivery by integrating primary care and behavioral health care and providing immediate help upon substance use disorder diagnosis during high volume periods.

**Vivitrol**

As researchers have gained a deeper understanding of the complex brain mechanisms that trigger alcohol dependence, medications are increasingly considered to be important treatment options for this disease. In 2005, the National Institute on Alcohol Abuse and Alcoholism (NIAAA) issued guidelines, recommending the combination of medications and psychosocial support as part of an integrated treatment program.[10]

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[5] Kline, A. & Falca-Dodson, M. (2007) Presentation on substance abuse and mental health problem in returning Iraqi veterans.

[6] Hoge, C., Auchterlonie, J. & Milliken, C. (2006). Military mental health problems: Use of mental health services, and attrition from military services after returning from deployment to Iraq or Afghanistan. J*ournal of the American Medical Association*, 295(9), 1023–1032.

[7] Hoge, C.W., Castro, C.A., Messer, S.C., McGurk, D., Cotting, D.I. & Koffman, R.L. (2004). Combat duty in Iraq and Afghanistan, Mental Health Problems, and Barriers to care. *New England Journal of Medicine*, 351(1), 13–22.

[8] Rhem, K. (2000, June 6) Alcohol abuse costs DoD Dearly. American Forces Press Service. Retrieved May 7, 2009 from: http://www.defenselink.mil/news/newsarticle.aspx?id=45284

[9] Johnson, S. et al (2007) The psychological needs of U.S. military servicemembers and their families: a preliminary report. Retrieved May 7, 2009 from: http://www.apa.org/releases/MilitaryDeploymentTaskForceReport.pdf

[10] U.S. Department of Health and Human Services, National Institutes of Health, *Helping Patients Who Drink too Much: A Clinician's Guide*, 2005.

One of the products currently approved by the U.S. Food and Drug Administration (FDA) for the treatment of alcoholism is VIVITROL, an extended-release naltrexone product developed and manufactured by Alkermes. Naltrexone is a non-addictive, non-aversive agent that binds to opioid receptors in the brain. In people with alcohol dependence, it is believed that this blockade diminishes craving for alcohol and leads to a greater ability to resist urges to drink excessively.[11] Eliminating the urge to drink allows patients the stability they need to focus on the psychosocial therapy component of their recovery.[12]

Approved by the FDA in April 2006, VIVITROL is the first and only once-monthly injectable medication for the treatment for alcohol dependence. It is intended for patients who are able to abstain from drinking in an outpatient setting in the week prior to initiation of treatment with VIVITROL; patients using VIVITROL in combination with psychosocial support have demonstrated significantly increased abstinence and decreased both drinking and heavy drinking days beyond what was achieved with counseling and placebo alone.[13]

In a 2005 study in the *Journal of the American Medical Association*, authors reported on the results of a 6-month phase III clinical trial on extended-release naltrexone. When extended-release naltrexone was added to counseling alone, the average patient experienced a 48-percent reduction in heavy drinking days compared to counseling plus placebo alone.[14] For those who had abstained from alcohol in the week prior to receiving their first dose of medication, there was a 90 percent or better reduction in heavy drinking, a two to three times greater likelihood of maintaining continuous abstinence and a 90-percent reduction in drinking days compared to the counseling plus placebo group over the 6-month period. VIVITROL is the only pharmacologic treatment for alcohol dependence that extends a medication's release over 30 days, which assures that measurable blood plasma concentrations are present in the patient's bloodstream every day during the expected treatment period.

In fact, studies show that VIVITROL, when combined with psychosocial therapy, triples the duration of initial abstinence and nearly triples the proportion of patients who maintain total abstinence over 6 months.[15] Even at times when alcoholics are most at risk for drinking—for example, the ten deadliest U.S. national holidays due to drunk driving—this once-monthly medication has been found to reduce the median level of drinking to virtually zero.[16,17]

While there are other pharmacologic treatments for alcohol dependence, a SAMHSA study found that the vast majority of patients with this disease have difficulty adhering to an alcohol pharmacotherapy that requires them to take a pill every day.[18,19] Anticipating this challenge, the National Institute on Drug Abuse NIDA) issued two reports in 1976 and 1981 calling for the development of sustained-release preparations.[20,21] The VIVITROL clinical development program was funded in part with a Small Business Innovation Research Program grant from NIAAA. The proprietary Medisorb® drug delivery technology in VIVITROL allows the medication to be gradually released into the body at a controlled rate, delivering

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[11] Oswald LK, Wand GS. Opioids and Alcoholism. *Physiology & Behavior* 2004; 81: 339–358.

[12] Vivitrol [prescribing information]. Cambridge, MA: Alkermes, Inc; 2007.

[13] Garbutt JC, Kranzler H, O'Malley S, Gastfriend D, Pettinati H, Silverman BL, et. al. Efficacy and Tolerability of Long-Acting Injectable Naltrexone for Alcohol Dependence: A Randomized Controlled Trial. *Journal of the American Medical Association*; 2005; 293:1617–1625

[14] Garbutt, J. et al (2005). Efficacy and tolerability of long-acting injectable naltrexone for alcohol dependence: a randomized controlled trial. *Journal of the American Medical Association*; 293: 1617–1625.

[15] O'Malley SS, Garbutt JC, Gastfriend DR, Dong Q, Kranzler H.R. Efficacy of extended-release naltrexone in alcohol-dependent patients who are abstinent before treatment. *J Clin Psychopharmacol* 2007 Oct;27(5):507–12.

[16] Lapham S, Forman R, Alexander M, Illeperuma A, Bohn MJ. The effects of extended-release naltrexone on holiday drinking in alcohol-dependent patients. *J Subst Abuse Treat* 2009 Jan;36(1):1–6.

[17] Rosenbloom DL. Holidays, triggers, and willpower—is there a role for medications? A commentary on "The effects of extended-release naltrexone on holiday drinking in alcohol-dependent patients". *J Subst Abuse Treat* 2009 Jan;36(1):7.

[18] Other pharmacologic interventions to treat alcohol dependence include: oral naltrexone, acamprosate, and disulfuram.

[19] Harris KM, DeVries A, Dimidjian K (2004). Trends in naltrexone use among members of a large private health plan. Psychiatric Services. http://ps.psychiatryonline.org. 55(3):221

[20] Willette R, Barnett G, editors (1976). *Narcotic Antagonists: The Search for Long-Acting Preparations*. NIDA Res Monogr DHEW Publication No. (ADM) 76–296. http://www.drugabuse.gov/pdf/monographs/04.pdf

[21] Willette R, Barnett G, editors (1981). *Narcotic antagonists: naltrexone pharmacochemistry and sustained-release preparations*. NIDA Res Monogr 28:1–273. http://www.drugabuse.gov/pdf/monographs/28.pdf

the naltrexone throughout the bloodstream and to the brain for 30 days after each injection. It provides patients the convenience of monthly dosing, which alleviates the difficulty of adhering to a daily medication regimen.

**Veterans Access to Vivitrol**

While Alkermes is pleased that many top tier addiction treatment centers have now adopted Vivitrol on their formularies as a first-line treatment for patients with alcohol dependence, the Committee should be aware that our Nation's veterans do not have the same access to the latest alcohol pharmacotherapies.[22]

The VA conducted a clinical review of VIVITROL from January 2007 through February 2008 and declined to grant the product formulary status. Although VA providers may prescribe non-formulary products for their patients, significant barriers may prevent VA patients from receiving treatment with VIVITROL. A longstanding VA directive limits the interaction that companies can have with VA physicians to discuss non-formulary products. This type of restriction may limit provider education and hamper patient access to novel therapies. Although some providers within the VA have fought for access to VIVITROL and have prescribed it for their patients with great success, the usage rate for VIVITROL within the VA is effectively zero.

To the credit of the VA, the agency published policy guidance, *Uniform Mental Health Services in VA Medical Centers and Clinics*, in June 2008. This document promotes the use of medication assisted treatment for alcohol dependent individuals; however, to date, few veterans have been able to obtain access to VIVITROL. While there are approximately 650,000 veterans who meet the criteria for alcohol dependence, only about one quarter of those individuals actually receive SUD treatment within the VA system.[23] In 2008, our estimates suggest that fewer than 125 patients in the entire VA system (less than 0.07 percent) have received VIVITROL.

In March 2008, the VA testified before this Committee that the VA/DoD Clinical Practice Guidelines for Substance Use Disorders would be published within 6 months.[24] These guidelines are a necessary element of educating providers about SUD treatment, which is key to broadening patient access and eliminating the stigma associated with this devastating disease. The guidelines were last updated in 2001 and, since their initial release, new medications for the treatment of alcohol dependence have been approved by the FDA. Nevertheless, in the absence of updated guidelines, our veterans appear to have enormous difficulty accessing these newer agents.[25,26]

The VA has outlined a performance measure to assess its success in continuity of care for veterans in treatment for SUD; however, by the VA's own admission, "Many VA SUD programs have found it difficult to meet the Office of Quality and Performance's Continuity of Care performance measure. The measure requires that patients entering a new episode of specialty SUD treatment receive at least two VA substance abuse clinic visits for each of three successive 30-day periods after qualifying as a new patient."[27] VIVITROL is a powerful tool that could improve continuity of care for veterans being treated for SUD and bring VA closer to meeting this performance measure.

Many people outside of the VA have had access to VIVITROL for some time. Beneficial results have been reported in state public treatment systems, in many other community-based treatment programs throughout the U.S., in primary care settings, in DUI and drug courts and in private commercial insurance patients.[28–32] In

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[22] Alcoholism and Drug Abuse Weekly; 2007; 19(23).

[23] U.S. Department of Veterans Affairs, *supra* note 2.

[24] John Paul Allen, Ph.D., Associate Chief Consultant for Addictive Disorders, Veterans Health Administration, U.S. Department of Veterans Affairs, in testimony before the House Committee on Veterans' Affairs Subcommittee on Health, March 11, 2008, available at http://veterans.house.gov/hearings/transcript.aspx?newsid=187.

[25] CAMPRAL® (acamprosate calcium) Delayed-Release Tablets were approved by the FDA on July 29, 2004.

[26] VIVITROL® (naltrexone for extended-release injectable suspension) was approved by the FDA on April 13, 2006.

[27] Schaefer J et al. (2007).Program and Patient Factors that Influence Continuity of Care Performance Measure Outcomes in VA Substance Use Disorder Treatment Programs, available at http://www.chce.research.va.gov/docs/pdfs/CoC__Providers__Survey.pdf.

[28] Colston S. Florida Advancing Recovery Project Implementing Medication Assisted Treatment using Vivitrol: November 2006–October 2008 Preliminary Results. Available from: Florida Substance Abuse Program Office, Stephenie__Colston@dcf.state.fl.us.

[29] Abraham AJ, Roman PM. Early Adoption and Implementation of Vivitrol. Addiction Health Services Research Annual Conference, Boston MA, Oct 21, 2008

Continued

these privately insured patients, this medicine was associated with the greatest reduction in hospitalization and emergency room visits while simultaneously increasing patients' utilization of counseling—leading Aetna Behavioral Health to introduce disease management with the medicine before patients even leave alcohol rehabilitation programs. Similar cost benefits were reported by a major state-wide Blue Cross Blue Shield health plan—a 49-percent reduction in hospital and pharmacy costs after VIVITROL treatment.[33] Improved outcomes and reduced costs are significant and attainable, but the VA must make SUD treatment a priority—both in policy and in funding.

**Real Patients, Real Success**

I would like to share with you a story, told to me by a physician, about the success one patient realized with VIVITROL. The patient's name is Chris, and he is currently 26 years old. Chris started drinking when he was in high school, on Friday nights after football games with his friends and fellow band members. After graduating from high school, Chris enrolled as a college freshman and soon found himself drinking more and more. Pretty soon, he started skipping classes and instead spent all his time drinking with his new friends. Unfortunately, Chris dropped out of school before the end of his freshman year and moved back to his father's home in Nashville, Tennessee.

Chris enrolled in a local community college, but his drinking continued to get out of control. Every day, he would take a cooler of beer with him to school in the back of his car, drinking between classes and later showing up to work drunk. During the summers, he would visit his mother and stepfather in Dallas, Texas, where his drinking led to arguments and a concern that he might assault his mother. His anger and drinking led to a total of six arrests for driving under the influence (DUI)—three in Texas and three in Tennessee—and one arrest for aggravated assault. Chris would get sober during his times in jail, and he attempted to get longer term treatment through the Salvation Army and numerous half-way houses. Each time he would "dust himself off" and try to stay sober, but, unfortunately, he relapsed every time. Finally, someone he knew convinced him to try VIVITROL.

Chris was hesitant at first, but he quickly saw the benefits of the medicine. He liked being able to see a doctor once a month to receive his injection, without having to worry about taking his medicine every day. He was able to get into and stay in counseling. Currently, he is back in school. He was recently invited to his family reunion for the first time in 4 years, and he has re-established good relationships with both his parents. He has a new girlfriend, is holding down a job and has remained sober for more than a year. Chris says that VIVITROL really helped him get back on the right track, and now he can't wait to get up and enjoy each day. The reason this physician's story means so much to me is because Chris is his son.

**Conclusion**

Alkermes and its investors took a risk in pursuing a difficult manufacturing process to produce medicines with innovative delivery systems in order to treat the unmet needs of patients with devastating diseases. If the company's work were assuredly profitable, companies much larger than ours would pursue the same approach. Patients, not profits, are the driving force behind what we do. Since 1987, Alkermes has continually focused on one goal—improving the lives of patients by developing therapies that improve outcomes. What started as a small research company is now a company that develops and manufactures treatments for diseases that others in the industry have largely ignored. The Federal Government, through NIH and NIDA, partnered with Alkermes in development of VIVITROL many years ago, but the government must remain an active partner, following through on its commitment to assist patients with accessible, affordable SUD pharmacotherapy. Our company is focused on the devastating problem of alcohol dependence among our veterans, and we believe that the VA must be equally committed. Meaningful clinical guidelines must be published and regularly updated to reflect emerging

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[30] Un H. Medication Assisted Treatment for Alcohol Use Disorder. SAMHSA/CSAT Invitational Conference on Economic Access to Treatment, Washington DC, Nov 3, 2008

[31] Lee JD, Grossman E, DiRocco D, Truncalil A, Rotrosen J, Hanley K, Stevens D, Gourevitch MN. Extended-release Naltrexone Injectable Suspension for Treatment of Alcohol Dependence in Urban Primary Care—A Feasibility Study: Preliminary Analysis. Addiction Health Services Research Annual Conference, Boston MA, Oct 21, 2008

[32] Hon J Kandrevas, Hon D Gruenburg. Testimony on Use of Medication in Selected Michigan DUI Courts to State of Michigan House Subcommittee on Corrections, March 6, 2008.

[33] Borawala AS, Gill P, Jan S. Utilization Patters of Vivitrol® (naltrexone for extended-release injectable suspension) for Alcohol Dependence. Horizon Blue Cross Blue Shield of New Jersey, Newark NJ and Rutgers U. Poster presented at Academy of Managed Care Pharmacy 21st Annual Meeting, April 17, 2009, Orlando FL.

therapies; performance measures must be developed, communicated and enforced in order to promote accountability; and the VA must make treatment of addiction among our Nation's veterans a real priority before we lose even one more veteran to the disease. In closing, thank you again for the opportunity to testify here today about the Alkermes story. We believe we offer a product that can dramatically improve the lives of our Nation's veterans; they deserve no less than the very best innovative technologies and treatments available.

**Prepared Statement of Mark Munroe, Senior Vice President, Sales and Marketing, Mobile Medical International Corporation, St. Johnsbury, VT**

Good day. First, I want to thank Chairman Filner and Congressman Buyer for allowing me to testify here today on behalf of my employer, Mobile Medical International Corp., Inc. (MMIC) of St. Johnsbury, Vermont. My name is Mark Munroe, Senior Vice President of MMIC. My sole purpose here today is to explain how MMIC is using an innovative approach to help Veterans Health Administration Medical Centers provide top-flight surgical care, keep VHA surgeons engaged with their patients and save significant amounts of time and money associated with the refurbishment of VHA operating rooms.

Mobile Medical is an international company that develops and manufactures commercial and military mobile surgical hospitals which meet U.S. health care standards. These mobile health care solutions are rapidly deployable, fully integrated, self-contained and present innovative solutions for today's health care delivery needs. To illustrate the versatility of this technology in various markets, note that MMIC has responded to a FEMA request to support the University of Texas Medical Branch (UTMB) in Galveston Texas after Hurricane IKE; provides on-site surgery at a maximum security prison in North Carolina with an MMIC staffed mobile unit; and has delivered eye-care and surgical care units to Armenia, Saudi Arabia, Oman and Iraq. As a point of reference, about 6 weeks ago Mobile Medical was featured on the international television program, Little People, Big World, where Iraqi dwarf children were shown receiving care on the MMIC mobile surgical unit in Southern Iraq.

Our flagship product, the Mobile Surgery Unit, can be driven to any VHA location and upon deployment triples in size to become a mobile surgical hospital that meets U.S. health care standards. These standards include those required for State licensure, Medicare Certification and Joint Commission on the Accreditation of Health care Organizations (JCAHO). MMIC's units meet all three of these standards. MMIC has provided mobile surgical capability to private, non-profit and university medical centers for over 12 years from California to Virginia and beyond. This service has most often been provided on a rental basis, and contract periods last anywhere from 6 months to several years. The primary reasons hospitals opt for this mobile solution are that it eliminates the cost of contracting out surgical cases to other hospitals and saves additional resources by trimming months from the duration of the project.

Over the past 18 months MMIC has successfully brought this cost-saving innovation to VHA medical centers which are undergoing hospital operating room renovations. Our conservative estimates indicate that VHA Medical Centers can save on average $12,000 per surgical case by maintaining control of these cases rather than contracting them out to local or regional hospitals. This approach also assures VHA management that VHA surgeons are handling the cases and maintaining their skills.

MMIC has successfully utilized this approach at the VAMC in White River Junction, Vermont, and has a unit actively working on endoscopic cases at the VAMC in Martinsburg, WV. MMIC is preparing to provide several units to cover a major operating room renovation project in Miami and is currently working on similar opportunities at VHA facilities in New Orleans, LA, Kansas City, MO, San Diego, CA, Clarksburg, WV and Fayetteville, NC. Many VHA facility leaders that have indicated interest in utilizing our units for this purpose have expressed a desire for a streamlined contractual process administered by VHA headquarters.

In order to address these expressed concerns, MMIC submitted an "Unsolicited Proposal" to the VA's National Acquisition Center in 2008. This submission proposed a pilot project utilizing 5 MSU's over 3 years saving $90 million. Those savings are summarized in the attached two-page executive summary. This request was ultimately denied. MMIC estimates that a more robust project utilizing 20 MSUs for currently scheduled operating room projects could result in total cost avoidance of nearly $700M over a 5-year period. (See one-pager also attached).

MMIC continues to attempt a dialog with the National Acquisition Center in order to emphasize the significance of the cost savings this approach offers, the benefits of keeping patients and staff inside the VHA system for their surgeries and the difficulties VHA Medical Center contract officers face as they attempt to fashion appropriate contract vehicles for this service.

Mobile Medical International Corp. stands ready to provide the Veterans Health Administration and its patients/clients with cost effective solutions for complex health care delivery concerns.

Thank you for taking the time to learn about MMIC's innovative work within the VHA system. It has been a pleasure being here today and an honor to testify before the Committee. Thank you.

**Prepared Statement of Stanley Stern, President, TeleMed Network, Ross, CA**

Chairman Filner, Ranking Member Buyer, and Members of the Committee, thank you for the opportunity to testify today on behalf of TeleMed Network. My name is Stanley Stern; I am President of TeleMed Network.

I want to outline for you today a technology that my company believes can significantly improve the treatment of behavioral health problems among veterans by better connecting them to the medical and community support they deserve.

A recent study by RAND estimated that 18.5 percent of troops returning from the wars in Iraq and Afghanistan—about 300,000 people—suffered symptoms of posttraumatic stress disorder.[1] Other studies have suggested that similarly large numbers of veterans show signs of depression, often in conjunction with PTSD.[2]

The Departments of Defense and Veterans Affairs, with the consistent support of this Committee, have dramatically increased efforts to restore our wounded, regardless of whether they were damaged in body or mind. Sometimes it has taken bad news to spur a response, but ultimately, I and most Americans believe, this Country does do the right thing for our veterans.

Unfortunately, the challenges to treating those warriors who are now fighting their own private battles against mental health conditions are complicated by culture, demographics, and geography.

Mental illness encourages isolation and flourishes in it, and the internal and external forces that drive troubled veterans into isolation are very strong. This is particularly sad when their illness is something like PTSD, which may respond better to personal therapy and interaction with veterans' groups than to drugs.[3]

Nationwide, relatively few Americans, compared with past generations, have been exposed to military life and its shared experiences, both good and bad. That's an unfortunate side effect of America's all-volunteer military. So when soldiers go home after battle, fewer and fewer people understand what they've been through. That goes for psychological counselors as much as anybody.

After being steeped in the pride and self-reliant ethos of America's Services, many veterans are understandably reluctant to admit their need for help, particularly when the wounds are invisible. They may even think, albeit incorrectly, that VA hospitals exist mainly for those graying veterans of past wars, not for otherwise healthy young men and women.[4]

The isolation can be even worse for those who served with the Reserves or National Guard, particularly when they go home to a small town or a community that's isolated by geography or culture. Qualified help, where caregivers understand what happens to men and women in war, may be miles away, compounding the self-protecting urge to stick it out, go it alone, to be a "soldier."

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[1] T. Tanielian and L. Jaycox, eds, *Invisible Wounds of War: Psychological and Cognitive Injuries, The Consequences, and Services to Assist Recovery*, 2008.

[2] D.G. Campbell et al., "Prevalence of Depression-PTSD Comorbidity; Implications for Clinical Practice Guidelines and Primary Care-Based Interventions," *Journal of General Internal Medicine* 22. no. 6 (2006); N. Breslau et al., "A Second Look at Comorbidity in Victims of Trauma: The Postraumatic Disorder-Major Depress Connection," *Biological Psychiatry*, 48, no. 9 (200), as referenced in M. Audrey Burnam et al., "Mental Health Care for Iraq and Afghanistan War Veterans," *Health Affairs*, 28, no. 3, (2009), p. 773.

[3] Institute of Medicine, Crossing the Quality Chasm: A New Health System for the Twenty-first Century (Washington: National Academies Press, 2001), as referenced in M. Audrey Burnam et al., "Mental Health Care for Iraq and Afghanistan War Veterans," *Health Affairs*, 28, no. 3, (2009), p. 776.

[4] Tanielian and Jaycox, eds., Invisible Wounds of War, referenced in M. Audrey Burnam et al., "Mental Health Care for Iraq and Afghanistan War Veterans," *Health Affairs*, 28, no. 3, (2009), p. 774.

Two years ago, the Department of Defense Task Force on Mental Health took a broad look at psychological care for veterans and candidly admitted that "the Military Health System lacks the fiscal resources and the fully trained personnel to fulfill its mission to support psychological health in peacetime or fulfill the enhanced requirements imposed during times of conflict."[5]

The Task Force reported that about one-third of the 686,306 veterans discharged between 2002 and 2006 who were eligible sought care at a VA facility. Of those, more than one-third were diagnosed or evaluated for mental disorders (17 percent PTSD, 14 percent drug problems, and 12 percent depression).

Among the specific failures in mental health care were an inability to overcome the stigma that veterans attach to reaching out for mental health care, the inaccessibility of qualified service providers, insufficient collaboration among providers, and other problems having to do with communication.

Indeed, the crux of many of the problems in dealing with military mental health problems is communication. So, why not use modern technology to relink the suffering veteran back into a supportive community that understands his or her problems and has the proper tools to solve them?

Simply put, TeleMed's system can provide veterans with a video teleconferencing capability in their homes, using a simple, scaleable, and affordable version of the technology common in corporate business.

Our TeleMed Internet Endpoint, what we call "TIE," currently costs less than $1,000, with the price expected to drop significantly. It is small, just three pounds, so it is portable and can be mailed. Yet, it provides a brilliant video conferencing image on a home television. The TIE and its secure network are mutually optimized for video. Simply plug it into a TV, connect it to the Internet and an inexpensive digital camera, and turn it on.

I invite you to imagine how this two-way visual and audio communication could be used.

First, with just one touch on a wireless keyboard, the veteran sees and speaks with a VA health care service provider whenever he or she needs help. The health care worker immediately appears full screen. The contact could be initiated by the veteran or the VA.

A second button could connect the veteran to an ongoing group therapy session, say on substance abuse or suicide prevention, perhaps one operating 24/7 with participants from around the globe. The caller might choose to participate, or simply observe his peers speaking about issues he also confronts. Imagine the psychological reassurance of this always-accessible confirmation that he is not alone. Help is available without an appointment, without travel, and most without stigma.

In recent months, increased attention has been paid to suicide among veterans. I have no way of knowing if the rates of suicide have gone up because of our wars in Afghanistan and Iraq and the increased deployments associated with them, but I do know that a functioning TIE Network could be ready when a potentially suicidal patient needs help most, at the moment of crisis, in the middle of the night.

Such group therapy conversations need not become part of a permanent medical record, and we know for certain that a major reason some military people are reluctant to seek help is because they fear a record of their outreach could damage their careers.

At the same time, the Obama Administration has placed a major emphasis on systematized electronic medical records as a way to improve care and drive down health costs. The VA has already taken the lead in this field, and the TIE Network takes this initiative even further. Doctors could record sessions with patients for later review and consultation. Patients could access medical records, receive reminders on medications, see instructional or inspirational videos. TIE is secure, encrypted, and data transmission is fully compliant with HIPAA. The system is ready to interface with VA electronic medical records.

Help, of course, is least accessible for our rural veterans who often must drive for hours to receive care. But studies have shown that mental health professionals in general are not distributed evenly across the county.[6] TIE offers a chance to link

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[5] Report of the Department of Defense Task Force on Mental Health, June (2007), Executive Summary, Findings.

[6] IOM, "Increasing Workforce Capacity for Quality Improvement," in Improving the Quality of Health Care for Mental and Substance-Use Conditions, Quality Chasm Services (Washington: National Academies Press, 2006), and President's New Freedom Commission on Mental health, "Subcommittee on Rural Issues: Background Paper" (Rockville, Md.: U.S. HHS, June 2004), as referenced in M. Audrey Burnam et al., "Mental Health Care for Iraq and Afghanistan War Veterans," *Health Affairs*, 28, no. 3, (2009), p. 775.

those best qualified to provide evidence-based quality therapy to those who need it most. Concurrently, it offers a chance for the government to use cost-effective treatment and not be tied to caregivers in specific areas.

My emphasis here today is on the many ways that the TIE Network can solve the difficult problems of treating the psychological problems of veterans, but TIE units are excellent vehicles for many other uses. They could be used for medical check-ups, evaluations, and counseling, while eliminating the driving, the waiting, and the mileage expense to the VA.

TIE is a conduit that connects the VA to its veterans, allowing the VA to provide its best treatments for PTSD, depression, and other problems directly to the vet's home. Our technology provides the quality and simplicity at a cost that allows these advantages to be scalable, benefiting both rural and urban veterans. We will measure these improvements with independent research that I am confident will quantitatively demonstrate improved medical benefits and access, and lower costs—all within 1 year.

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**TeleMed Network is led by:**

**The Executive Team**

*Stanley Stern*–President

- Founder of two companies:
  - Cobalt Communications–video conferencing integration
  - PRN–largest in-store advertising network

*Janette Gitler*–COO

- Senior Program Director–Gordon and Betty Moore Foundation
  - Responsible for $300M Environmental Fund
- Director of Programming–KRON & KQED (2 largest media in SF Bay Area)

*Dr. Mervyn Silverman*–SVP & Medical Director

- Director of Health, City of San Francisco
- President, American Foundation for Aids Research
- Director Consumer Affairs, U.S. FDA
- Awarded: Public Health Hero, "Heroes in Medicine Award, Award of Courage"

*David Wellstone*–Director

- National spokesperson on health care & mental health

**The Technical Team**

*Ed Yoon*–CTO

- Chief Technology Officer–Gordon & Betty Moore Foundation (Intel)
- Senior Technology Evangelist for Microsoft
- Developed/installed communication systems for Congress, FBI, CIA, DoD, NATO
- Microsoft–Senior Consultant to CINCPACFLT (Commander-in-Chief, U.S. Pacific Fleet)–developed technology road-map for next decade
- Awarded: Architectural Engineer of the Year from Microsoft's executive Committee

*Ken Novak*

- 25 years of experience in Wide Area Network (WAN) design and implementation
- Digital Vision Fellow at Stanford University
- Chief Technology Officer at CGNET–IT services to non-profits around the globe

*Bill Lattin*

- Chief Technology Officer, Certicom Corp.
- Managing Director of SecureField, an information security consultancy that specializes in cryptographic design and network security.
- Chair of the Standards for Efficient Cryptography Group (SECG)

**Advisory Board**

*Jim Omura*

- Professor of electrical engineering at UCLA for 15 years
- Designer of a number of spread spectrum communications systems, and the Massey-Omura cryptosystem
- Fellow of the IEEE and a member of the National Academy of Engineering
- Awarded the IEEE Alexander Graham Bell Medal

*Scott Minick*

- Board Chairman–California Pacific Medical Center
- Board Member of approx. 12 biotech companies

*Susan Porth*

- 20 years with Kaiser Permanente
- 10 years as SVP & CFO for 10 years

**Prepared Statement of David Scadden, M.D., Scientific Founder, Fate Therapeutics, Inc., La Jolla, CA**

Mr. Chairman, ladies and gentlemen of the Committee, on behalf of Fate Therapeutics, I would like to thank all of the Members for inviting Fate Therapeutics to testify today. We would like to ask that this document be considered our formal testimony and have it submitted into the record through David Scadden, Founder, Fate Therapeutics.

**CREATING TOMORROW'S MEDICINES FOR WOUNDED SOLDIERS USING THE MOST ADVANCED STEM CELL TECHNOLOGY**

**Executive Summary:**

Many diseases and injuries involve the death of cells that the body cannot naturally replace. Sometimes cell death can occur suddenly, as when a soldier sustains traumatic injuries in the battlefield. Other times it is slow and inexorable, as in Parkinson's disease; a consequence that can be attributed to the exposure to chemical agents used in warfare. The great promise of stem cells—the body's equivalent of renewable energy—is that they could be coaxed into becoming and then replacing cells lost to disease or injury. While initial efforts centered on the use of embryonic stem cells, we believe the breakthrough creation of induced pluripotent stem cells (known as iPS cells) and deeper understandings in adult stem cell biology have enabled us to create and develop tomorrow's medicines for veterans.

The transformative discoveries that led to the creation of iPS cells occurred in parallel with new understandings of adult stem cells and their roles in developmental and regenerative biology. iPS cells are created by using technologies that can turn a mature adult cell—like a skin cell—into a cell that has similar properties of self-renewal and pluripotency as embryonic stem cells, without using human embryos. Adult stem cells are found in almost all the tissues or organs in the body and are primarily responsible for maintaining and repairing the tissue in which they reside. Specifically, it was found that adult stem cells essentially lie in a reactive state; triggered into action by disease or injury. These remarkable discoveries were the basis for Fate Therapeutics' drug discovery and development strategy to create new medicines.

Scientists at Fate Therapeutics are working to quickly unlock the true potential of iPS and adult stem cells by using a two-prong approach. Fate is establishing technologies to ensure safe, efficient methods to create iPS cells to enable disease modeling, drug discovery and development and personalized cell replacement therapy. The second approach is to apply conventional drug approaches, whether in the form of pills or by injection, to activate specific mature adult cells to restore health. By leading this area of research, Fate is answering the underlying questions of how cells in the body activate and transform in normal, disease or injured states and then applying these understandings to develop tomorrow's medicines for veterans and the general public.

For veterans, we believe the near term applications for such a strategy to generate wound healing therapies are especially applicable. While improved technological advances in armor have increased the survivability of our soldiers, it has come with the unintended cost of our armed servicemen and women sustaining more severe injuries. Traumatic brain injury, non-union bone fractures, deafness and

blindness are unfortunately injuries that are found to be common place in today's battlefields and unfortunately have limited to no treatment options. Programs underway at Fate Therapeutics have indicated that cells in the areas of the body that suffer damage from such wounds, can be activated through the traditional applications of medicines to guide the body to heal itself. While these initiatives are in the early stages, we continue to strive to fully realize the potential of the discoveries in stem cell biology and develop them as safe and curative therapies for our wounded soldiers who so honorably deserve them.

**Fate Therapeutics:**

Founded in 2007 on the leading stem cell and developmental biology research, Fate Therapeutics is using the fundamental biological mechanisms that guide cell fate to develop regenerative medicines. The company has brought together the foremost scientists from the Nation's research hotbeds (Boston, San Francisco, San Diego and Seattle) who have demonstrated the potential to create and modulate stem cells to restore health. While embryonic stem cells opened the possibility for regenerative medicine, Fate Therapeutics is focusing on adult stem cells and induced pluripotent stem cells (iPSCs). Adult stem cells naturally exist in tissues or organs and are responsible for maintaining and repairing the tissue in which they are found. iPSCs are stem cells created from fully mature differentiated cells, like a skin cell, and are being developed as personalized cell replacement therapies (See Background on Stem Cell Research below for more on stem cell types and applications). Fate is using conventional drug discovery and iPSC technology to identify small molecules that can specifically activate these stem cells to repair and regenerate tissue for veterans' health.

**Scientific Founders of Fate Therapeutics:**

Fate's scientific founders are working with the company to collaboratively research and develop innovative therapeutics to modulate cell fate. By partnering with the leading academic labs in stem cell and developmental biology, Fate has exclusive access to the most advanced biological assays, models and research to illuminate the biology of stem cells and deliver on the promise of regenerative medicine.

- ***Philip Beachy, Ph.D.***–Ernest and Amelia Gallo Professor of Developmental Biology at Stanford University School of Medicine and an Howard Hughes Medical Institute (HHMI) Investigator
- ***Randall Moon, Ph.D.***–William and Marilyn Connor Chair and director of the Institute for Stem Cell and Regenerative Medicine at University of Washington and an HHMI investigator
- ***David Scadden, M.D.***–Gerald and Darlene Jordan Professor at Harvard Medical School, co-director of Harvard Stem Cell Institute, and director of Massachusetts General Hospital Center for Regenerative Medicine
- ***Leonard Zon, M.D.***–Grousbeck Professor of Pediatric Medicine at Harvard Medical School, director of the Stem Cell Program at Children's Hospital Boston, and an HHMI Investigator
- ***Sheng Ding, Ph.D.***–Associate professor in the departments of chemistry and cell biology at The Scripps Research Institute
- ***Rudolf Jaenisch, M.D.***–Founding member of the Whitehead Institute, professor of biology at MIT, and member of the National Academy of the Sciences

Drs. Beachy and Moon are leading developmental biologists who understand how to activate specific stem cell pathways to differentiate stem cells in vivo and in vitro. Drs. Scadden and Zon are renowned scientists and doctors who are researching ways to guide cells to treat various diseases and identifying means to explore the adult stem cell niche, locations where naturally occurring stem cells are found in the body. Drs. Ding and Jaenisch are the foremost investigators finding small molecules and other non-genetic methods to guide cell fate.

***DIRECTING CELLS TO RESTORE HEALTH:***
**FATE THERAPEUTICS' REGENERATIVE MEDICINE PROGRAMS FOR SOLDIERS AND VETERANS**

**Hearing Restoration**

Among veterans, hearing loss is the most common service-connected disability.[1] A 2004 survey showed that 28 percent of troops coming home from a war zone have

[1] Fausti SA, et al. Hearing health and care: The need for improved hearing loss prevention and hearing conservation practices. J Rehabil Res Dev. 2005 Jul-Aug; 42(4 Suppl 2):45–62.

diminished hearing.[2] In 2004, the Veterans Administration (VA) paid $633.8 million to 378,982 veterans whose main disability was hearing loss, according to the Army's Center for Health Promotion and Preventive Medicine (Figure 1). That number has since grown to more than $1.2 billion annually in compensation costs for hearing loss and hearing related injuries.

In a 2005 study, the Center for Naval Analyses found that permanent hearing loss is one of the most common disabilities among sailors and recommended expansion of active military hearing-conservation programs that work to reduce noise exposure.[3] In 2005, it may have not seemed possible to recommend funding research to restore hearing, but today stem cell research and its applications in regenerative medicine offer that opportunity. Fate Therapeutics, a private biotechnology company, has converged the leading scientific expertise and research in stem cell and developmental biology to discover and develop regenerative medicines to treat a number of diseases and conditions that currently have little to no therapeutic options, including acute hearing loss.

**Fate's Program to Cure Acute Deafness:**

Hair cells in the ear are specialized cells responsible for sensing sound and transmitting those signals to the brain. Once damaged, usually due to loud or sustained noise exposure, these specialized cells die and are not replaced, causing deafness; however, stem cells have been identified in the adult ear (Figure 3).

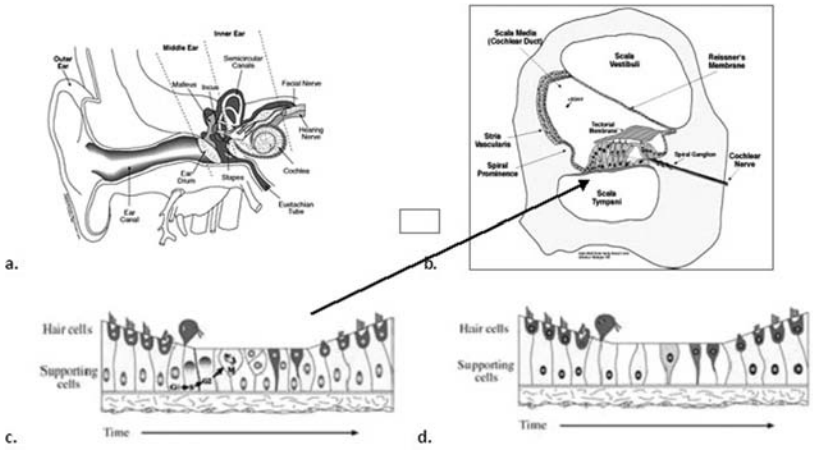


*Figure 3a: Cross section through the ear anatomy; 3b: Expanded depiction of red box in 3a to show cochlear structure and hair cells (orange cell), the specialized sensory cell for hearing; 3c: Supporting cells upon activation can divide and differentiate into hair cells (blue cells); 3d: Supporting cells have also been seen to change form or transdifferentiate into hair cells (Images: University of Washington).*

Research in cell culture and animal models has shown that upon activation these stem cells can differentiate into the specialized cells needed to restore hearing. Fate Therapeutics has proprietary research around the pathways that modulate stem cell activation and differentiation and is evaluating the company's library of drug candidates to identify ways to efficiently activate these pathways. We are currently performing preclinical validation experiments in 0cochlear explant cultures to confirm our small molecule drug candidates activate progenitor cells in the inner ear to grow and differentiate into hair cells. We hope to advance the development of therapeutics to regenerate cochlear hair cells, which are lost as a result of noise damage sustained during military service.

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[2] Schulz, TY. Troops Return with Alarming Rates of Hearing Loss. Hearing Health vol 20:3; Fall 2004.

[3] Geoffrey B. Shaw and Robert P. Trost. "Statistical Analysis of Hearing Loss Among Navy Personnel." February 2005. CRM D0011228.A2.

**Vision Restoration**

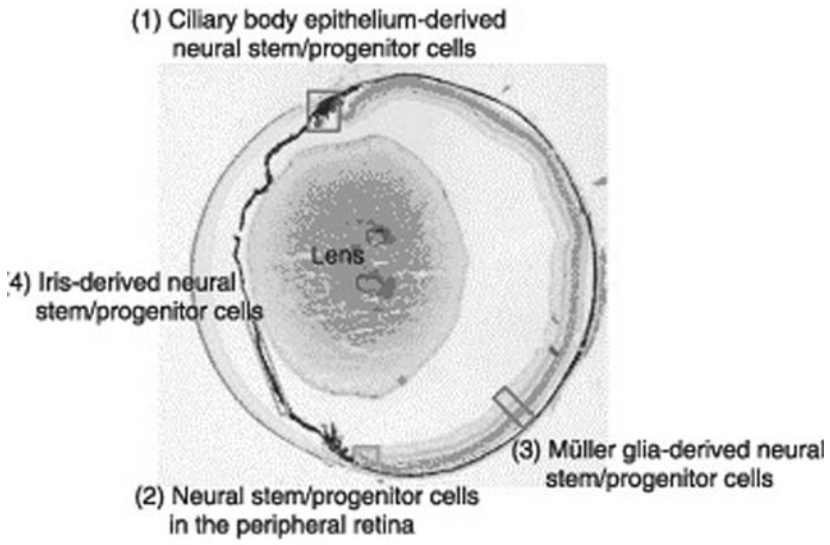
One in 10 veterans from military operations in Iraq and Afghanistan have sustained serious traumatic eye injuries, which is the highest percentage for eye wounds among any other major conflict dating to World War I.[4] In 2007, it was reported that more than 1,100 veterans from these two military conflicts have undergone surgery for damaged eyes.[5] While body armor improvements are saving more lives, eyes, limbs and heads still remain extremely vulnerable. In fact, eye wounds occur at almost twice the rate as wounds that require amputations. Moreover, troops who sustain combat injuries leading to sudden blindness lose a greater degree of independence and have a much longer rehabilitation time to regain the ability to perform simple life tasks.

While science is still a long way from regrowing new limbs, stem cell research and its applications in regenerative medicine can now offer an opportunity to restore sight. Fate Therapeutics, a private biotechnology company, has converged the world's leading scientific expertise and research in stem cell and developmental biology to discover and develop regenerative medicines to treat a number of diseases and conditions that currently have little to no therapeutic options, including acute blindness.

**Fate's Program to Cure Acute Blindness:**

Rods and cones in the eye are specialized cells responsible for sensing light and transmitting those signals to the brain. Once damaged, these specialized cells die and are not replaced, causing blindness; however, stem cells have been identified in the adult eye (Figure 2).

a.




[4] Wong, TY, et al. "Eye Injuries In Twentieth Century Warfare: A Historical Perspective." (1997) Survey of Ophthalmology. (1997) 41:433–459.

[5] Zoroya, G. "Blinded by War: Injuries Send Troops into Darkness." USA Today. November 14, 2007.

b.

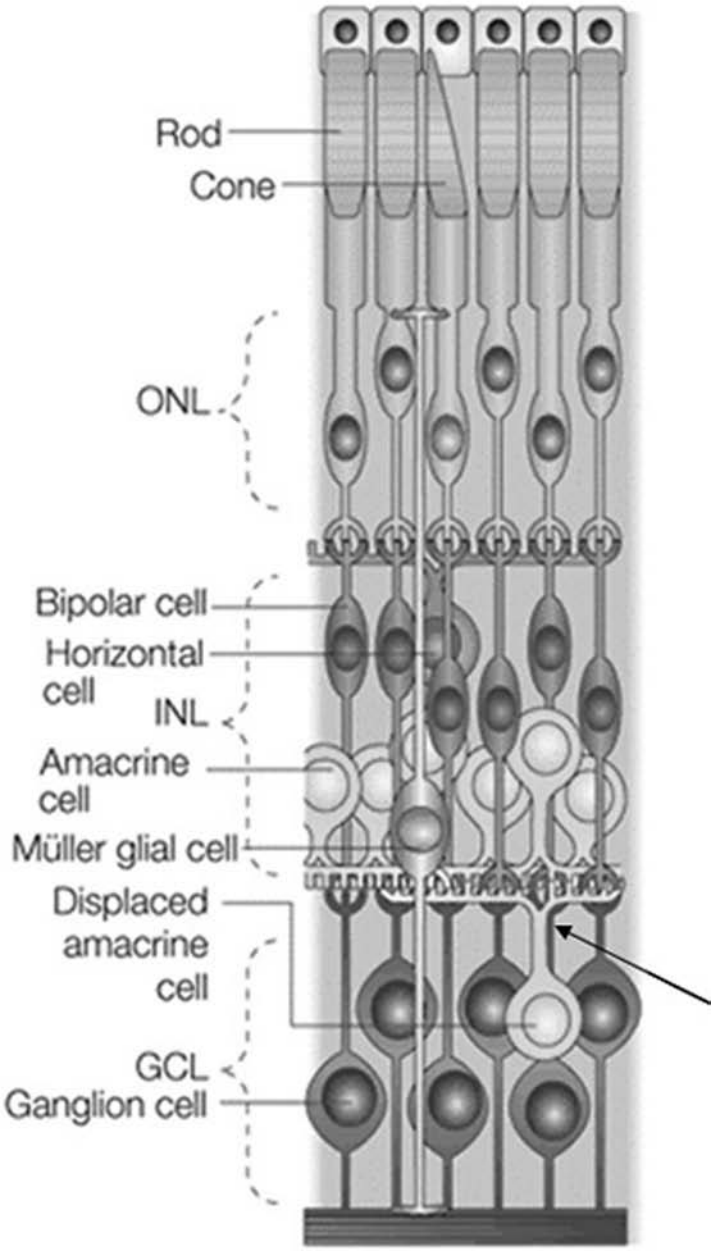



*Figure 2a: Location of stem cells in the eye; 2b: Expanded depiction of red box in 2a to show a Muller glial cell (arrow: orange cell), a type of stem cell in the eye that can upon activation divide and differentiate into rods (light blue cells) (Images: Nature).*

Research in cell culture and animal models has shown that upon activation of the Wnt or Hedgehog pathway these stem cells can differentiate into the specialized cells needed to restore sight. Fate Therapeutics has proprietary research around the pathways that modulate these stem cells and is evaluating the company's library of drug candidates to identify ways to efficiently activate these pathways. We are currently performing preclinical validation experiments in retinal explant cultures to confirm our small molecule drug candidates activate progenitor cells in the eye to grow and differentiate into rods and cones. We hope to advance the development of therapeutics to regenerate photoreceptors lost as a result of choroidal hemorrhage and retinal detachment consequent to traumatic eye injury sustained in combat.

**Bone Regeneration**

Advances in medical care and improvements in both body and vehicle armor have resulted in increased soldier survival, from 76.4 percent during the Vietnam War to 90.4 percent in Iraq. However, the price of this survival has led to the rise in soldiers sustaining more severe, traumatic injuries: orthopedic musculoskeletal injuries account for approximately 70 percent of war wounds; fractures account for 26 percent of combat injuries; and 82 percent of all fractures are open fractures.[6] Most civilian orthopaedic treatment approaches cannot be applied to battlefield medicine because combat injuries often involve high-velocity shells or explosives, which injuries are generally very different from low velocity bullet wounds more often seen in civilian trauma centers. The challenge in these battlefield injuries is the high degree of tissue loss and contamination combined with limited treatment resources. The specific treatment protocol includes surgical debridement, leaving all wounds open, early fracture stabilization, broad-spectrum antibiotics, and rapid evacuation to higher levels of care.

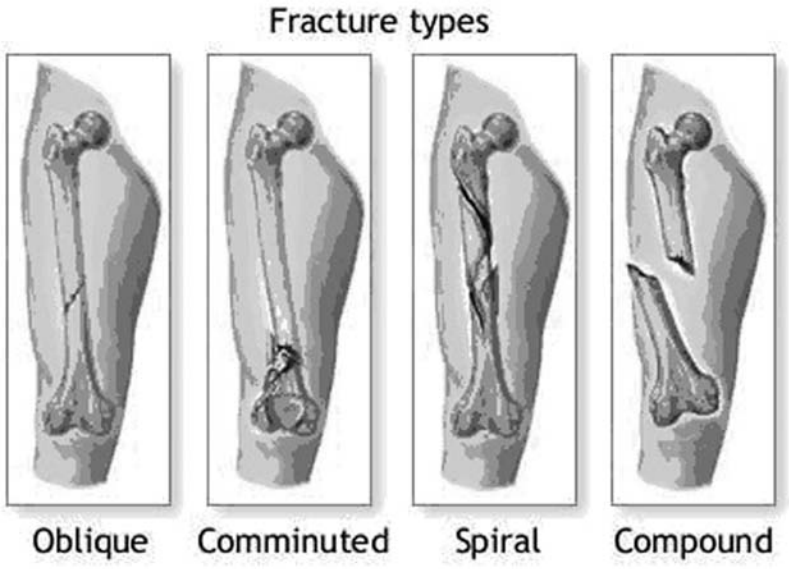
While science is still a long way from regrowing new limbs, stem cell research and its applications in regenerative medicine can now offer an opportunity to develop therapeutics that can activate the body's own stem cells to advance healing and repair of bone and cartilage. A regenerative medicine treatment supplement to support orthopedic medicine at either battlefield or surgical care level could provide quicker healing times and better overall recovery. Fate Therapeutics, a private biotechnology company, has converged the leading scientific expertise and research in stem cell and developmental biology to discover and develop regenerative medicines to treat a number of diseases and conditions that currently have little to no therapeutic options, including traumatic orthopedic injuries.

**Fate's Program for Non-Union Fracture:**

Non-union bone fractures are large breaks in the bone that cannot heal without further intervention. These fractures represent a major challenge for battlefield medicine because treatment often requires multiple surgeries and medical procedures (Figure 2a).

[6] Peter Pollack and Carolyn Rogers. "A brief background of combat injuries." *AAOS NOW*. March/April 2007. American Association of Orthopaedic Surgeons.

a.




b.

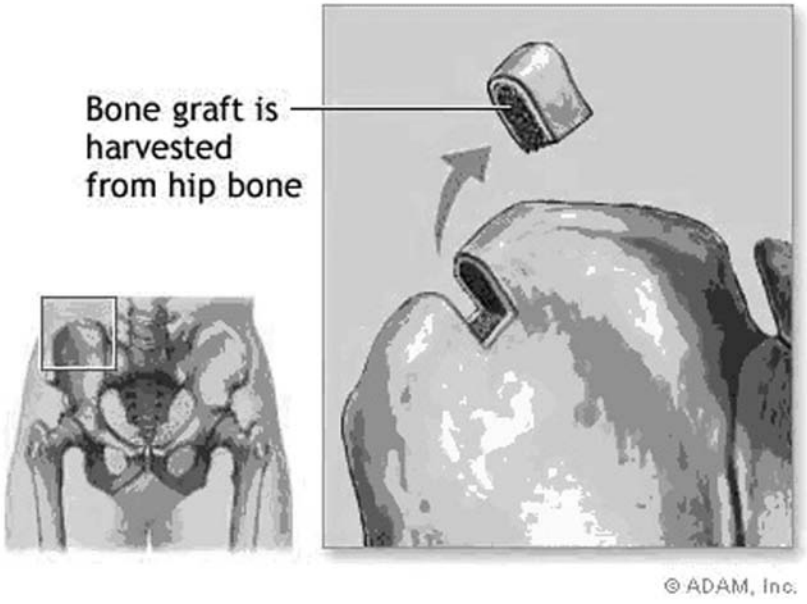


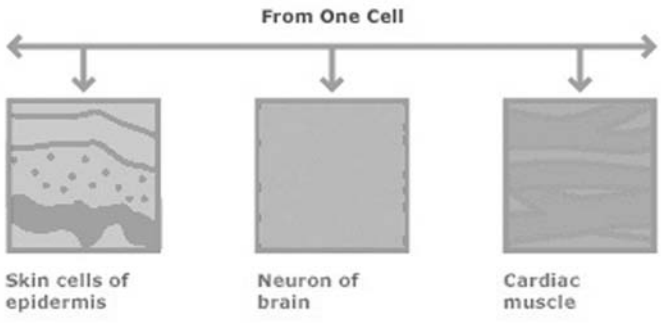

*Figure 2a: Except for oblique, these different types of fractures take longer to heal and often need surgeries and other medical interventions to heal properly. 2b: A schematic of bone graft.*

The most common means of fixing a non-union fracture is to add a bone graft taken from the patient's own pelvis (Figure 2b). However, this increases pain, medical procedures, hospital time and potential complications, such as donor site wound infection, bleeding or numbness. The most advanced FDA-approved product, a bone growth factor, reduces the usage of bone graft but does not reduce healing time. Developing small molecule drugs that can selectively activate and guide stem cells in the body will be the best chance at a successful solution to reduce non-union fracture healing time. We hope to advance the development of therapeutics to regenerate bone in cases of high energy weapon injuries and blast injuries. These combat injuries are often associated with highly fragmented fractures and infection that increase the failure rate of bone to heal.

***Background on Stem Cell Research***

**Embryonic Stem Cells:**

In 1998, the first human embryonic stem cell (hESC) line was created from a fertilized egg. This was a significant milestone in regenerative medicine because hESCs are pluripotent, meaning they can become any cell in the body, and stem cells could conceivably be grown and differentiated into replacement cells for any applicable therapeutic need (Figure 1).




*All the Cells in the Body to Restore Health*

*Figure 1: The promise of regenerative medicine*

However, the seemingly unlimited therapeutic potential associated with hESCs were tempered with the sobering safety issues that hESCs presented. Specifically, because of the limited population source from which hESCs are derived, potential patients would be exposed to similar immune rejection risks as those of organ transplant recipients when receiving organs from donors of not identical genetic matches. Moreover, hESC recipients would face increased risks to potentially unknown genetic diseases of the donor. Accordingly, the ability to generate patient-specific replacement cells with pluripotent capabilities became the next sought after milestone to fully realize the therapeutic potential of regenerative medicine.

Scientists tried to address this hurdle with a technique that replaces an egg cell's nucleus with the nucleus from a patient's skin cell (Figure 2). Since the nucleus of an adult skin cell has a full set of chromosomes, the egg cell would in a sense be fertilized with an exact copy of the patient's DNA. The embryonic stem cell line derived from this "fertilized" egg cell would be a genetic match to the patient and likely to not be rejected. However, this technique was highly inefficient and relied on donated egg cells, which are from a limited population source and difficult to obtain.

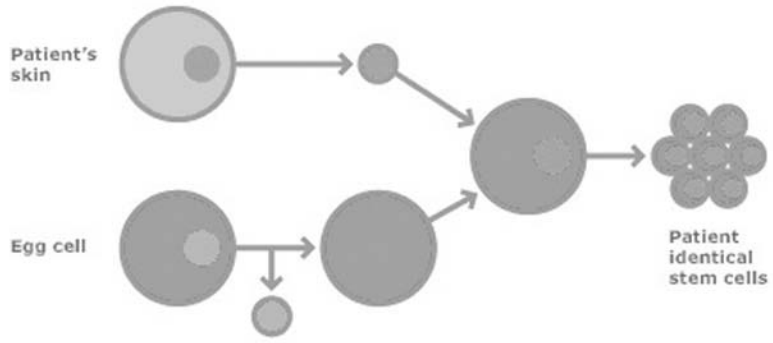



*Figure 2: Schematic of nuclear transfer, a previously explored method to generate genetically matched stem cells.*

**Induced Pluripotent Stem Cells (iPS cells):**

In 2007, in separate publications Drs. Yamanaka and Jaenisch, the later a scientific founder of Fate Therapeutics, reported that fully differentiated adult cells, such as a skin cell, could be "reprogrammed" to become embryonic-like stem cells by forcing expression of four transcription factors (Figure 3). Called induced pluripotent stem cells (iPS cells), as iPS cells were derived from the potential patient's own cells, the issue of creating patient specific cells was addressed. Furthermore, ethical issues involving the use of embryos or eggs had been avoided.

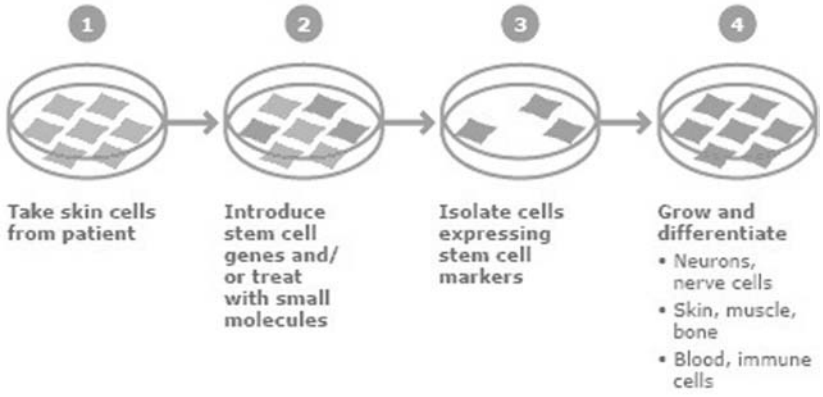



*Figure 3: A schematic of creating iPS cells, a more efficient and reproducible process for generating personalized cell replacement therapies.*

iPS cells were first created by genetic manipulation using viruses, which carry risks from insertion and makes the cells unsuitable for clinical use. Fate Therapeutics and the company's scientific founders have found safer and more efficient ways to create iPS cells using non-genetic methods, such as small molecules and biologics. As iPS cells can potentially be made from any adult cell and differentiate into any cell type, iPS cells are considered to be the best means to create personalized cells for regenerative medicine. Beyond cell therapy, Fate Therapeutics believes iPS cells are of essential importance to research how to control cell fate with small molecules to develop conventional therapeutics.[7] These small molecules could poten-

[7] All drugs in pill form, like aspirin, are composed of small molecules. Small molecules are easier to turn into drugs because they can be tested for safety and efficacy. Thus, they follow a conventional pharmaceutical drug development approach with a well-defined regulatory and commercialization path.

tially be applied to modulating adult stem cells to stimulate the body's own healing process to repair and regenerate tissues.

**Adult Stem Cells Are Naturally Found in the Body:**

While ESCs and iPS cells are types of stem cells made in the lab, adult stem cells naturally occur in the human body. Adult stem cells are found in tissues or organs and primarily maintain and repair the tissue in which they are found. Some populations of adult stem cells are also thought to remain quiescent (non-dividing) in areas of the body called "niches" until they are activated by disease or tissue injury. Adult stem cells can renew themselves and can differentiate to yield the major specialized cell types of the tissue or organ. Some researchers are trying to grow adult stem cells in the laboratory for cell replacement therapy; however Fate Therapeutics is taking a different approach. Fate is using conventional drug discovery[8] and iPS cell technology to identify small molecules that can specifically activate these adult stem cells in the body to repair and regenerate tissue.

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**Prepared Statement of Howard J. Federoff, M.D., Ph.D., Executive Vice President for Health Sciences, Executive Dean of the School of Medicine, Georgetown University Medical Center, Washington, DC**

Chairman Filner, Ranking Member Buyer and Members of the Committee. Thank you for holding this hearing, for the work you are doing on behalf of America's brave veterans, and for allowing me to testify this morning. I will be focusing on innovative work that from my perspective is critically important to addressing the long term implications of traumatic brain injury (TBI) both to ensure that we are serving the long term needs of returning veterans who have experienced TBI and to do so in ways that are wise for the Department of Veterans Affairs health care programs.

The Defense and Veterans Brain Injury Center makes the point on its Web site that "America's armed forces are sustaining attacks from explosions or blasts . . . almost daily in Iraq and Afghanistan." It also notes that screenings at Walter Reed have found that 32 percent of servicemembers evacuated from theater had TBI. Those statistics obscure the reality, also referenced on that webpage, that "Sometimes, in the case of mild TBI, there may be no outward sign of injury. Over 90 percent of combat-related TBI's are closed brain injuries."

Indeed, TBI has been termed "the silent epidemic." While 1.4 million Americans suffer from TBI from a variety of sources each year, many of these injuries—with potential long term consequences—are not reported. Even in mild cases of trauma, the central nervous system can suffer permanent, often debilitating damage.

There can be no dispute that our military is moving aggressively to respond as best they can to the flood of very visible and tragic traumatic brain injuries that our men and women in uniform are experiencing in these 21st century conflicts. Just as the nature of these injuries has changed from the "shell shock" suffered by those serving in earlier conflicts, medical science has made significant strides. But we owe it to those who are serving and have served our Nation in uniform to act on the important realization that, notwithstanding the attention they are receiving, there are all too many who have suffered mild to moderate traumatic brain injuries that pose serious, but hidden threats to their long term well-being. We need to act to:

- Develop methodologies for more rapid and accurate diagnosis of TBI and its associated risks;
- Determine the most effective approaches to triaging TBI patients; and
- Pursue the rational design and screening of new therapies, including novel drug discovery and development targeting the prevention or minimizing of cognitive impairments which can impact learning capabilities, the ability to hold down a job, and predispose to post-traumatic stress disorders.

Years of neurological research have taught us a great deal about the human brain, and, therefore, there is information relevant for TBI victims:

- First, the plasticity of the human brain permits unique recuperative responses to trauma. We must fully understand these responses to better understand when to intervene and when to allow the body to heal itself.

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[8] Conventional drug discovery relies on a deep understanding of the biological pathways and mechanisms which control a specific cell or cellular process. Small molecules and biologics are developed into drugs based on their selectivity to modulate these cellular processes in a way that has therapeutic benefit.

- Second, research to date indicates that, unlike in the case of a stroke, in at least some types of TBI, there is a longer timeframe from the time of injury for a possible therapeutic intervention before permanent loss of brain function.
- And, third, research on Alzheimer's and Parkinson's diseases makes clear that blood and its circulating cells may serve as an important window into the human brain, helping us better understand the impact of neurological disease and injury. For example, understanding the neuropathology of brain inflammation through analysis of blood based proteins and distinct populations of leukocytes may help us better determine the extent to which the brain has been injured and the degree to which the body is responding and possibly recovering. These observations are generally invisible absent a molecular analysis of the blood of an injured person, but they potentially hold the key to effective and timely interventions.

Recently, the Department of Defense through its Neurotoxin Exposure Treatment Program (NETRP) has awarded a 5-year grant to Georgetown University Medical Center neuroscientists to perform systematic and extensive bio-molecular profiling of brain tissues and peripheral blood to identify and validate robust, specific and sensitive biomarkers for TBI. Those bio-molecular "signatures" can be read from the blood and, early on, may aid in diagnosis of the variety and severity of brain injuries and guide therapeutic responses. Indeed, this research, I am confident, will inform the rational design of new drugs and therapies to prevent both short-term and lasting brain damage. Our work will be carried out in conjunction with the Seattle-based Institute for Systems Biology and researchers at the University of Rochester. As someone who believes in the tremendous benefits that are possible through broad collaborations, I am pleased that we are planning to work with the Uniformed Services University of the Health Sciences as they pursue their direction from Congress to focus on TBI, as well as with the National Institute for Nursing Research, the National Institute of Neurological Disorders and Stroke, and the Washington Hospital Center.

Our research for the Department of Defense will initially rely on civilian sector TBI patients for our clinical studies in recognition of the reality that we will be able to recruit civilian patients without the delays that are inherent in working with patients injured in combat. However, I am following up on a recommendation from Chairman Filner that we reach out to the DC VA Medical Center (WVAMC), to pursue approaches to ensure longitudinal follow up between the care received in the cases from the military and ongoing DVA medical care. Given the on-going work on traumatic brain injury at WVAMC, as well as the over 30 Georgetown Medical Center faculty who hold joint appointments with WVAMC, I am confident that we will actively engage WVAMC in this research. To provide the best possible care for TBI victims now relying on the Department of Veterans Affairs for medical services, ongoing monitoring of their conditions and well-documented longitudinal follow up will be critical. It will likewise enrich our research.

Members of this Committee know very well that the vast majority of military personnel who are returning from the field having experienced TBI are very young. God willing, they have long lives ahead. Therefore it is incumbent upon us to ensure that we are aggressive in just this kind of research endeavor that looks beyond the immediate consequences of even mild TBI. With this kind of research, we can address the "silent epidemic" before it takes a toll on the long-term quality of life of those who are serving our country. I urge you to ensure that the Department of Veterans Affairs, in close concert with both the Department of Defense and the Department of Health and Human Services, remain vigilant in pursuing the identification both of these bio-molecular signatures and of effective therapeutic responses to TBI.

Again, thank you for giving me this opportunity to testify before you.

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**Prepared Statement of Nelson M. Handal, M.D., FAPA, Founder, Chairman, and Medical Director, Harmonex, Inc., CliniCom, Atlanta, GA, Board Certified Child, Adolescent and Adult Psychiatrist, and Fellow, American Psychiatric Association**

[Good Morning.] Mr. Chairman, Members of the Committee, thank you for the opportunity to share information about innovative treatments and technologies that are today serving to enhance quality of care in mental health.

As you know, information and the way it is used is at the core of psychiatric assessment and diagnosis. Typically patients requiring mental health care are interviewed in what is commonly referred to as a traditional face-to-face psychiatric interview. Practicing mental health clinicians know that too often, time constraints,

volume and complexity of the information, limited access to care, and other factors, if not properly identified and addressed, often end up limiting the accuracy of their face-to-face assessments.

*The key question is* how to gather information comprehensively, in a reasonable amount of time, utilizing an easy to use tool that generates a valuable report to facilitate disposition and the clinician's initial face-to-face interview.

Our organization, Harmonex is the developer of a patient self administered and computer based assessment tool known as CliniCom. CliniCom is comprehensive, easy to use and allows the clinician to verify suggested diagnoses. The technology resides in a secure platform that comprehensively screens for 56 possible mental illnesses and Traumatic Brain Injury (TBI). CliniCom also includes a powerful suicide alert that is unlike anything available in mental health today. CliniCom is based on the DSM–IV standard and incorporates clinical research and widely accepted community standards of care.

CliniCom is being used successfully across our Nation at private outpatient clinics and hospital settings alike. The technology can be equipped to run in most clinical environments using tablets, desktops or kiosks. CliniCom evokes the appropriate question sets based on the user type and the patient's age. It does not replace the mental health professional. It simply allows them to significantly enhance the face-to-face interview, its outcomes, and quality of care.

CliniCom does not forget to ask pertinent mental health questions each and every time. It gathers complete medical, social, and family histories and can also identify concerns associated with suicide, violence, and traumatic events. CliniCom will also quantify severity of symptoms and conditions automatically. It allows for secure and uniformed documentation by organizing clinical information in a standard History and Physical (H&P) format.

Once patients complete the assessment, clinicians can devote much of their initial interview toward validating the CliniCom report and helping patients understand the nature of their condition.It is very difficult to gather all of this information during a single, traditional face-to-face psychiatric interview. Our technology can gather all clinically relevant and necessary information in a responsible and quantifiable manner.

The "Clinical Decision Making Process" overall is significantly enhanced by allowing CliniCom to identify individuals that may have "co-morbid conditions," meaning the presence of one or more disorders (or diseases) in addition to a primary disease or disorder. An example would be an individual with depression in addition to PTSD and Substance Abuse. With CliniCom, clinicians can better ensure that both primary and co-morbid problems are identified simultaneously, leaving no stone unturned.

A recent independent survey of 1109 CliniCom users indicated that 92 percent of users reported that CliniCom was very easy to use. In addition, survey results indicated that 87 percent of users found CliniCom to be very easy to understand, while 88 percent found it to be extremely thorough. Seventy percent of users completed the assessment in 60 minutes or less. This is a function of the severity of their case.

While CliniCom has served to enhance care in the private sector, we have confidence that the technology can also serve to enhance care within military mental health. CliniCom has unique characteristics that make it well suited for use both as a pre—and post-deployment screening tool and also as a comprehensive mental health assessment tool.

Soldiers can effectively be screened with CliniCom prior to deployment to establish a mental health base-line. The technology can then be used in-theatre, to address any changes to that base-line or post-deployment in an effort to identify any changes in mental health status. As a post-deployment screening measure, CliniCom's methodology offsets some of the drawbacks inherent in screening methods currently in use; most of which are simply paper or online checklists consisting of only a few questions. We believe CliniCom would also assist the clinical assessment and care of soldiers in outpatient and inpatient behavioral health settings.

CliniCom works to identify individuals with possible Post Traumatic Stress Disorder (PTSD), Traumatic Brain Injury (TBI) or suicidality in a thorough manner. Certain algorithms are triggered if the individual endorses trauma of any sort in the social history items; so for example, PTSD is identified not just by combat related trauma but also trauma that may have existed prior to deployment, even traumas occurring earlier in life.

Another very important benefit of CliniCom is its suicide alert capabilities. When an individual endorses suicide presenting complaints or screening items, a complex algorithm for suicide assessment is automatically engaged.

By implementing a technology like CliniCom, DoD and VA can use this valuable clinical resource to help mitigate the overarching issues of stigma and access to care

and ensure that every member of our armed forces is given a complete, comprehensive and responsible mental health assessment.

In summary, CliniCom is a unique, information gathering tool designed to assess mental health conditions, TBI and suicidality. The technology is comprehensive, easy to use and its conclusions can easily be verified by mental health professionals. In addition, what is learned from these cases can be used to conduct research that could lead to even greater advances in mental health care, truly modernizing the way we help people of all walks of life, who today suffer with illness.

We are grateful to the Members of this Committee for the work you do on behalf of our veterans and soldiers. Thank you for your time and for the opportunity to introduce you to CliniCom. We look forward to answering your questions and are prepared to help in any way we can.

**Prepared Statement of James A. Schoeneck, Chief Executive Officer, BrainCells Inc., San Diego, CA**

Chairman Filner, Ranking Member Buyer, Ladies and Gentlemen of the Committee:

Thank you for the opportunity and the honor of appearing before this distinguished Committee today. I wish to commend you for your attention to the compelling issues surrounding Military Post Traumatic Stress Disorder, or PTSD.

I have served as Chief Executive Officer of BrainCells Inc since 2005, and have worked on successful drugs in the biotech and pharmaceutical industry for almost 30 years. BrainCells is a San Diego biotech founded on the discovery made only 10 years ago that new nerve cells, specifically neurons, grow in certain parts of the human brain. This new science of neurogenesis has linked emotional disorders to the failure to create and develop new cells located in a specialized part of the brain. In fact, new neuron production is a requirement for normal emotional responses that mentally healthy people take for granted. By way of groundbreaking studies, the founding scientists of BrainCells from Columbia University and the Salk Institute have demonstrated that stress can arrest the formation of these new cells (neurogenesis) resulting in a measurably shrunken site within the brain called the hippocampus. We now have the first physical understanding of biologic processes involved in psychiatric diseases. Image studies performed on PTSD patients confirm that they, also suffer from abnormal changes in the hippocampus. Although these methods are not yet available to diagnose and study the progress of all clinical PTSD patients, they will be someday soon.

Importantly, BrainCells has designed a drug screening platform to search for new classes of drugs that will help this nerve cell growth function return to normal—restoring neurogenesis with the intention of improving emotional integration with few side effects. BrainCells believes that its compounds provide alternatives to traditional anti-depressants and anti-anxiety drugs by directly increasing neurogenesis. BrainCells believes we have excellent drug candidates to treat PTSD.

Over the past few years, the U.S. Department of Defense and the Veterans Health Administration have taken steps to improve mental health services for personnel returning from deployments and veterans. Expanded screening and treatment for PTSD and depression and new efforts to reduce the stigma surrounding mental illness among servicemembers are to be commended. But since October 2001, approximately 1.6 million U.S. troops have been deployed for Operations Enduring Freedom and Iraqi Freedom in Afghanistan and Iraq, and according to last year's Rand Study one in seven servicemembers has returned from deployments with symptoms of PTSD. That leaves us 230,000 servicemen and women and veterans *known* to be suffering from mental injuries. (PTSD can be regarded parenthetically as a chronic wounding of the brain just as Traumatic Brain Injury bruises the brain.) Recent reports published in the Journal of the American Medical Association placed numbers even higher.[i] The radiating social effects of so many PTSD sufferers are mind-boggling when one considers that families also must experience the impact of their loved ones returning with mental illness. Violence, divorce, and domestic abuse have skyrocketed among returnees and suicide rates in the military now exceed those in the civilian population—unheard of as historic suicide rates have always been lower among soldiers, sailors, marines, and airmen.

PTSD is classified as an anxiety disorder with symptoms of chronic anxiety and fear that serve no purpose. It is often accompanied by typical or atypical depression.

[i] Bridget M. Keuhn, "Soldier Suicide Rates Continue to Rise" JAMA March 18, 2009 301 (11): 1111–1113.

Treatments for PTSD have had mixed results. Non-drug treatment is regarded as the first-line option for PTSD and is routinely incorporated into management plans for patients with PTSD. Many patients do not achieve a sufficient response to non-drug therapy or are left with disabling residual symptoms.[ii] The selective serotonin reuptake inhibitors (SSRIs) are considered the first-line pharmacological treatments. These are the familiar class of anti-depressants like Prozac or Paxil. Response rates for these medications rarely meet 60 percent in the general population, and less than 20–30 percent of PTSD patients achieve remission.[iii] This class of drugs routinely causes side effects like insomnia, weight gain, and most significantly for young returning servicemembers, sexual dysfunction. This is because the increased serotonin resulting from this medicine affects many tissues in the brain and body—most of which do not need extra serotonin. Less than 40 percent of servicemembers diagnosed with PTSD receive mental health care—and some of those voluntarily forego treatment or compliance because of sexual function effects or worries. Many soldiers use alcohol or illegal drugs to deal with symptoms rather than take SSRI anti-depressants.

Combat veterans are now shown to suffer a more severe form of PTSD than civilian victims of trauma. Military trauma is generally associated with greater depression, more anger and irritability, more aggression, more problems with one's sense of personal identity, and a far greater tendency toward suicide or violence.[iv] Additional studies are needed, but experts are moving to the conclusion that military PTSD is both different from civilian trauma, and it is also more difficult to treat. Methods used to treat civilian PTSD are at times inadequate to address military syndromes. The numbers of refractory or resistant cases are rising. It is disturbing to realize that we still have thousands of Viet Nam veterans in the full throws of chronic PTSD and simultaneously we are being advised by the military that currently deployed troops are experiencing unprecedented severity and incidence of the condition. Often if left untreated, PTSD is a lifetime disorder.

Probably because of the nature of the unique psychological insult, military PTSD is a different mental syndrome than civilian trauma induced PTSD. It is not just depression and anxiety combined, but has its own set of symptoms that require medicines designed for and tested in the affected population. Presently, it is unlikely that the civilian pharmaceutical industry can or will invest resources to address this specialized "orphan-like" condition of military PTSD that includes suffering from extreme anxiety, depression and memory processing disorders. Our investors at BCI, for example, anticipate that we will use our resources to develop drugs to treat the large civilian market for major depressive disorder. This market may provide investors with their anticipated return on investment in exchange for the high financial risks taken in the development of new drugs. Unless the government provides collaboration, incentives and funding directly to the biotech and pharmaceutical industry to deliver FDA approved drugs labeled for military Post Traumatic Stress Disorder, clinicians will be left with combinations of existing drugs tested in and approved for people with different medical conditions. I wish to respectfully suggest to the Committee that the members of our military who voluntarily protect the Nation from harm are deserving of a well-funded pharmaceuticals development program directed specifically to military derived PTSD. The Congress has generously funded significant amounts for research into determining organic causes and best existing practices for treating PTSD, but has yet to fully engage those of us who are singularly and professionally dedicated to identifying and testing safe new compounds that treat tough diseases.

Members of the Committee are undoubtedly aware of the myriad ways that private enterprise can be provided incentives, as exemplified by the orphan drug laws that offer tax credits and patent extensions to illnesses affecting small populations. Tragically, military PTSD has already exceeded the statutory 200 thousand patients that define the orphan drug laws, but surely our warfighters are deserving of the best that our creative laboratories can provide.

I am deeply grateful for this opportunity to share my views with the Committee. In closing I wish to summarize with the following thoughts and recommendations:

1. PTSD is a disease with great personal and social cost that dramatically impacts the lives of our troops and returning veterans, their families and the soci-

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[ii] Expert Review of Clinical Pharmacology January 2009, Vol. 2, No. 1, Pages 77–86.

[iii] William Berger et al., "Pharmacologic alternatives to antidepressants in posttraumatic stress disorder: A systematic review", Dec. 24, 2008, Progress in Neuro-Psychopharmacology and Biological Psychiatry Volume 33, Issue 2, 17 March 2009, Pages 169–180.

[iv] Naifeh, James et al., "Clinical Profile Differences Between PTSD—Diagnosed Military Veterans and Crime Victims," Journal of Trauma and Dissociation, 9(3): 321–334.

ety around them. Unfortunately, current therapies fail to sufficiently treat a large proportion of those afflicted with the disorder.
2. There are wonderful new developments in the field of neurobiology and neuropharmaceuticals that may make a huge difference to sufferers of PTSD and other mental disorders without some of the side effects that dissuade veterans and military personnel from seeking treatment.
3. We must respond with a sense of urgency around testing new classes of drugs to treat the patients who do not respond to existing therapies for military PTSD. Our collective goal should be to have new medicines for the veterans of these conflicts, not future ones.
4. A clear pathway to new drug development engaging the pharmaceutical industry as a full partner, including regulatory and financial incentives for orphan-like drug development, including clinical trials is required.
5. Improved screening of patients for early diagnosis and treatment must continue and expand since early diagnosis predicts far better outcomes.
6. We must also invest time and resources in improved tools to diagnose and differentiate PTSD from TBI, and the creation of tools that evaluate treatment effectiveness, thereby reducing treatment failures and suicides.

Once again, my thanks for the opportunity to speak before you.

**Prepared Statement of Joseph Califano III, M.D., Professor, Department of Otolaryngology-Head and Neck Surgery and Oncology, Johns Hopkins Medical Institutions, Baltimore, MD**

Mr. Chairman and Members of the Committee, I am Dr. Joseph Califano, MD.:

As a Professor of Otolaryngology-Head and Neck Surgery and Oncology, a researcher in Molecular Biology, and a practicing head and neck surgeon, I routinely see patients who present at their initial consultation with advanced head and neck cancers. Many head and neck cancers are already at an advanced stage in the disease process before the lesion is discovered during examination or the patient presents with a specific complaint. As an example, 50 percent of cancers of the tongue have already metastasized before they are diagnosed. It is typically only at relatively advanced stages that most patients become aware of any signs or symptoms associated with oral malignancies (except for lip cancer, which is usually obvious because any change in appearance is in a visually prominent area). While the survival rates for breast, lung and prostate cancers have improved over the last three decades, this is not true for oral cancer overall. Recurring and second primary tumors contribute to the devastating mortality and morbidity associated with oral cancers.

Late diagnosis contributes to the low 5-year relative survival rates for all oral and oropharyngeal cancers, even as treatment modalities have improved. For example, the 5-year relative survival rate for localized cancer of the lip is 97 percent, but only 35.3 percent when distant metastases are present at the time of diagnosis. For cancer of the tongue, the corresponding 5-year relative survival rates are 73.6 percent and 25.9 percent. It is also difficult to diagnose recurrent malignancies or second tumors close to a treated site, since irradiation and surgery each result in changes to the mucosa that could result in observed early pre-malignant and malignant abnormalities being dismissed as scarring or radiation-induced changes. For all types of oral cancers, the more localized the lesion at the time of diagnosis the better the patient's chance of survival and the less invasive and destructive treatment will be, leading to better quality of life. A recent pilot study at the University of Washington involving specialists trained to identify oral cancer found that their sensitivity in detecting lesions with atypical cellular changes using an unaided visual examination was just 21 percent, and 50 percent for lesions with moderate or greater dysplasia or carcinoma. Techniques with high sensitivity and specificity that aid earlier diagnosis of oral cancer have the potential to reduce both mortality and morbidity.

**Carcinogenesis: a molecular process characterized by genotypic changes followed by phenotypic change**

Malignancies develop through molecular changes at the cellular level. Cell cycles become deregulated, with genetic changes and tissue dysplasia of varying severity occurring. Loss of heterozygocity in pre-malignant lesions, with chromosomal abnormalities and allelic loss on specific arms of chromosomes, is predictive of malignant transformation. Loss of heterozygocity in the 3p, 9p and 17p arms of chromosomes in particular is predictive for malignant transformation, and secondary malignancies are more likely in cases where multiple chromosomal arms are affected.

**ViziLite Plus**

Adjunctive technology aids the detection of lesions at an early stage. ViziLite Plus is used to help identify pre-malignant and malignant lesions by differentially staining the tissues and has been found to offer high sensitivity and specificity. The stain used is pharmaceutical-grade toluidine blue (TBlue) which binds to a pre-malignant or malignant lesion. Recent studies have shown that the differential uptake of TBlue in lesions is associated with chromosomal changes and loss of heterozygocity, and predictive of malignant transformation. In addition to aiding the detection of lesions requiring biopsy for histopathology and diagnosis, T-blue staining has been shown to delineate the margins of lesions such that the area of resection at the time of surgery encompasses the full extent of the lesion and all identified abnormal tissue.

**Use of ViziLite Plus in the Erbitux study**

The ViziLite Plus system is currently being utilized as part of an ongoing Phase II clinical trial at multiple cancer sites for determining the efficacy of the head and neck cancer drug, Cetuximab (trade name Erbitux). ViziLite Plus was selected as part of the inclusion criteria for patient admittance into the study to identify lesions consistent with specific chromosomal deletions in patients with previous histories of oral and oropharyngeal cancer. Previous work with this pharmaceutical-grade toluidine blue has demonstrated an affinity for the dye to bind to sites of allelic loss that are consistent with cancer progression of low-grade epithelial dysplasia. To be admitted, positive differential staining must occur followed by histological and molecular analyses. The role of the blue dye is to identify those lesions with the greatest likelihood of presenting the necessary allelic loss for progression.

**The value of adjunctive screening technologies in the VA**

Specific behaviors, and advancing age, increase an individual's risk for oral cancer. Smoking tobacco or drinking alcohol increases an individual's risk by up to 600 percent. Tobacco use is by far the single greatest risk factor, with over 75 percent of all cases occurring in tobacco users (smoking, spit, and chew tobacco). The combination of smoking and drinking further increases risk, as demonstrated by Mashberg's study on Veterans. The prevalence of tobacco smoking has historically been higher among Veterans than in the general population, and alcohol abuse is one of the most common mental health problems Veterans experience. Veterans are therefore a high-risk population for oral and oropharyngeal cancers.

Since earlier detection aids earlier treatment and would improve patient outcomes and quality of life, adjunctive technology that improves the rate of detection and that helps predict which lesions will undergo malignant transformation is warranted. Screening technologies such as ViziLite Plus help the examiner detect lesions that would otherwise be missed, and help predict which lesions will undergo transformation. It is strongly suggested that ViziLite Plus be considered for inclusion into clinics examining high-risk populations, such as the Veterans Administration, so that more effective examination and biopsy procedures may be performed to diagnose disease earlier.

Thank you for the opportunity of sharing my views on this important subject. I will be pleased to respond to any questions you may have.

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**Prepared Statement of Joel Epstein, DMD, MSD, FRCD(C), FDS, RCS, Director, Interdisciplinary Program in Oral Cancer Biology, Prevention and Treatment, College of Medicine, Chicago Cancer Center, University of Illinois, Chicago, IL**

Mr. Chairman and Members of the Committee, I am Dr. Joel Epstein, DMD:

Over the past few years dentistry has been introduced to visual diagnostic adjuncts to the conventional head and neck and oral examination for oral cancers. Light-based technologies have been developed with the goal of assisting practitioners in identification and evaluation of mucosal changes that include premalignant lesions and cancer. Health care providers have been and continue to be challenged with identifying abnormal oral conditions, which may represent premalignant and malignant disease. Until recently we have had to rely solely on visual examination in order to identify these abnormal changes and only through meticulous and time consuming oral examination. The result has been that the majority of oral cancer is not diagnosed until symptomatic and with advanced stage of disease, when extensive treatment is required and prognosis is guarded. While conventional visual examination remains the cornerstone for the oral cancer screen-

ing process, adjuvants are available that may facilitate lesion identification and guide subsequent testing for diagnosis and may be of assistance to experienced health care providers and patients such as those found in the VA system.

Worldwide clinical trials have been conducted to determine the sensitivity of the visual examination in identifying neoplasias presenting with precancerous dysplasia or invasive carcinoma. Sensitivity is determined by number of true positive (dysplasias and cancers identified) results and the number of false negative (dysplasias and cancer missed) results recorded during visual examination. A large general population in India was studied where an oral examination was conducted and early detection of cancers was shown, and reduced mortality was seen at 2 year follow-up. However, oral lesions at early stage are subtle and may appear benign and have few symptoms thereby limiting the attention of the examining health care worker. The advanced stage of cancer at diagnosis in ⅔ of the population in studies in developed countries including the USA, demonstrates the difficulty in detection and diagnosis of premalignant lesions or early stage cancer.

The most widely used light technology available and supported with the most peer-reviewed literature is chemiluminescence. Tissue reflectance using a chemiluminescent light source (ViziLite®) emitting low-intensity, diffuse wavelengths of light may provide additional information. The light is reflected off of tissue surface and sub-layers, and is affected by keratin and tissues that contain cells with nuclei that take up a larger volume of the cell than normal (hallmark of dysplasia and cancer). Normal tissue absorbs this light and abnormal tissues will reflect the light. Chemiluminescent light is non-discriminatory and will be reflected by nearly all abnormalities. Clinical studies to date conducted at different centers show that approximately 60 percent of lesions will show enhanced contrast, brightness and surface texture with chemiluminescent light compared to standard white light illumination. To date, the literature has demonstrated a sensitivity of 100 percent for this type of technology in the detection of pathologic lesions. It has been further demonstrated that increased brightness may reduce the potential for not identifying a potentially significant mucosal lesion. These studies were conducted in patient populations likely comparable to those which are found in the VA to assess visibility and increased visual characteristics that may increase detection, but were not studies where identified lesions were biopsied to assess cellular change (histopathology).

In studies involving oral chemiluminescence, lesions meeting the definitions of 'clinically suspicious' for dysplasia or cancer were captured in lieu of biopsy and histological analyses, with the exception of two studies,[i,ii] which had histological outcomes. Additionally, all published studies have been conducted by specialists in Oral Medicine, Oral Pathology and/or Oral Surgery. In the majority of studies, chemiluminescence (ViziLite) examination identified lesions suspicious for pathology that remained unidentified after conventional visual examination. In four (4) studies involving 885 patients, thirteen (13) lesions in thirteen different patients (1.46 percent) were not identified during visual examination and categorized as clinically suspicious for dysplasia or worse. Further, in one these studies[iii] an occult lesion detected by ViziLite alone was later biopsied post-study during routine patient care and proved to be squamous cell carcinoma of the lateral tongue.

Another adjunct for visualization and clinical assessment is vital tissue staining, where a product is applied to the oral surface in patients and evaluated. Toluidine blue has a long history of study. More recently, a medical grade toluidine blue has been developed and the more recent studies have used this product as a single agent for detection and evaluation or in combination with chemiluminescence. As a clinical researcher with experience in conducting research and publishing study results on diagnostic aids for the detection of oral cancer and its precursor lesions, it is clear from the literature that the use of toluidine blue is the most reliable adjunct we employ to assist in a differential diagnosis, biopsy site selection, to accelerate the decision for biopsy, and to assist in detection of lesion margins. Without performing tissue biopsy for H&E analysis, toluidine blue and it's preferential staining of nucleic acids (DNA) helps to identify lesions with the likelihood of presenting pathol-

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[i] Ram S, Siar CH. Chemiluminescence as a diagnostic aid in the detection of oral cancer and potentially malignant epithelial lesions. Int J Oral Maxillofac Surg. 2005 Jul;34(5):521–7. Epub 2005 Jan 26.

[ii] Epstein JB et al. Analysis of oral lesion biopsies identified and evaluated by visual examination, chemiluminescence and toluidine blue. Oral Oncol. 2008 Jun;44(6):538–44.

[iii] Epstein JB, et al. The Efficacy of Oral Lumenoscopy (ViziLite) in Visualizing Oral Mucosal Lesions. Spec Care Dentist. 2006 Jul–Aug;26(4):171–4.

ogy. Cross-sectional studies[iv,v] and a prospective study[vi] have shown that toluidine blue binds to sites of genetic change that predicts progression of premalignant lesions to cancer and in lesions that already represent cancer at first diagnostic biopsy. Toluidine blue has been shown to assist in clinical evaluation, biopsy site selection and to provide guidance of the risk of progression of premalignant lesions to cancer.

The screening technology utilizing chemiluminescence and pharmaceutical-grade toluidine blue (TBlue) is ViziLite Plus. This device has been studied in patient populations similar to those found in the VA system. The combination device utilizes chemiluminescence for the identification of abnormalities in patient populations at increased risk for oral cancer (its FDA intended use). The ViziLite examination is performed only after conventional visual examination. ViziLite Plus also contains TBlue and is applied to those lesions differentially identified by the ViziLite light source and present with clinical suspicion.

Based upon the body of evidence in the peer-reviewed literature it can be recommended that ViziLite Plus be used in a higher risk patient population by experienced providers, as seen in VA clinics. ViziLite Plus technology should be considered for clinical use in the evaluation of lesions previously identified during conventional head and neck examinations. Although this type of application may not realize the full potential of the combination device, the Veteran population could be well-served by reducing the number of false positive findings associated with visual examination thus potentially reducing the number of unnecessary biopsies. This outcome has been shown in a multicenter study[ii], in a risk population similar to the VA population, where a reduction in the number of biopsies by approximately half would have still identified clinically significant lesions. Additionally, the system may be used in conjunction with clinical suspicion, for the monitoring of pathologic lesions over time as an indicator for repeat biopsy and histologic examination.

Thank you for the opportunity of sharing my views on this important subject. I will be pleased to respond to any questions you may have.

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**Prepared Statement of William L. Balanoff, DDS, MS, FICD, SmilePerfect, Fort Lauderdale, FL**

Mr. Chairman and Members of the Committee, I am William L. Balanoff, DDS, MS, FICD.

Visual examination has often been referred to as the "Gold Standard" examination for oral cancer screening, but has not been successful at achieving early detection rates of pre-cancerous and cancerous lesions to the point of reducing incidence and death. As such, the incidence rate of oral cancer remains virtually unchanged and mortality rates have not significantly decreased over the same time period. I like to think that dental practitioners are not remiss and don't want to do a thorough job of screening patients at increased risk for oral cancer, but rather that it's just that we haven't had the benefits of adjunctive screening technologies to help us identify early cancers and precancerous lesions such as those used by our colleagues in the medical community for other cancer types.

The reality is that the general practitioner is charged with the responsibility of identifying potentially harmful lesions and referring that patient to a specialist in oral diseases for further evaluation and possible treatment. Whether it is private practice dentistry or VA dentistry, the demands and complexities are great. Given the inherent difficulties associated with oral soft tissue examination (patient's ability to provide adequate access, pooling of saliva, multiple structures of varying color and working knowledge of oral pathology), the inclusion of a diagnostic adjunct is critical to ensure that all abnormalities have been visually captured.

The idea of not using diagnostic adjuncts to screen patients for oral abnormalities is the equivalent to a philosophy of a medical doctor using only his eyes and hands to assess a patient's health when diagnostic adjuncts are available. All patients expect their doctors to use every tool and test available to assess their health.. Much is the same for the practicing dentist and the availability of medical devices to assist

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[iv] Epstein JB, Zhang L, Poh C, Nakamura H, Berean K, Rosin M. Increased allelic loss in toluidine blue-positive oral premalignant lesions. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2003 Jan;95(1):45–50.

[v] Guo Z, Yamaguchi K, Sanchez-Cespedes M, Westra WH, Koch WM, Sidransky D. Allelic losses in OraTest-directed biopsies of patients with prior upper aerodigestive tract malignancy. Clin Cancer Res 2001;7(7):1963–1968.

[vi] Zhang L, Williams M, Poh CF, et al. Toluidine blue staining identifies high-risk primary oral premalignant lesions with poor outcome. Cancer Res 2005;65(17):8017–8021.

in the screening for oral lesions which can be missed during visual examination. Rates of death associated with cancers encountered by my MD counterparts were not adequately reduced until adjuvant screening devices were introduced. Cancer death rates from prostate, breast and cervical cancer did not begin to show substantive decreases until adjunctive screening technology allowed physicians to see or feel things they could not see or feel with their unaided eyes or hands. Mammograms, PAP smears and PSA tests have reduced death rates by 40 percent, 80 percent and 17 percent respectively. These dramatic improvements in lives saved was only realized when physicians were given scientifically based technological advancements to aid in the discovery of these diseases.

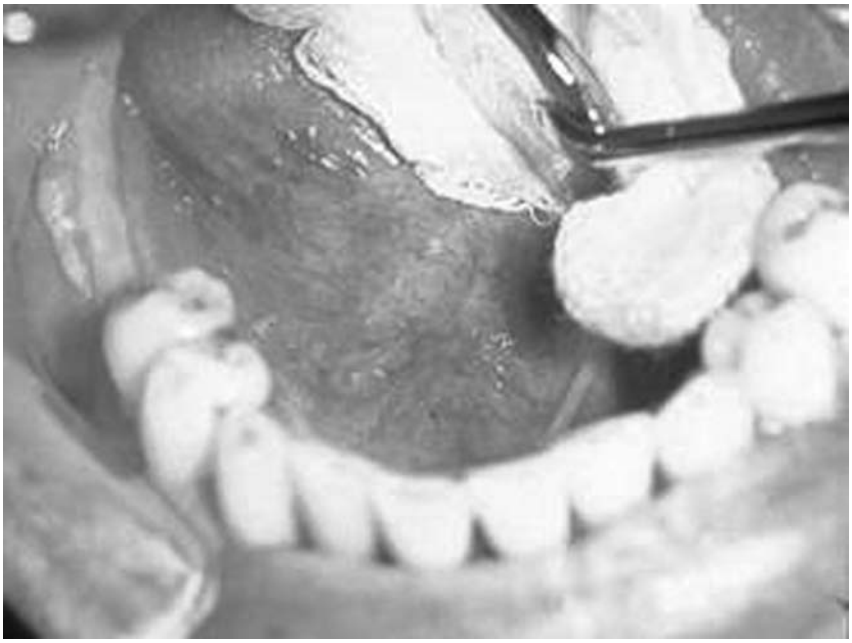
Since leaving dental school, I have performed thousands of head and neck examinations to detect the presence of disease which requires treatment. Disease states such as periodontal disease and dental caries (cavities) are diagnosed with the aid of adjunctive technology. Periodontal probing, X-rays, and microbiology are standard regimens for the diagnosis of periodontal disease and X-rays are at the heart of diagnosing dental caries. As a dental professional, my decisions have been grounded in science and research to help detect and treat these disease states. Oral cancer and premalignancies can now be addressed in the same manner with the advent of devices for improving the efficacy of visual soft tissue examination.

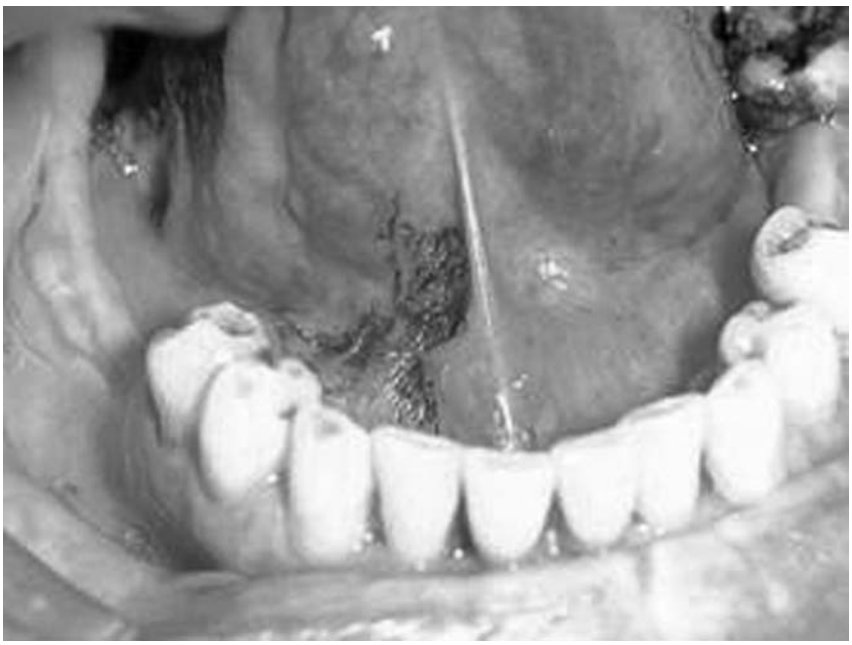
Of concern to me are those professing to be pundits of oral cancer screening and accepting the status quo as acceptable care. Of even greater concern is during my routine research of new products available to a practitioner that I read articles or reviews recommending that diagnostic adjuncts not be used and that visual examinations remain the only test required. Unfortunately, too often these recommendations are made by those who have never tried oral cancer screening adjuncts and are making recommendations based upon another's opinion or by those who do not see patients and only write about that which they themselves are inexperienced.

For the past 5 years, the use of chemiluminescence (ViziLite) has allowed me to identify lesions that were otherwise missed during previous conventional oral examination. This adjunctive screening device is now the standard of care, along with conventional visual examination, in my conduct of dentistry and its use is ideally suited for patients identified at being at increased risk for oral cancer.

The technology was first tested on thousands of women in worldwide clinical studies and was shown to significantly improve the sensitivity for identifying cervical intraepithelial neoplasias, the precancerous lesions of the female cervix. In four studies it was shown to improve the sensitivity of identifying cervical pathology from 92 percent to 99.1 percent. The FDA cleared the light technology for dentistry in 2001 because the visual response to lesions treated with a mild acetic acid followed by chemiluminescent illumination was nearly identical for the same kind of cells making up both areas. More recently, a medical grade toluidine blue (TBlue®) was added to the ViziLite light source and cleared by the FDA for use as the combination device ViziLite Blue Oral Lesion Identification and Marking System (ViziLite Plus)by Zila Pharmaceuticals, Inc.

Toluidine blue has been used clinically for many years and is well documented in its utility for use in identifying high grade dysplasia. It has been reported that toluidine blue may be preferentially retained by nuclear and mitochondrial DNA associated with oral premalignant lesions (OPLs) and "frank" cancer. It is because of this that staining suspicious lesions differentially identified during ViziLite examination is of great benefit to higher risk patients, such as those found in the VA hospitals. It allows me to refer patients with a greater likelihood of pathology present.





My job as a general dentist is to find everything "abnormal" in my patients and to refer to specialists those conditions presenting with a great deal of clinical suspicion. Primarily, clinical suspicion is determined by direct visualization under normal patient lighting. As an adjunct, ViziLite Plus is critical for 1) initial identifica-

tion of a lesion missed during visual examination and/or 2) to provide me with additional information to make an informed referral.

General dentists, including those who treat our Nation's Veterans, are responsible for the detection of abnormalities that present as pathosis. And because there is a screening adjunct that has helped me to identify precancerous lesions that I missed during visual examination, I strongly recommend the ViziLite Plus system for use within the Veterans Administration system.

**MATERIAL SUBMITTED FOR THE RECORD**

Committee on Veterans' Affairs
Washington, DC.
*May 14, 2009*

Honorable Eric K. Shinseki
Secretary
U.S. Department of Veterans Affairs
810 Vermont Avenue, NW
Washington, DC 20420

Dear Mr. Secretary:

In reference to our Full Committee hearing entitled "Innovative Technologies and Treatments Helping Veterans" on May 13, 2009, I would appreciate it if you could answer the enclosed hearing questions by the close of business on June 27, 2009.

In an effort to reduce printing costs, the Committee on Veterans' Affairs, in cooperation with the Joint Committee on Printing, is implementing some formatting changes for materials for all full Committee and Subcommittee hearings. Therefore, it would be appreciated if you could provide your answers consecutively and single-spaced. In addition, please restate the question in its entirety before the answer.

Due to the delay in receiving mail, please provide your response to Debbie Smith by fax at 202–225–2034. If you have any questions, please call 202–225–9756.

Sincerely,

BOB FILNER
*Chairman*

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**Questions for the Record**
**The Honorable Bob Filner, Chairman**
**House Committee on Veterans' Affairs**
**Innovative Technologies and Treatments Helping Veterans**
**May 13, 2009**

During the Full Committee hearing on May 13, 2009, I received testimony from Alkermes, a small biotechnology company that manufactures a drug called VIVITROL. VIVITROL is an extended-release naltrexone product. It is a non-addictive, non-aversive agent that binds to opioid receptors in the brain. It was recently approved by the U.S. Food and Drug Administration (FDA). It is my understanding the drug VIVITROL was used on a limited basis in the Veterans Integrated Service Network 8, particularly in the Gainesville facility. Please provide answers to the following questions:

**Context of Response:** Vivitrol® is not on the Department of Veterans Affairs (VA) formulary. Its use is very limited and VA does not systematically collect patient data that would definitively respond to several of the questions you raise. In these instances, we are summarizing peer reviewed literature on Vivitrol®. At present, no VA medical centers in the Veterans Integrated Service Network (VISN) 8 are performing research on Vivitrol®.

**Scientific Evidence:** When the Food and Drug Administration (FDA) approved Vivitrol®, the Veterans Health Administration (VHA) Pharmacy Benefits Management Service (PBM) initiated a review of the scientific evidence to evaluate its efficacy and safety compared to other standard therapies available to VA patients. VA formulary committees, the PBM medical advisory panel (MAP) and VISN pharmacy executives reviewed the scientific evidence supporting the use of Vivitrol®. There are limited data showing better medication adherence with injectable naltrexone relative to orally administered naltrexone. Unfortunately, there is no definitive evidence showing that injectable naltrexone is safer or results in better patient outcomes compared with oral naltrexone. Very limited data suggest a possibility that injectable naltrexone might be less safe than oral naltrexone. VA also recognizes that patients must be amenable to traveling to a VA clinic to receive intramuscular injections of naltrexone every month. Overall, there is a lack of definitive evidence that injectable naltrexone improves patient outcomes relative to oral naltrexone.

**Availability:** Vivitrol® is available for non-formulary use and VHA PBM and the MAP/VISN pharmacist executives committee have issued guidance for the non-for-

mulary use of injectable naltrexone. VA and Department of Defense (DoD) guidelines for the management of substance use disorders provide recommendations for the use of both oral and injectable naltrexone. Prior trials of oral naltrexone or other anti-alcoholic agents (e.g., acamprosate or disulfiram) are not required before injectable naltrexone can be considered. Further, clinical guidelines recommend that addiction-focused counseling be offered in addition to naltrexone, regardless of route of administration.

The responses to the questions below reflect information based on VA prescription data and a thorough literature review. As noted, there are no systematically collected data available specific to VISN 8 that can be used to respond to the questions.

**Question 1:** What is the total number of patients in your network receiving VIVITROL as part of their treatment for alcohol dependence?

**Response:** Within VISN 8 the total number of patients receiving Vivitrolr is 45. The James A. Haley Veterans' Hospital in Tampa, Florida currently has one patient and the North Florida/South Georgia Veterans Health System currently has 44 patients receiving Vivitrol®. In fiscal year (FY) 2008, VA-wide, 71 Veterans were prescribed Vivitrol®. Oral naltrexone is more widely used, with 5,827 unique patients receiving it in FY 2008.

**Question 2:** Does VIVITROL improve the patients' urges to drink?

**Response**: Based on review of the available literature, both oral naltrexone and Vivitrol® result in decreased urges to drink for some patients.

**Question 3:** What percentage of patients experienced a decrease in their urge to drink?

**Response**: The FDA approved labeling for Vivitrol® suggests that it decreases heavy drinking (and, presumably, urges to drink) in those patients who were able to achieve abstinence for at least 1 week prior to starting treatment.

**Question 4:** Does VIVITROL decrease drinking?

**Response:** Review of the existing literature suggests that both oral naltrexone and Vivitrol® are effective at decreasing rates of heavy drinking among patients.

**Question 5:** Does VIVITROL promote abstinence from drinking?

**Response:** Both oral naltrexone and Vivitrol® are shown to significantly reduce use of alcohol. Both medications are appropriate for use in treatment programs that promote abstinence or programs that promote decreased use of alcohol.

**Question 6:** What percentage of patients remain abstinent during treatment?

**Response:** Based on findings from a small post-hoc subgroup analysis of individuals included in an industry-sponsored clinical trial who were able to achieve abstinence prior to drug treatment, Vivitrol® treatment was associated with approximately 32 percent abstinence at 6 months, compared to 11 percent for those who received placebo.

**Question 7:** What is the average duration of persistence on VIVITROL?

**Response:** Vivitrol® is administered on a monthly basis. Review of utilization data for FY 2007 indicates that approximately 50 percent of those Veterans who were prescribed Vivitrolr received no more than 1 injection. We are not aware of any direct research data on the average duration of persistence on Vivitrol®.

**Question 8:** Do patients engage in behavioral counseling while receiving VIVITROL? If so, what percentage of patients are receiving counseling?

**Response:** Vivitrol is currently prescribed and administered within VA specialty care for alcohol use disorders. Given that this treatment is provided within a specialty care program, Veterans who have been prescribed Vivitrol® would also receive counseling.

**Question 9:** What happens to hospital utilization (specifically emergency department visits and inpatient admissions) in patients using VIVITROL?

**Response:** We are not aware of any studies that have evaluated emergency department visits and rates of hospital utilization among patients using Vivitrol®.

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