OFFICE OF THE UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

PERSONNEL AND READINESS

MAR - 9 2016

The Honorable John McCain
Chairman
Committee on Armed Services
United States Senate
Washington, DC 20510

Dear Mr. Chairman:

The enclosed final report responds to Senate Report 113-85, page 190, which accompanied S. 1429, the Department of Defense Appropriations Bill for Fiscal Year (FY) 2014, requesting the breakdown of funding in the Congressionally Directed Medical Research Program (CDMRP) between basic and advanced research.

The CDMRP's recent research award portfolio is shifting to emphasize more applied and advanced clinical research. The portfolio reflects a significant shift in the type of research funded when comparing FYs 2012-2014 to FYs 2010-2012. The percent change in the number of awards funded in basic research has decreased by 31percent, while awards funded in advanced and applied research have increased by 16 and 27 percent, respectively.

Thank you for your interest in the health and well-being of our Service members, veterans, and their families. A similar letter is being sent to the other congressional defense committees.

Sincerely,

Brad Carson
Senior Advisor to the Under Secretary of Defense for Personnel and Readiness, Performing the Duties of the Principal Deputy Under Secretary of Defense for Personnel and Readiness

Enclosure:
As stated

cc:
The Honorable Jack Reed
Ranking Member

OFFICE OF THE UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

PERSONNEL AND
READINESS

MAR - 9 2016

The Honorable William M. "Mac" Thornberry
Chairman
Committee on Armed Services
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

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Brad Carson
Senior Advisor to the Under Secretary of Defense for Personnel and Readiness, Performing the Duties of the Principal Deputy Under Secretary of Defense for Personnel and Readiness

Enclosure:
As stated

cc:
The Honorable Adam Smith
Ranking Member

PERSONNEL AND READINESS

OFFICE OF THE UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

MAR - 9 2016

The Honorable Thad Cochran
Chairman
Subcommittee on Defense
Committee on Appropriations
United States Senate
Washington, DC 20510

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Brad Carson
Senior Advisor to the Under Secretary of Defense for Personnel and Readiness, Performing the Duties of the Principal Deputy Under Secretary of Defense for Personnel and Readiness

Enclosure:
As stated

cc:
The Honorable Richard J. Durbin
Vice Chairman

OFFICE OF THE UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

PERSONNEL AND READINESS

MAR - 9 2016

The Honorable Rodney P. Frelinghuysen
Chairman
Subcommittee on Defense
Committee on Appropriations
U.S. House of Representatives
Washington, DC 20515

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Brad Carson
Senior Advisor to the Under Secretary of Defense for Personnel and Readiness, Performing the Duties of the Principal Deputy Under Secretary of Defense for Personnel and Readiness

Enclosure:
As stated

cc:
The Honorable Peter J. Visclosky
Ranking Member

REPORT TO THE CONGRESSIONAL DEFENSE COMMITTEES IN RESPONSE TO SENATE REPORT 113-85, PG 190, ACCOMPANYING S. 1429, THE DEPARTMENT OF DEFENSE APPROPRIATIONS BILL, 2014

"CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS"

July 2015

The estimated cost of this report or study for the Department of Defense is approximately $4,790 for the 2015 Fiscal Year. This includes $1,500 in expenses and $3,290 in DoD labor.
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Congressionally Directed Medical Research Programs

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PURPOSE OF REPORT

Senate Report 113-85 (page 190) requested that the Assistant Secretary of Defense for Health Affairs "provide a report to the congressional defense committees within 180 days of enactment of this Act on the breakdown of funding in the Congressionally Directed Medical Research program between basic and advanced research." Specifically, Senate Report 113-85 stated that the committee "remains supportive of the medical research being conducted by the Department that yields medical breakthroughs for servicemembers and often translates to the civilian population, as well."

BACKGROUND

The Congressionally Directed Medical Research Program (CDMRP) is the program execution and management agent for multiple Congressional Special Interest programs, and is responsible for program planning, coordination, integration, budgeting, evaluation, administration, and reporting for each program. The CDMRP uses a flexible execution and management cycle that is designed to tailor each program's research portfolio to the rapidly-changing knowledge gaps and discoveries within each relevant research field. The cycle follows the appropriations from cradle to grave, and includes the receipt of annual Congressional appropriations, stakeholder meetings for new research programs, vision setting, release of funding opportunities, soliciting research applications, pre-proposal screening and invitation to submit full applications, full application receipt and review, recommendations of applications for funding, and oversight of research awards.

At the center of the program cycle is a two-tier review process, which assures each of the CDMRP research portfolios reflects not only the most meritorious science, but also the most programmatically relevant research. This process was adopted from the recommendations set forth in 1993 by the National Academy of Science's Institute of Medicine (IOM) (1). Scientifically sound applications that best meet each program's goals are recommended to the Commanding General, U.S. Army Medical Research and Materiel Command (USAMRMC), and the Director, Research, Development, and Acquisition Directorate of the Defense Health Agency, for funding. Once approved, funding notifications are sent to investigators; awards are typically made in the form of one- to five-year assistance agreements and are assigned to the CDMRP staff for full-cycle oversight of research progress and outcomes. The CDMRP protects the integrity of the review process and provides transparency by publishing lists of funded applications, programmatic panel members, peer review panelists, abstracts, and research accomplishments on the CDMRP website: http://cdmrp.army.mil. The programs that comprise the CDMRP are scientifically sound, innovative, and responsive to Congressional intent and the needs of the military and the public. The USAMRMC and the CDMRP have been praised by the IOM, which issued a report in 1997, stating it was favorably impressed with the processes implemented by the CDMRP and supported its continuation (2).

The programs that comprise the CDMRP are scientifically sound, innovative, and responsive to Congressional intent and the needs of the military and the public.

Each CDMRP program is guided by a programmatic panel (typically called an Integration Panel or Joint Program Committee) comprised of scientists and clinicians with renowned expertise in relevant areas of research and medicine, consumers from advocacy communities, and members of the military and other Government organizations (3). In Fiscal Year (FY) 2014, over 460 scientists, clinicians, and consumers, which included Service members in all capacities, served as full or ad hoc members of programmatic panels across 19 Congressional Special Interest research programs. At the time this report was written, programmatic panels for the FY 2015 programs to be managed by the CDMRP are being constituted, so data on their composition was not yet available. Each program has a vision statement that reflects its overarching goals of ending or curing its respective disease, condition, or injury, ameliorating the consequences, and/or having a major impact on the quality of life of the survivors. On an annual basis, each programmatic panel examines its program's goals and vision statement, and refines them as appropriate to reflect the current state of science and medicine. Following a comprehensive review of the program's portfolio, the present-day research landscape, and potential directions, the investment strategy for the program is developed, as well as the award mechanisms that will be offered as funding opportunities to fulfill the investment strategy. In addition, the programmatic panel provides recommendations on how the application review process can be best tailored to select applications that will achieve the investment strategy.

Establishment of a program's goals, vision statement, and investment strategy leads to the development of funding opportunities that describe the intent of each award mechanism. Funding opportunities are published and advertised broadly to solicit research applications aimed at making scientific advances that have a significant impact for the individuals affected by the relevant diseases, injuries, and conditions. The CDMRP's diverse funding opportunities enable and support at all stages of research, including exploring early-stage concepts, developing a foundation to understand disease biology and etiology, investigating therapeutic efficacy in disease models, advancing technological innovations, and conducting clinical trials and studies in human populations.

The current report covering FY 2014 provides a summary of the funding invested by the CDMRP along the continuum of basic, translational (applied), and advanced research. The report focuses on the 19 Congressional Special Interest programs that have been managed by the CDMRP since their inception. Congressional Special Interest programs previously executed by the Telemedicine and Advanced Technology Research Center and now under management of the CDMRP are not included as the transition of program portfolios and data is still in process. Information on those programs is expected to be included in any future reports.

CDMRP FUNDING OPPORTUNITIES BY TYPE OF RESEARCH

As noted above, each of the programs managed by the CDMRP develops a research investment strategy that is responsive to the dynamic changes in its respective field and is adapted yearly to meet emerging needs of patient and research communities, fill gaps in research, and address other barriers to progress. The programmatic panel of each program recommends how to implement the research investment strategy through specific and clearly defined award mechanisms designed to address research focus areas. The types of research supported by the

CDMRP's award mechanisms range from early-stage concepts and ideas at the basic research level, to translational projects at the applied research level, to advanced research supporting clinical trials. Thus, the CDMRP enables investigators to submit proposals at every stage of idea and research development through the award mechanisms offered across its different programs. Since its inception, the CDMRP has developed and released over 900 Program Announcements to the public as funding opportunities for the solicitation of research proposals focused on the specific goals of each research program.

The CDMRP has offered award mechanisms that support all types of research, which can be grouped into four major categories. For this report, each award mechanism was assigned to one of the following:

- Basic research: Discovery-driven research for the generation of new ideas, knowledge, hypotheses, or preliminary data to support applied and more advanced research. Examples of this research category include "bench-science" and development of animal models.
- Applied research: Research that includes utilizing basic research findings to develop material and knowledge products to prevent, diagnose, or treat diseases, conditions, and injuries. Examples of this category include validation using animal models, technology development, and clinical research without an intervention.
- Advanced research: Late-stage applied research, including testing and refinement of material and knowledge products in human subject populations. Examples include clinical research with an intervention and clinical trials.
- Combination research: Research utilizing a variety or blend of basic, applied, or advanced research approaches. Award mechanisms and individual awards that span across Basic, Applied, and Advanced research fall into this category. Combination mechanisms are designed to be flexible to allow the research community to propose research at any stage that has the potential for high impact.

Table 1 depicts the types of award mechanisms offered by the CDMRP since FY 1993. The estimated funding in the investment strategy to support basic, applied, and advanced research is closely matched to the actual award funding investments. Over the lifetime of the CDMRP, the largest percentage of all of the CDMRP research awards were made in the combination research category, which includes basic, applied, and advanced research. CDMRP's strong investment in combination-type research reflects the responsive approach it takes to research management, as such award mechanisms allow for maximum flexibility in supporting research in areas where the research landscape is highly dynamic. Basic research is generally funded using award mechanisms in the lower dollar range of $100,000 to $500,000; whereas advanced research involving clinical trials requires more funding, typically in the $1M to $10M per award range. It is important to note that the sum of the estimated funding for applied

The high percentage of funding opportunities that seek translational research applications, as well as the corresponding actual awards funded, indicates that supporting translational research is a high priority for the CDMRP.

and combination research (80% combined) in the investment strategy nearly matches the actual award funding invested in these research categories (84%). The high percentage of funding opportunities that seek translational research applications, as well as the corresponding actual awards funded, indicates that supporting translational research is a high priority for the CDMRP.

Table 1. Investment Strategy and Research Funded by Type of Research FY 1993 – FY 2014**

Type of Research	Award Mechanisms in Investment Strategy	Estimated Funding In Investment Strategy	% of Actual Awards	% of Actual Award Funding
Basic	28%	11%	35%	10%
Applied	13%	8%	7%	13%
Advanced	11%	9%	2%	6%
Combination	48%	72%	56%	71%

** At the time this report was written FY 2014 awards are in negotiations and are not final.

For a more detailed analysis of the individual CDMRP research programs, Appendix A shows the planned investment strategy in the left column compared to the actual research awards funded in the right column. The differences in investment strategies among the programs are the result of several factors. The feasibility of offering award mechanisms that support advanced research (which includes clinical trials) may be limited due to gaps in the basic science knowledge of the specific disease or condition, limited availability of funds to support advanced research such as clinical trials, or strategic decisions based on program focus within the broader research landscape. Research programs with less mature areas of research generally focus primarily on basic or applied research in an effort to fill gaps and create the foundations needed for advanced research. Moreover, each CDMRP research program's investment strategy is defined on an annual basis, when the program receives Congressional funding, to identify and target the areas that are most critically in need of research. Therefore, the award mechanisms and research types supported by a program may shift and evolve over time.

The number of research awards made and funds invested in each type of research varies by program. Each research program's investment strategy is used as a guide when its programmatic panel recommends applications for funding. The number of awards recommended for funding and the amount invested within each award mechanism and research type is highly dependent on the number, quality, and type of applications received, as well as each application's relevance to the program's goals, relative innovation or impact, portfolio balance or composition, and adherence to the intent of the award mechanism.

RECENT INVESTMENTS AT A GLANCE: FY 2012 – FY 2014

To examine more recent CDMRP investments over the last three years, Table 2 depicts the research awards made by the CDMRP programs during FY 2012 – FY 2014. The largest percent of all of the CDMRP research awards made (based on number of awards) are in the categories of

basic and combination research. Because validation in animal models, clinical research, and clinical trials is generally more costly than basic research, the percentage of research awards made per research type is not directly correlated to the amount of funding invested in each research type. While 25% of the CDMRP's FY 2012 – FY 2014 research awards were in basic research, this represented only 8% of the research funding invested. In contrast, while only 4% of these FY 2012 – FY 2014 research awards were specifically in advanced research (clinical trials), this represented 13% of the research funding invested. Moreover, in comparison to the data in Table 1, it is evident that the CDMRP's recent research award portfolio is shifting to emphasize more applied and advanced clinical research. For example, applied research represents 13% of the award funding within CDMRP's entire portfolio (FY 1993 to FY 2014), and 21% of the award funding in the more recent time period of FY 2012 to FY 2014. Similarly, the investment in advanced research has grown from 6% of the award funding from FY 1993 to FY 201[4], to 13% of the award funding in FY 2012 to FY 2014.

Table 2. Recent Investments by Type of Research, FY 2012-FY 2014

Type of Research	% of Actual Awards	% of Actual Award Funding
Basic	25%	8%
Applied	20%	21%
Advanced	4%	13%
Combination	51%	58%

** At the time this report was written FY 2014 awards are in negotiations and are not final.

Further evidence of a shift toward more applied and advanced research is seen in comparing the types of research funded over the most recent past three-year intervals. As shown in Table 3, the CDMRP's portfolio reflects a significant shift in the type of research funded when comparing FYs 2012-2014 to FYs 2010-2012. The percent change in the number of awards funded in basic research has decreased by 31%, while awards funded in advanced and applied research have increased by 16% and 27%, respectively.

Table 3. Variance Analysis of Research Funded in FY 2010-FY 2012 and FY 2012-FY 2014

Type of Research	% Change of Actual Awards Funded
Basic	-31%
Applied	+27%
Advanced	+16%
Combination	-4%

** At the time this report was written FY 2014 awards are in negotiations and are not final.

Appendix B breaks down the recent three-year investments for each of the CDMRP's research programs. Each program has a unique vision that targets the most critical aspect along the pipeline of basic to advanced research. The fundamental understanding of the biology and etiology of many diseases is still underdeveloped and requires delineation before the gap between basic and advanced research can be bridged. In addition, the research and funding

landscape in certain diseases may warrant an emphasis on funding the earlier stages of research, where novel discoveries are critical and urgently needed. A greater emphasis on basic and applied research is evident in programs such as amyotrophic lateral sclerosis (ALS), bone marrow failure, multiple sclerosis, lung cancer, and ovarian cancer. In contrast, other programs such as breast cancer, neurofibromatosis, orthopaedic, spinal cord injury, and Gulf War Illness (GWI), are positioned to solicit for and select research proposals that are closer to clinical translation, through funding opportunities targeting advanced research and/or the entire translational research continuum (combination research).

TRANSLATING CUTTING-EDGE BASIC RESEARCH INTO CLINICAL PRACTICE

In an era of numerous biomedical advancements, the increased ability to prevent, detect, and treat diseases, injuries, and medical conditions is providing patients with an array of clinical and preventative interventions and an overall better quality of life. While these advances have been extraordinary in moving medicine forward, the vast majority of conditions do not have a cure or cannot be prevented. Thus, the need to accelerate the pace of current biomedical research efforts remains urgent. Advanced research in the form of clinical trials is the engine that drives progress against disease by rigorously testing the safety and efficacy of new products and potential treatments in patients. However, prior to the translation of scientific findings into clinical trials, an increase in the basic understanding of key disease processes must occur and must be substantiated through preclinical investigations in *in vitro* systems and in more complex systems including animal disease models.[4] Therefore, success in translational medicine demands a continuous pipeline of basic and applied research discoveries that can advance to clinical application.

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Many of the CDMRP-managed basic and applied projects have the potential to become fielded products for the Warfighter and civilian populations. One process that helps facilitate this transition is called Decision Gate, a process designed and implemented by the USAMRMC to effectively manage medical product development in a cost-effective, consistent, and transparent process. Decision Gate, which is grounded in the Department of Defense Directive 5000 series, Food and Drug Administration (FDA) regulations, and best industry practices, allows the USAMRMC to remain responsive to the changing needs of the Warfighter. Research products identified as having sufficient scientific maturity and potentially filling a documented Service member need enter into Decision Gate. During the continued development of a research product, the product proceeds through a series of decision points (called Milestones) in which the Milestone Decision Authority decides whether product development continues as planned, continues with a revised plan, or is terminated. The CDMRP has participated in the formation of several teams in the Decision Gate process that are working to improve transfusion safety and diagnosis, neurocognitive assessments, diagnosis of traumatic brain injury, and treatment of traumatic brain injury.

As another approach to maintain movement of promising basic and applied research along the translational research continuum, some of the CDMRP programs such as the breast cancer, lung cancer, and orthopaedic research programs offer Expansion Awards. These Expansion Awards

are open only to investigators previously funded under specific CDMRP award mechanisms and provide support for the continued investigation of successful innovative ideas and expansion to translational and clinical research. Expansion Awards are competitive, undergo the CDMRP's rigorous two-tier review, and support further development of research that will impact patient care.

Funding from the CDMRP has enabled several investigators to bridge the gaps between basic science, applied science, and clinical medicine in a broad spectrum of patient-centered areas including treatment, prevention, early detection and screening, diagnostic, and quality of life/supportive care. Appendix C provides an extensive list of CDMRP-funded research efforts that were initiated as basic or applied research, and are currently in or entering a more advanced phase of development such as clinical trials, have been commercialized, or have already been implemented as standard of care. Selected examples of CDMRP-funded research that began as basic research and was then translated into advanced research or standard of care are highlighted below:

Funding from the CDMRP has enabled several investigators to bridge the gaps between basic science, applied science, and clinical medicine in a broad spectrum of patient-centered areas.

- Amyotrophic Lateral Sclerosis: Supported an FY 2010 award to perform large screens of FDA-approved drugs and identify chemical modifiers of the Tar DNA binding protein of 43 kDa (TDP-43) associated with ALS. The neuroleptic compound pimozide was found to improve neuromuscular transmission and restore mobility in all TDP-43 models tested. These findings led to a Phase IIb clinical trial to test the effectiveness of pimozide in ALS patients.
- Autism: Supported an FY 2010 pilot clinical trial award investigating whether Cognitive Enhancement Therapy or Enriched Supportive Therapy improved outcomes for adults with Autism Spectrum Disorder. After 18 months the adults in the Cognitive Enhancement Therapy group had significantly higher gains in neurocognition, social cognition, and social adjustment. The results have led to a large follow-on clinical trial funded by the National Institutes of Health.
- Bone Marrow Failure: Supported an FY 2009 study that used Myelodysplastic Syndrome (MDS) bone marrow samples to develop an MDS gene expression repository. This study led to a pending clinical trial of LY-2157299, an inhibitor targeting the receptor of transforming growth factor-β.
- Breast Cancer: Supported an FY 2004 study that discovered the ability of a small molecular inhibitor of cyclin-dependent kinases (PD-0332991) to inhibit estrogen receptor-positive (ER+) breast cancer. Clinical trials supported by Pfizer showed that that PD-0332991 (palbociclib) combined with letrozole improves overall survival (Phases I and II), and the ongoing Phase III clinical trial has shown improved progression-free survival. These promising results led to accelerated FDA approval, in February 2015, of palbociclib in combination with letrozole to treat metastatic ER+ breast cancer in postmenopausal women.

- Deployment Related Medical Research: Supported an FY 2008 preclinical study that successfully demonstrated low-level light as a potential therapy for treating traumatic brain injury. These investigations are being expanded in a pilot study that will further inform the design of a Phase III clinical trial.
- Gulf War Illness: Supported an FY 2008 award to develop and characterize a mouse model of exposure to agents associated with GWI. In a subsequent FY 2010 award, the mouse model was used to assess neurobehavioral outcome following treatment with the anti-inflammatory anatabine. These investigations led to a FY 2014 clinical evaluation of anatabine in a small population of GWI patients.
- Lung Cancer: Supported an FY 2009 study which discovered that inhibiting focal adhesion kinase (FAK) in lung cancer models inhibits tumor growth. These findings provided the rationale for opening a Phase II clinical trial in K-Ras mutant non-small cell lung cancer patients using the FAK inhibitor defactinib (VS-6062).
- Multiple Sclerosis: Supported an FY 2009 project that developed an effective myeloperoxidase (MPO) targeted magnetic resonance imaging agent for detection of multiple sclerosis disease activity, setting the stage for clinical investigations into MPO as an early detection strategy for multiple sclerosis.
- Neurofibromatosis: Supported an FY 2000 project that resulted in the discovery that FDA-approved Gleevec, a competitive tyrosine-kinase inhibitor already approved for use in the treatment of multiple forms of cancer, could block the ability of NF1+/- mast cells to stimulate fibroblast proliferation in an animal model, suggesting that it might work to prevent neurofibromas in patients. The results of this study allowed for the fast track approval for a Phase II trial of Gleevec in children and adults with NF1.
- Ovarian Cancer: Supported an FY 2003 study in which preliminary investigations identified 5 new biomarkers for ovarian cancer. These biomarkers were validated in more than 3,000 samples and subsequently incorporated into an *in vitro* diagnostic multivariate index test. This blood test, labeled OVA1^{TM}, was approved by the FDA in 2009, and is currently the only approved blood test to help determine if an ovarian mass is malignant or benign prior to surgery. This diagnostic test allows physicians to more easily identify patients for referral to a gynecologic oncologist and aids in facilitating surgical planning for those women who need treatment.
- Peer Reviewed Cancer Research Program: Supported an FY 2011 research award investigating immunity signaling dysregulation in MDS that has led to the development of an antibody to Toll-like Receptor 2. In partnership with Opsona Therapeutics the antibody is being manufactured and tested in Phase I/II clinical trials.
- Peer Reviewed Medical Research: Supported an FY 2009 award that demonstrated that combining multiple polyamine-targeting drugs with conventional chemotherapy is more effective in eliminating neuroblastoma in cell lines and animal models. This work lead directly to an ongoing Phase I trial using difluoromethylornithine and Celecoxib together with the chemotherapy agents Cyclophosphomide and Toptecan in children with relapsed neuroblastoma (NCT02030964).

- Peer Reviewed Orthopaedic: Supported an FY 2011 award that enabled development of the Force Limiting Auto Grasp (FLAG) for use in upper extremity prosthetic devices. FLAG is a two component system that 1) limits pinch force of the terminal device when desired, and 2) has an auto grasp that detects socket slip and automatically increases grip force to compensate. FLAG is now available in the Motion Control Electric Terminal Device and the Motion Control Hand.
- Prostate Cancer: Supported an FY 2002 study which demonstrated that inhibition of the protein RANKL blocks progression of prostate cancer bone metastases in an animal model. This study led to FDA approval for denosumab as a treatment for cancer-related bone loss, and standard of care treatment for osteoporosis (PROLIA®) and cancer (XGEVA®).
- Psychological Health and Traumatic Brain Injury: Supported an FY 2007 pilot study to develop and evaluate a brief cognitive-behavioral therapy (CBT) protocol for treating post-traumatic stress disorder (PTSD). The results of this study led to a current randomized, controlled clinical trial of CBT in Service members and veterans from Operation IRAQI FREEDOM and Operation ENDURING FREEDOM with PTSD symptoms.
- Spinal Cord Injury: Supported an FY 2009 study showing that high Schwann cell concentrations are effective in treating spinal cord injury in an animal model. This led to initiation of a Phase I clinical trial of Schwann cell therapy for sub-acute treatment of spinal cord injury.
- Tuberous Sclerosis Complex (TSC): Supported an FY 2006 study investigating the role of the mTOR signaling network in TSC. A landmark discovery that mTORC1 signaling regulates TSC led to subsequent clinical trials, resulting in the first drug approved by the FDA specifically for the treatment of TSC.

The above-mentioned research represents only a small portion of the clinical products or approaches that have arisen from basic and applied research supported by the CDMRP, and have made, or have the potential to make, a significant clinical impact. Notably, these advancements demonstrate the time it takes to move a discovery from basic or pre-clinical testing to clinical trials and underscore the importance of encouraging and funding high risk, innovative research ideas.

MAKING PROGRESS THROUGH CLINICAL TRIALS

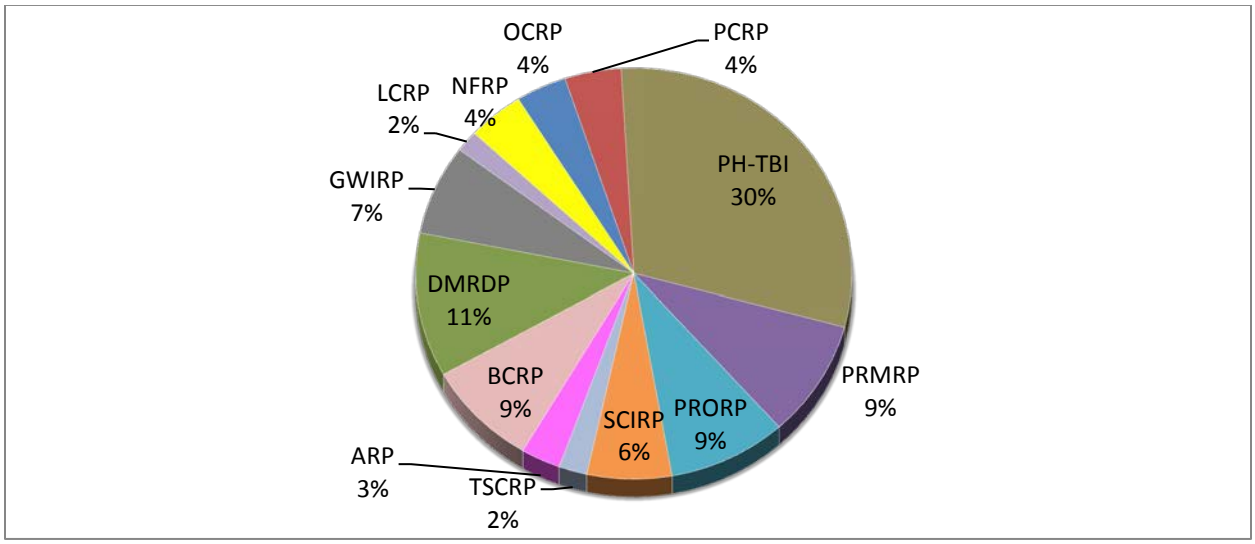
Another aspect of the CDMRP's research portfolio that demonstrates commitment to making clinical improvements is the significant funding invested in clinical trials. As of July 10, 2015, 233 clinical trials are being funded in active or pending awards across the 19 programs that are the subject of this report. While the number of active awards with clinical trials represents 9% of the total number of awards in these programs, notably the percent of funding invested in active awards with clinical trials represents 25% of the total investments. The types of clinical trials include, among others, innovative detection

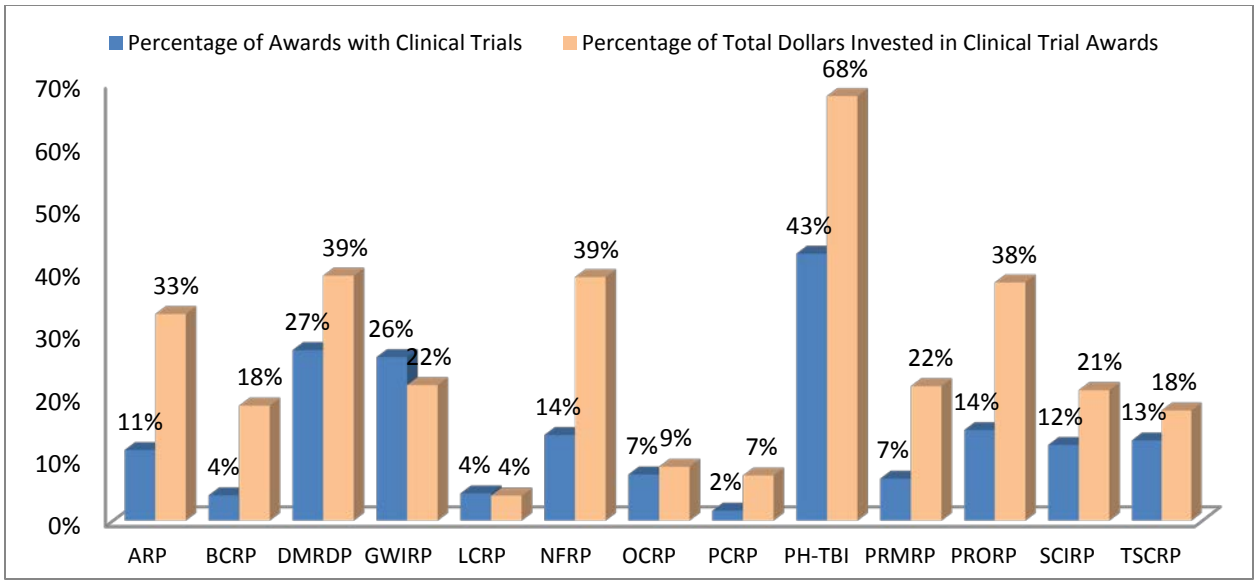
Advanced research supporting clinical trials constitutes a significant portion of the CDMRP's research and funding investments.

methods, novel cognitive treatments, vaccines and immunotherapies, physical therapies, and therapeutic drug interventions.

As shown in Figure 1, nearly one-third of the clinical trials are being supported by the Psychological Health and Traumatic Brain Injury (PH-TBI) Research Program, while the other clinical trials are distributed across twelve different programs. The bar graph in Figure 1 depicts the program-specific data on the percentage of awards and dollars invested in clinical trials within each program's current research award portfolio. The dollars invested in clinical trials represent as much as 68% of the current research portfolios of these CDMRP programs. Taken together, these data demonstrate that advanced research supporting clinical trials constitutes a significant portion of the CDMRP's research and funding investments.

Figure 1. Distribution of CDMRP's Active Awards with Clinical Trials, by Research Program





SUMMARY

Research programs managed by the CDMRP establish an annual investment strategy that targets the type of research that not only will meet each program's vision and goals, but fills gaps in the research field and funding landscape. The CDMRP's programs are able to shift the focus of their award mechanisms as needed to target the most critical needs along the pipeline of translating basic research to the clinic**.** Translational research is a high priority of the CDMRP, as evidenced by the funding mechanisms which seek translational research projects in applied and combination research, as well as the significant funding invested in these translational research categories. Moreover, with about one-quarter of the CDMRP's current investments in awards that include a clinical trial, it is clear that supporting advanced research is also a priority of the CDMRP. Importantly, many investments made in basic or applied research projects have successfully achieved advanced development and are now clinical standards of care, resources, or products benefiting patients or the research field. By enabling funding of high-gain research efforts in all phases of the research pipeline, and supporting investigators that possess the passion and creativity to pursue transformative research, the outcomes of the CDMRP funded research have a high probability to continue making translational research advancements and clinical breakthroughs.

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