United States Government Accountability Office

Report to Congressional Requesters

June 2015

REGENERATIVE MEDICINE

Federal Investment, Information Sharing, and Challenges in an Evolving Field

Accessible Version

GAO-15-553

GAO Highlights

Highlights of GAO-15-553, a report to congressional requesters

June 2015

REGENERATIVE MEDICINE

Federal Investment, Information Sharing, and Challenges in an Evolving Field

Why GAO Did This Study

Regenerative medicine is an interdisciplinary field with a focus on conducting research and developing treatments for a vast assortment of previously untreatable diseases and conditions through self-healing—a process by which the body uses its own systems to recreate cells and rebuild tissues and organs.

GAO was asked to review the federal involvement in this field. This report describes (1) which federal agencies conducted or funded regenerative medicine research in recent years and how these agencies invested their resources; (2) the activities these federal agencies undertake to share information across agencies; and (3) the challenges to advancing the field of regenerative medicine identified by federal agencies and other stakeholders and the steps taken, if any, to address them.

GAO analyzed funding data from seven federal agencies active in regenerative medicine research in fiscal years 2012 through 2014, the 3 most recent years for which full funding data were available; reviewed agency documents, including reports and strategic plans, and an interagency working group's meeting agendas and minutes. GAO also interviewed officials from the seven agencies, as well as nonfederal stakeholders, representing academic and state-funded research institutions, patient advocacy groups, and trade organizations.

In commenting on a draft of this report, the federal agencies that conduct, fund, or otherwise play a role in regenerative medicine research provided technical comments, which GAO incorporated where appropriate.

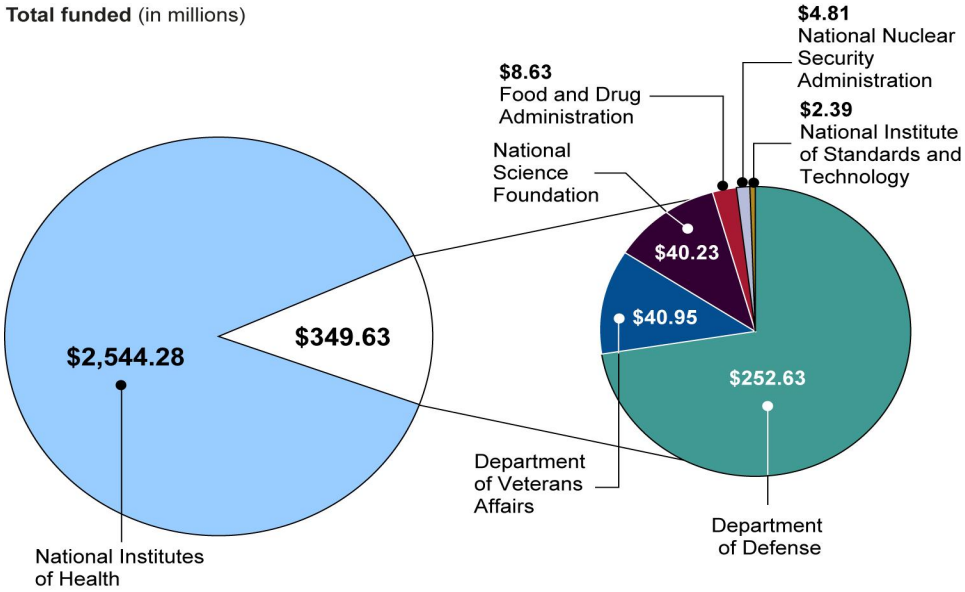
View GAO-15-553. For more information, contact Marcia Crosse at (202) 512-7114 or crossem@gao.gov.

What GAO Found

Seven federal agencies invested—that is, conducted or funded—approximately $2.89 billion in regenerative medicine research in fiscal years 2012 through 2014. Most (88 percent) was invested by the National Institutes of Health. Agencies funded research related to their missions, including basic research to enhance general scientific knowledge, clinical research to move scientific discoveries into practical applications, and research to develop regulatory science.

Federal Funding for Regenerative Medicine Research, Fiscal Years 2012 through 2014

Total funded (in millions)



Source: GAO analysis of agency funding on regenerative medicine research. | GAO-15-553

These agencies have established mechanisms for sharing information on the wide array of research they fund. These mechanisms include participating in regular meetings of an interagency working group, cofunding research, and cosponsoring workshops. Although some nonfederal stakeholders expressed a desire for greater coordination of federal regenerative medicine activities, agency officials reported that the current approach to sharing information is appropriate given the diverse missions of the agencies involved, the broad range of research conducted in this field, and the variety of diseases and conditions that may benefit from new discoveries.

Agency officials and nonfederal stakeholders have identified a variety of challenges in advancing regenerative medicine. These include establishing effective collaborations between federal and nonfederal stakeholders; recruiting scientists versed in regenerative medicine to become federal employees; navigating the regulatory review and product approval process; and making decisions about Medicare coverage and reimbursement rates, mechanisms, and processes for newly approved products. Some steps have been taken to address these challenges, including recruiting postdoctoral fellows and providing training for them specifically to build the needed mix of interdisciplinary skills for research in regenerative medicine to address workforce challenges.

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Abbreviations

AFIRM	Armed Forces Institute of Regenerative Medicine
CMS	Centers for Medicare & Medicaid Services
DOD	Department of Defense
FDA	Food and Drug Administration
HHS	Department of Health and Human Services
MATES	Multi-Agency Tissue Engineering Sciences Interagency Working Group
NIH	National Institutes of Health
NIST	National Institute of Standards and Technology
NNSA	National Nuclear Security Administration
NSF	National Science Foundation
VA	Department of Veterans Affairs

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U.S. GOVERNMENT ACCOUNTABILITY OFFICE
441 G St. N.W.
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June 23, 2015

Congressional Requesters

Regenerative medicine is an interdisciplinary field with a focus on conducting research and developing treatments for a wide range of previously untreatable diseases and conditions through self-healing—a process by which the body uses its own systems to reprogram cells and rebuild tissues and organs. Regenerative medicine has been proposed as an approach to treat a vast array of diseases and conditions, including diabetes, heart disease, renal failure, Parkinson's disease, osteoporosis, limb loss, burn damage, and spinal cord injuries. Virtually any disease that results from malfunctioning, damaged, or failing tissues may be potentially cured through regenerative medicine treatments. While there are some regenerative medicine treatments that are currently being used—such as tissue-engineered products used to heal wounds and to induce bone and connective tissue growth and replace damaged cartilage—this area of science may yield many more products in the future.

The federal government has had a long-standing interest in regenerative medicine. In 2000, the White House Office of Science and Technology Policy established the Multi-Agency Tissue Engineering Sciences Interagency Working Group (MATES)—a forum for member agencies to exchange information and collaborate on issues related to tissue engineering and regenerative medicine. In 2005, the Department of Health and Human Services (HHS) published *2020: A New Vision—A Future for Regenerative Medicine*, which encouraged the federal government to play a direct role in advancing regenerative medicine. In 2007, in part to address the HHS report, MATES issued a multiagency strategic plan outlining opportunities for federal agencies to advance the field of regenerative medicine.[1]

You asked us to study current federal activities that impact the field of regenerative medicine. This report focuses on these activities and

[1]Multi-Agency Tissue Engineering Sciences Interagency Working Group, *Advancing Tissue Science and Engineering: A Foundation for the Future and A Multi-Agency Strategic Plan* (Washington, D.C.: June 2007).

describes (1) which federal agencies conducted or funded regenerative medicine research in recent years and how these agencies invested their resources; (2) the activities these federal agencies undertake to share information across agencies; and (3) the challenges to advancing the field of regenerative medicine identified by federal agencies and other stakeholders, and the steps taken, if any, to address them.

To describe which federal agencies conducted or funded regenerative medicine research and how these agencies invested their resources, we reviewed federal documentation on regenerative medicine, such as the MATES website and strategic plan and the HHS report. We contacted all federal agencies that were listed on the MATES website to determine if they had conducted or funded regenerative medicine research from fiscal years 2012 through 2014, the 3 most recent years for which full funding data were available. For the agencies that had conducted or funded regenerative medicine research during this time frame, we interviewed agency officials and reviewed relevant agency reports to determine their activities in regenerative medicine. We also analyzed funding data for regenerative medicine research during this period, which agencies provided to us or we obtained from publicly available databases. We used a standard definition of regenerative medicine—to include research on tissue engineering, stem cells, and cell and gene therapies—which we discussed with each federal agency. We assessed the reliability of data from each agency by reviewing related documentation, performing data reliability checks (such as examining the data for missing values), and interviewing agency officials. After taking these steps, we determined that the data we used were sufficiently reliable for our purposes.

To describe the activities federal agencies that have conducted or funded regenerative medicine research undertake to share information across agencies, we reviewed reports and other relevant documentation from these agencies. We also reviewed the strategic plan, agendas, and meeting minutes for MATES from fiscal years 2012 through 2014 and interviewed agency officials about their information sharing activities. Evaluating the effectiveness of these information sharing activities was not within the scope of our review.

To describe the challenges that federal agencies and other stakeholders in regenerative medicine research have identified and what steps, if any, have been taken to address them, we interviewed agency officials from those agencies that conducted or funded regenerative medicine research in fiscal years 2012 through 2014. We also sought to obtain input from a variety of knowledgeable nonfederal stakeholders, including those

representing academic and state funded or supported research institutions, such as the California Institute of Regenerative Medicine, University of Washington Institute for Stem Cells and Regenerative Medicine, and Wake Forest Institute for Regenerative Medicine. We also interviewed representatives from patient advocacy groups, such as the Genetics Policy Institute and the Parkinson's Action Network, and trade organizations—the Alliance for Regenerative Medicine and the Regenerative Medicine Foundation. We identified these nonfederal stakeholders from a literature review and by asking the nonfederal stakeholders we interviewed to provide referrals to others knowledgeable about regenerative medicine.

We conducted this performance audit from July 2014 to June 2015 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Background

Regenerative medicine offers the possibility of new and highly individualized treatments for a variety of diseases and conditions; scientists believe that the promise of regenerative medicine is to provide cures for virtually any disease that results from malfunctioning, damaged, or failing tissues. Regenerative medicine incorporates self-healing—where the body uses its own systems, sometimes with help from added biological material from outside the body—to reprogram cells or rebuild organs. Scientists are working in the field of regenerative medicine to develop products that could help manage many pressing problems in health care. For example, a shortage of organ donors means many people die while waiting for an organ transplant; however, scientists are pursuing ways for organs to be restored by using therapies to regenerate the cells of the organ itself or applying tissue engineering strategies to grow a replacement organ outside of the body for transplantation. Similarly, the steady increase of diabetes in the population could result in more patients seeking treatment for complications from that disease. Scientists are exploring techniques to foster regeneration of pancreatic cells, which could help address the cause of diabetes—inadequate insulin secretion. Discoveries from regenerative medicine research might be used to treat patients of all ages. For example, work done with engineered heart cells could lead to discoveries for pediatric patients who suffer from congenital heart defects, as well as adult patients with

damage caused by heart disease. Regenerative medicine might also lead to treatments for people with limb loss or damage and severe burns. Scientists are working to find ways to improve bone restoration to reduce the pain, bleeding, and scars created through current bone harvesting techniques, as well as developing a system to decrease the amount of skin that would need to be harvested to treat a burn patient.

In order to develop products for a broad range of conditions and diseases, regenerative medicine brings together a wide variety of scientific disciplines—including biology, chemistry, engineering, and physics—to advance knowledge and conceive new clinical applications. Regenerative medicine research encompasses the use of the following:

- **Tissue engineering**. This includes the practice of combining cells, biologically active molecules, and scaffolds—which support the tissue growth—into functional tissues. The goal of tissue engineering is to restore, maintain, or improve damaged tissues or whole organs. Scientists may develop tissues using a patient's own cells, which can reduce the possibility of infection or tissue rejection. According to the National Institutes of Health (NIH), an agency within HHS, tissue engineering currently plays a relatively small role in patient treatment, although bladders, small arteries, skin grafts, cartilage, and even a full trachea have been implanted in patients. Work in the field of tissue engineering has resulted in skin and cartilage products, which contain cells grown in tissue cultures outside of the patient, that have been approved by the Food and Drug Administration (FDA), another agency within HHS.
- **Stem cells**. Cells are the building blocks of regenerative medicine research. Scientists must first understand and control the cells that make up tissues in the body in order to build tissues. Stem cell research can contribute to the understanding of how cells form different tissues. Stem cells are unique in that they are pluripotent—they can self-renew or be developed into many different cell types in the body, such as a muscle cell, a red blood cell, or a brain cell. According to NIH, there are many ways to categorize stem cells. One system, which takes into account the source of the original cell, divides stem cells into two kinds: embryonic stem cells— which have the ability to form potentially any cell type that makes up the body—and nonembryonic "somatic" or "adult" stem cells—which are found within existing tissues and organs and can form some or all of the cell

types to maintain and repair the tissue or organ in which they are found.[2] Scientists also work with induced pluripotent stem cells—adult cells that have been genetically reprogrammed to an embryonic stem cell–like state.

- **Gene or cell therapies**. These therapies are considered regenerative medicine products and can result from stem cell research. Gene therapy and cell therapy aim to repair the direct cause of genetic diseases in the DNA or cells by modifying individual genes or cell populations for the treatment of a disease. FDA has approved some cell therapies for use, such as one to repair cartilage damage, through cell biopsy and reimplantation.[3]

Given the diverse scientific disciplines involved in this research and the array of diseases and conditions it may impact, stakeholders must employ multiple approaches for developing regenerative medicine products. For example, these approaches include using 3D printers to create experimental muscle tissue for reconstructive surgery or to create a skin equivalent that can be used for burn wounds; infusing cells from donated human cord blood to treat patients with blood disorders; and developing composite bone scaffolds—structures to support bone regeneration. There is a consensus that regenerative medicine may be defined as the development of products to repair or replace human cells, tissue, or organ function lost due to age, disease, damage, or congenital defects.

[2]There have been limitations on the use of federal funds for research on human embryonic stem cells since 1996. Over time, some of these limitations have changed. Most recently, in 2009, in response to an Executive Order, NIH issued new guidelines for conducting embryonic stem cell research and subsequently created a registry of human embryonic stem cell lines that are eligible for use in federally funded research. Exec. Order No. 13,505. 74 *Fed. Reg*. 10667 (Mar. 9, 2009).

[3]Drugs, medical devices, and biologics are subject to a risk-based regulatory approach before they can be marketed in the United States. The level of FDA regulatory oversight is dependent on the characteristics (chemical and physical makeup) of the product and the intended use of the product. For many regenerative medicine products, the level of oversight includes premarket review to support clearance, approval, or licensure prior to marketing.

Seven Federal Agencies Conducted or Funded a Range of Regenerative Medicine Research

We identified seven federal agencies that conducted or funded regenerative medicine research in fiscal years 2012 through 2014. In addition to FDA and NIH, the Department of Commerce's National Institute of Standards and Technology (NIST), the Department of Defense (DOD), the Department of Energy's National Nuclear Security Administration (NNSA), the Department of Veterans Affairs (VA), and the National Science Foundation (NSF) conducted research on regenerative medicine during this time period.

Regenerative medicine research conducted or funded by federal agencies falls into several categories. Some agencies conduct basic research, which is designed to provide general scientific knowledge that may provide a foundation for other research related to their unique missions. One such example is developing new techniques to preserve organs and large tissues. Some conduct translational research to move laboratory-generated research into practical applications in humans and the development of best practices. Some agencies also fund clinical research, such as testing a new treatment of amyotropic lateral sclerosis, also known as Lou Gehrig's disease. In addition, certain agencies perform research focused on a specific population, such as research to develop treatments for wounded military personnel. Finally, some agencies conduct research to advance regulatory science and to develop consensus and measurement standards, for example improving measurements of certain cell characteristics.[4]

It is important to note that while agencies focus on research related to their individual missions, they may conduct research in more than one category. For example, NIH funds some research that could be considered basic research in addition to its translational and clinical research. Table 1 summarizes information regarding the efforts of the seven federal agencies that conducted or funded regenerative medicine research in fiscal years 2012 through 2014.

[4]Consensus standards are voluntary documentary standards developed by interested stakeholders, such as industry, government, and academia, using a consensus-based process; measurement standards ensure reliability and repeatability of measurements. The Office of Management and Budget establishes policies on the federal use and development of voluntary consensus standards. See Office of Management and Budget, *Federal Participation in the Development and Use of Voluntary Consensus Standards and in Conformity Assessment Activities, Circular A-119 Revised* (Washington, D.C.: Feb. 10, 1998).

Table 1: Federal Agencies That Conducted or Funded Regenerative Medicine Research, Fiscal Years 2012 through 2014

Federal agency	Agency mission	Regenerative medicine research conducted includes
Department of Defense	Provide the military forces needed to deter war and to protect the security of the country	Research and applications for active-duty personnel including limb repair, traumatic brain injury, and battlefield injuries
Department of Veterans Affairs	Provide veterans and eligible beneficiaries with benefits and services	Research and applications for the veteran population, including limb repair, traumatic brain injury, and care for wounded warriors, as well as for stroke, glaucoma, and other conditions for an aging veteran population
Food and Drug Administration within the Department of Health and Human Services	Protect the public health by ensuring the safety, efficacy, and security of human drugs, biological products, medical devices, food supply, cosmetics, and products that emit radiation	Safety and effectiveness research related to regulation of regenerative medicine products and standards development
National Institute of Standards and Technology within the Department of Commerce	Promote innovation and industrial competitiveness by advancing measurement science, standards, and technology	Measurement science and development of consensus documentary standards and standard reference materials to facilitate commercialization of regenerative medicine products [Note A]
National Institutes of Health within the Department of Health and Human Services	Seek knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability	Biomedical applications and basic, clinical, and translational research, including stem cells and tissue engineering
National Nuclear Security Administration within the Department of Energy	Enhance national security through the military application of nuclear science; responsible for issues of nuclear defense, nonproliferation, and naval research	Research and development, including basic research and experiments designed to determine the utility of new scientific ideas, technical concepts, or devices
National Science Foundation	Promote and advance fundamental scientific progress	Basic research with a focus on expanding current scientific knowledge

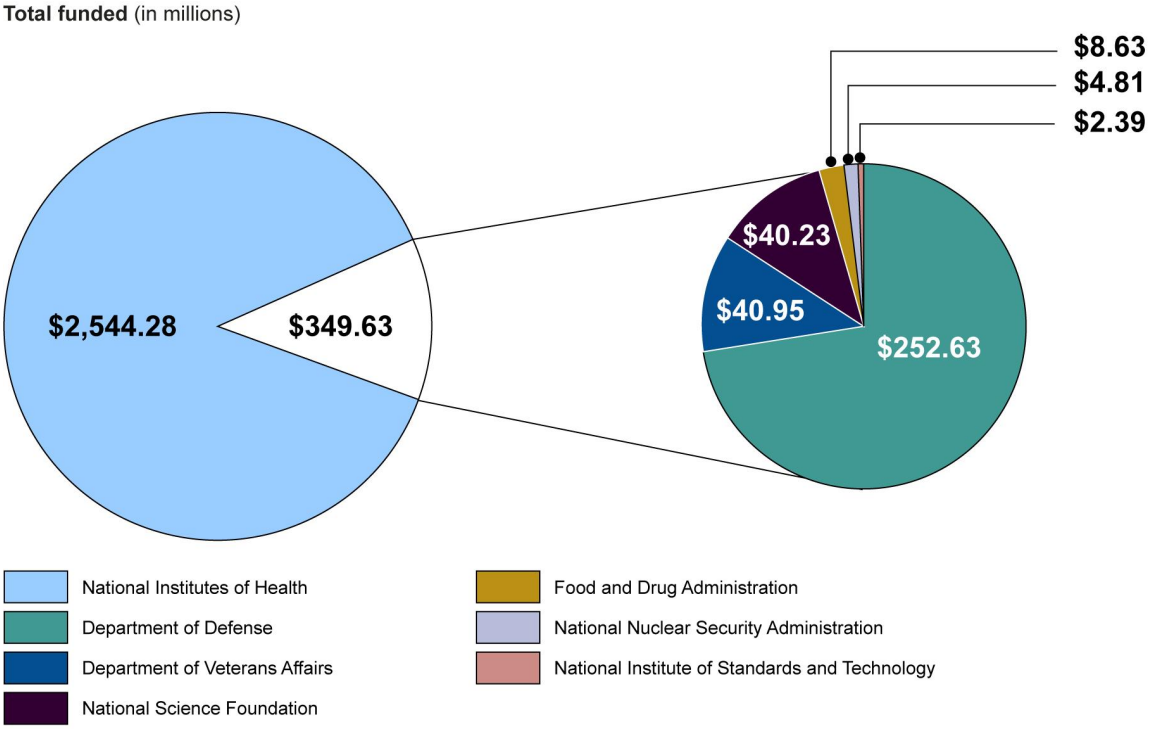
Source: GAO analysis of agency interviews and information. | GAO-15-553

Note A: Consensus standards are voluntary documentary standards developed by interested stakeholders, such as industry, government, and academia, using a consensus-based process; measurement standards ensure reliability and repeatability of measurements.

Federal funding for regenerative medicine varies considerably among these seven federal agencies. They have invested a total of approximately $2.89 billion in regenerative medicine research from fiscal years 2012 through 2014, 88 percent of which was invested by NIH, as

shown in figure 1. The agencies' funding ranged from $2.39 million funded by NIST to $2.54 billion funded by NIH during this period.[5]

Figure 1: Federal Funding for Regenerative Medicine Research, Fiscal Years 2012 through 2014



Source: GAO analysis of agency funding on regenerative medicine research. | GAO-15-553

Note: For purposes of this report, we use the term "funding" to refer to obligations. An obligation is a definite commitment that creates a legal liability of the federal government for payment of goods and services ordered or received. A federal agency incurs an obligation, for example, when it awards a grant.

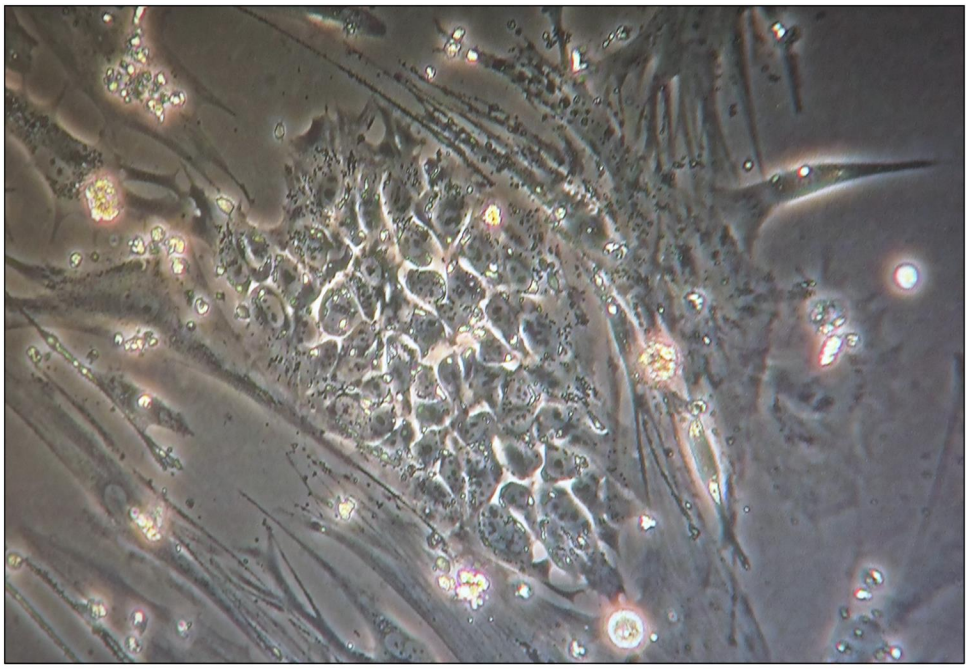
[5]NSF collects and makes publicly available its research funding data; however, the agency does not routinely categorize its awards and projects as regenerative medicine research. This information can be obtained through a search of award abstracts on its publicly-available database of research projects. To generate a list of NSF regenerative medicine awards, we searched this database and asked NSF to review our findings. In some instances, we identified research efforts that included applications relevant to regenerative medicine, even though this may not have been the purpose of the study. NSF officials did not always agree that a project should be categorized as related to regenerative medicine. They emphasized that the agency's mission is to conduct basic research, not research for a particular disease, condition, or treatment type. However, based on our definition of regenerative medicine research, we included these research efforts in the total reflected for NSF.

NIH, which funds basic, translational, and clinical research, made the largest investment in regenerative medicine during this period. Its $2.54 billion resulted in about 2,400 awards per year from fiscal years 2012 through 2014. Over 80 percent of NIH's overall research funding goes to extramural research, which supports scientists and research personnel working at universities, medical schools, and other research institutions; however, it also funds intramural research—that is, research performed by NIH scientists in NIH laboratories. Within NIH, 22 of its 27 institutes and centers, which are focused on particular diseases, conditions, or research approaches, funded some regenerative medicine research, demonstrating the breadth of the field. In addition, funding for regenerative medicine research came from the Office of the Director and the NIH Common Fund.[6] The single biggest investment in NIH's regenerative medicine research was from its National Heart, Lung, and Blood Institute, which is responsible for about 24 percent of NIH's regenerative medicine funding in this time period. One example of research funded by this institute is a project that tests the effectiveness of a new technique for developing engineered heart cells for cardiac regeneration and restoration of vascular function. Figure 2 shows a colony of pluripotent stem cells that could be used for the development of engineered heart cells. Following the National Heart, Lung, and Blood Institute, the next largest investments in regenerative medicine research from NIH came from the National Institute of Diabetes and Digestive and Kidney Diseases, the National Cancer Institute, and the National Institute of Neurological Disorders and Stroke, having each funded over $200 million in research for fiscal years 2012 through 2014. NIH's investments by these institutes further illustrate the broad range of conditions and diseases being studied within the field of regenerative medicine. Examples of the research conducted by these institutes include work to develop transplantable liver grafts for curing or treating liver dysfunction and failure, develop novel strategies to treat a variety of cancers through stem cell transplantation, and determine the extent to which cell grafts can improve recovery in stroke patients. (See app. I for

[6]The Office of the Director is responsible for coordinating some programs and activities that span NIH components, particularly research initiatives and issues involving more than one of the institutes or centers. The NIH Common Fund, formerly the NIH Roadmap for Medical Research, is a series of initiatives designed to speed the movement of scientific discoveries. According to NIH, it provides a framework of the priorities the NIH must address in order to optimize its entire research portfolio and lays out a vision for a more efficient and productive system of medical research.

more details on NIH's funding for regenerative medicine by institute or center from fiscal year 2012 through fiscal year 2014.)

Figure 2: A Colony of Human Pluripotent Stem Cells That Could Be Used to Create Engineered Heart Muscle Cells



Source: GAO. | GAO-15-553

Note: The colony of cells was produced through the National Institutes of Health-funded research at the University of Washington Institute for Stem Cell and Regenerative Medicine.

DOD is the second largest funder of regenerative medicine research, and its investment in regenerative medicine research totaled almost $253 million, or about 9 percent of the total federal investment in regenerative medicine, in fiscal years 2012 through 2014.[7] DOD funded approximately 178 projects focused on the health needs of active-duty military personnel. Within DOD, the Defense Health Program is the largest funder of regenerative medicine research, having invested more

[7]Although DOD's research efforts are led by individual components within the department, all of its research is focused on active-duty personnel. As a result, we have chosen to report DOD activities at the department level.

than $120 million in fiscal years 2012 through 2014.[8] The Defense Health Program funds a variety of projects, including research on regeneration of cochlear hair cells—damaged through loud noises and blasts—to aid in hearing restoration. After the Defense Health Program, the Office of Naval Research and the U.S. Army are the next largest funders within DOD, each having invested over $42 million. During fiscal years 2012 through 2014, the U.S. Army, the Defense Health Program, and the Office of Naval Research invested in the Armed Forces Institute of Regenerative Medicine (AFIRM).[9] AFIRM in turn awarded $42.66 million in funding for regenerative medicine research at U.S. academic institutions and private companies during this same time period. AFIRM currently supports research on topics related to developing advanced treatment options for severely wounded warriors.[10] An example of research funded by AFIRM is work focused on developing approaches to improve burn treatment (see fig. 3).

[8]The Research, Development, and Acquisition Directorate in the Defense Health Agency provides oversight of Defense Health Program funding and focuses on, among other things, advancing medical research and development for wounded warriors, expediting the delivery of products and solutions to servicemembers and their families, and advancing the state of medical science in areas of the most pressing need.

[9]AFIRM is a multi-institutional, interdisciplinary network—including U.S. Army; U.S. Navy, Office of Naval Research; U.S. Air Force; NIH; VA; and DOD—working to develop advanced treatment options for wounded servicemembers.

[10]AFIRM's research currently focuses on five specific areas: (1) extremity injury treatment to decrease the need for amputation; (2) craniomaxillofacial reconstructions to help servicemembers who have experienced massive bone and tissue loss to the face and head; (3) skin injury treatment to improve burn and wound healing; (4) vascular composite tissue allotransplantation and immunomodulation to improve and preserve the functionality and sustainability of hand, arm, and face transplants; and (5) repair and reconstruction needed to treat certain genitourinary and lower abdominal injuries caused by explosions.

Figure 3: A Mannequin's Burned Forearm Being Used in DOD-Funded Armed Forces Institute of Regenerative Medicine Research to Develop Skin-Cell Printing Techniques for Burn Victims

Source: Wake Forest Institute for Regenerative Medicine. | GAO-15-553

VA, the third largest funder of federal regenerative medicine research, funded 94 regenerative medicine projects in fiscal years 2012 through 2014. According to VA, all of the research is awarded through a competitive process and takes place within the VA health care system, funding practicing clinicians who are aware of the research needs that will improve veterans' health. VA's average annual award amount was around $225,000 and was as much as $1.66 million during this time period. Among the projects VA funded was a study to develop a minimally invasive therapy that could normalize disc function in the lower back while promoting tissue regeneration using stem cells. The results of this study could impact both wounded warriors and aging veterans suffering from chronic lower back pain. Another VA research project is evaluating whether replacement of damaged cells in the eyes with induced pluripotent stem cells could help preserve vision for patients suffering from glaucoma. VA has also conducted research to reprogram blood cells into stem cells and other types of cells to rebuild injured bones and regenerate organs.

The remaining federal agencies—NSF, NNSA, FDA, and NIST—combined make up less than 2 percent of the federal investment in regenerative medicine research in fiscal years 2012 through 2014. NSF

and NNSA focus on basic research, while FDA focuses on both regulatory research and consensus standards development and NIST on standards development.

- **NSF**, which supports extramural research, funded 107 projects, totaling approximately $40.23 million, which includes basic scientific research that may have applications beyond regenerative medicine. One example of NSF-funded research includes a project designed to improve efficacy of stem cell transplantation into the brain for tissue regeneration.
- **NNSA**, which also conducts basic scientific research, undertook one project, totaling about $4.81 million, and examined increasing the biocompatibility of polymers, which could be used as implantable sensors in some regenerative medicine applications, to decrease rejection of these polymers from the body.[11]
- **FDA** scientists conduct the majority of the regenerative medicine research the agency funds, and it has invested about $8.63 million to help advance regulatory science for regenerative medicine products. For example, one such project is to develop improved methods for evaluating experimental cell-based products to reliably predict product performance.
- **NIST** conducts research to advance measurement science and standards, and it invested about $2.39 million for 8 regenerative medicine projects to advance the field. One example of NIST's work is developing statistical tests that will allow determination of the accuracy of cell counts for the development of cell therapies.

[11]NNSA officials told us the agency does not plan to conduct additional regenerative medicine research in the foreseeable future.

Agencies Have Established Mechanisms for Sharing Information on Their Diverse Investments in Regenerative Medicine Research

Agencies that have conducted or funded regenerative medicine research have established mechanisms for sharing information across agencies on the wide range of research they undertake. These information-sharing mechanisms include regular meetings of MATES and more collaborative ad hoc activities such as cofunding research and cosponsoring workshops related to regenerative medicine.[12] Given the broad range of disciplines and research missions represented by the agencies that are members in MATES, monthly meetings provide a forum for participants to stay informed about regenerative medicine research and other activities undertaken by member agencies. Six of the seven federal agencies with investments in regenerative medicine research from fiscal years 2012 through 2014 are current or former members of MATES: NIH, FDA, DOD, VA, NSF, and NIST.[13] According to meeting minutes from fiscal years 2012 through 2014, discussion topics included presentations on research conducted by MATES member agencies, updates from scientific conferences and meetings attended by MATES members, ideas for updating the 2007 MATES strategic plan,[14] and updates from attendees on current and planned regenerative medicine research.

One recent activity undertaken by MATES was a joint workshop its members coordinated as part of an international tissue engineering and regenerative medicine conference held in December 2014 in Washington, D.C. Officials noted that the goal of the event was to show how the various federal agencies supported a range of regenerative medicine activities consistent with their individual missions. Officials from MATES member agencies NSF, NIH, DOD, NIST, and FDA presented information on the regenerative medicine research conducted or funded by their agencies, demonstrating the diversity of approaches taken by each. An

[12]MATES is currently chaired by a representative from FDA. According to officials, the position of chair rotates among member agencies.

[13]Officials from NNSA told us that they do not consider their agency to be a member of MATES, although the Department of Energy remains on the membership roster on the MATES website. In addition, the Environmental Protection Agency, National Aeronautics and Space Administration, Department of Agriculture, and Centers for Medicare & Medicaid Services remain on the membership roster on the MATES website. However, these agencies are not currently members of MATES nor did they conduct or fund regenerative medicine research during fiscal years 2012 through 2014.

[14]*Advancing Tissue Science and Engineering*. As of April 2015, MATES officials told us the effort to update the plan was underway, but no draft or interim documentation on this effort was available for our analysis.

official from NSF emphasized the agency's basic research—funding novel ideas for eventual application in regenerative medicine such as fundamental studies on cells and disease modeling. An NIH official presented work the agency has funded to develop clinical trials for stem cell therapies, emphasizing its role in translational research. An official from DOD's AFIRM discussed the primary goals for the agency's investments in research focused on applications for its specific population—military personnel—such as tissue salvage, restoration, and regeneration. The NIST presentation at the workshop focused on that agency's role in performing research in measurement science for advancing technology by bringing partners together to develop standards, including measurement standards related to regenerative medicine. The presentation communicated results from NIST's partnership with a private company to develop methods for improving the measurement confidence of cell counting—a key cell attribute for research and development and quality control in bioprocessing—to facilitate product development.

Participation in MATES is voluntary and agency representatives attend as their interest and availability allows. A review of available MATES meeting minutes from fiscal years 2012 through 2014 shows regular attendance by officials from some member agencies, with less regular attendance by other participating agencies. Specifically, of the 29 meetings for which minutes were archived over the 3-year period, officials from NIH and FDA attended all 29. In addition, officials from NIST, DOD, NSF, and VA attended 21, 11, 7, and 3 meetings, respectively. Officials from agencies who attend the meetings regularly told us they believe this venue is a highly effective way to share information with colleagues across agencies.

In addition to participation in MATES, agencies engage in a range of ad hoc activities for sharing information and collaborating with one another in the area of regenerative medicine such as cofunding research, serving as advisors to each other on certain projects, and cosponsoring workshops related to regenerative medicine. For example, in 2006, three agencies—NIH, NSF, and NIST—issued the joint funding announcement, "Enabling Technologies for Tissue Engineering and Regenerative Medicine," which resulted in a diverse set of funded applications, including one for the development of an artificial liver in mice and technology to extend liver preservation. NIH and VA have cofunded research projects with DOD's AFIRM and also serve on advisory committees for its programs including on traumatic brain injury and spinal cord injury. Another example of interagency advising for regenerative medicine projects is DOD's and VA's participation as ex-officio members of NIH's National Institute of Neurological Disorders and Stroke Advisory Council, which oversees all

of that institute's activities, including regenerative medicine research. In addition, there are numerous examples of agencies collaborating on jointly held regenerative medicine workshops such as the 2012 Functional Imaging for Regenerative Medicine workshop held by NIST, in conjunction with MATES, to identify imaging needs and challenges in tissue engineering and regenerative medicine and FDA and NIH jointly held workshops in 2011 and 2012 on stem cell research, product development, and regulatory issues.

Officials from the agencies that conduct or fund regenerative medicine research reported that the current methods in place for sharing information across agencies are appropriate given the diverse missions of the agencies involved, the broad range and type of research conducted and funded in this field, and the variety of diseases and conditions that may benefit from new discoveries. Some officials reported that there are benefits to the federal government's decentralized approach to not only sharing information, but also to conducting and funding this research. For example, some officials we spoke with said the decentralized nature of regenerative medicine activities generates diversity of thought in regenerative medicine studies and allows agencies the flexibility to make their own plans and priorities for advancing the field according to each agency's mission. In addition, it allows the research and science to progress on multiple fronts simultaneously, according to each agency's expertise. Further, some officials told us that a more formalized approach to information sharing and collaboration across agencies that added bureaucracy—such as a requirement to have certain information cleared through formal channels which may slow communication—could inhibit the flow of information rather than enhance it.

In contrast to the current approach to information sharing and coordination across federal agencies, some nonfederal stakeholders we spoke with expressed a desire for greater coordination of federal regenerative medicine activities with the hope that more focused attention in this area could attract more resources and faster advancement in the field. For example, an official from one nonfederal stakeholder group suggested that a statement of commitment from the federal government to a given set of regenerative medicine priorities could help to invigorate the field and encourage greater support for the research. An official from another nonfederal stakeholder group told us that the organization encourages a national strategy for regenerative medicine research as a means to enhance information sharing across agencies, ensure the research funding allocated to this field is used wisely, speed the development of new regenerative medicine products, and keep the United

States at the forefront of innovations in this field. However, these organizations did not provide any specific examples of how the current level of coordination among federal agencies has prevented a specific regenerative medicine therapy from reaching patients or otherwise had a negative effect on the field.

Agency Officials and Other Stakeholders Have Identified Challenges in Advancing the Field of Regenerative Medicine and Have Taken Some Steps to Address Them

Agency officials and nonfederal stakeholders have identified a range of challenges impacting the field of regenerative medicine. Specifically, they noted challenges with establishing effective collaboration mechanisms between federal and nonfederal stakeholders; finding qualified scientists versed in regenerative medicine and recruiting them to become federal employees; navigating the regulatory review process when seeking FDA approval of a new product; and setting payment policies and Medicare reimbursement mechanisms, processes, and rates for FDA-approved regenerative medicine products. In some cases, federal and nonfederal stakeholders have found strategies for addressing these challenges.

Federal collaboration with nonfederal stakeholders. Officials from three of the seven agencies we spoke with that conducted or funded regenerative medicine research in fiscal years 2012 through 2014, as well as representatives from some nonfederal stakeholder groups we interviewed, noted it is challenging for federal agencies to collaborate with nonfederal entities. Although some agencies described mechanisms they can use—such as memoranda of understanding or other formal agreements—to collaborate with individual nonfederal entities,[15] some officials and representatives from nonfederal stakeholder groups pointed out that there is no systematic mechanism for federal agencies to collaborate with nonfederal entities that may also be conducting or funding regenerative medicine research, such as state-funded research institutions and private foundations. Some officials noted that stronger relationships and communication among federal and nonfederal stakeholders could help federal agencies stay informed about nonfederal research and help ensure the best use of those agencies' investments in research in the field. Officials from one agency noted that interacting with

[15]For example, NIH officials noted that they can and do form public-private partnerships and establish memoranda of understanding with nonfederal research organizations to accomplish specific research goals on an as-needed basis. In addition, officials said they can use public workshops and conference calls to discuss items of mutual interest with a foundation or industry partner.

officials from state-funded research institutions and foundations at national meetings and conferences helps to build relationships that allow federal officials to stay connected to the work happening outside of the federal sector. Officials from multiple agencies cited recent restrictions on travel to, and therefore, reduced attendance at, scientific meetings and conferences as a barrier to their work in regenerative medicine. They told us that their previous conference participation allowed them to maintain connections to the wider scientific community.[16]

To address this challenge, agency officials said they try to make the most of the very limited travel opportunities they have, while largely relying on their personal and professional relationships and networks to stay informed about relevant nonfederal funding and program updates. To increase their opportunities for maintaining connections to nonfederal stakeholders, FDA officials said they try to persuade conference organizers to hold meetings in the Washington, D.C., area where many federal scientists are employed, so that limited travel funds can be preserved. For example, FDA officials noted that MATES was able to present its December 2014 joint workshop as part of an international tissue engineering and regenerative medicine conference when conference organizers agreed to hold the event in Washington, D.C. Officials from FDA also suggested that convening a group of regenerative medicine stakeholders from across the federal government, industry, and academia to discuss progress in the field and opportunities for collaboration across stakeholder groups could be a valuable endeavor. To that end, FDA is discussing the possibility of holding a forum for stakeholders with the Institute of Medicine to discuss topics ranging from the state of the science to commercialization of regenerative medicine products. Officials noted that other federal agencies would be welcome in

[16]We recently reported that for those working in defense science and technology, conference participation can promote communication with peers in other U.S. agencies and academia, as well as those from other countries. In addition, this communication helps to provide leadership across an array of individual technical fields, ensure the technical quality of research, and recruit new scientists and engineers to work for the federal government. DOD and Department of Energy officials have identified risks associated with reduced conference participation including a potential decline in the quality of scientific research, difficulty in recruiting and retaining qualified scientists and engineers, and a diminished leadership role for both agencies within the global science and technology community. See GAO, *Defense Science and Technology: Further DOD and DOE Actions Needed to Provide Timely Conference Decisions and Analyze Risks from Changes in Participation,* GAO-15-278 (Washington, D.C.: Mar. 4, 2015).

such a forum that would also include leaders in the field from academia and industry.

Federal regenerative medicine workforce. According to federal officials we interviewed from two agencies, attracting and hiring researchers with the appropriate expertise is challenging, given that the field changes very rapidly and the federal hiring system can move slowly. In addition, some officials noted that finding researchers with suitable interdisciplinary expertise is difficult. Also, an official at one agency told us that there may be a belief among some scientists that the federal government is not supportive of stem cell-related research. To address workforce challenges, officials from two agencies have recruited postdoctoral fellows and provided training for them specifically to build the needed mix of interdisciplinary skills. Officials from one agency noted that high profile fellowships can also serve to highlight interagency collaborations that could enhance staff members' knowledge and expertise. They suggested that postdoctoral fellowships such as one that existed in the past between NIH and NIST that allow scientists to work across agencies could be focused on regenerative medicine to build expertise in this area of research. Officials from one agency said they have recruited postdoctoral fellows to work in regenerative medicine through the National Research Council Postdoctoral Fellowship Program. In 2008, FDA initiated a multicenter fellowship in regenerative medicine to bring in scientists with advanced degrees to enhance multidisciplinary training within the agency. This fellowship provides the opportunity for collaboration between FDA's Center for Biologics Evaluation and Research and its Center for Devices and Radiological Health. Though the exact number of fellows varies based on budget and availability of projects, officials noted there are typically two to six fellows at a time who actively participate in the regulation of devices and biologics. According to FDA, the agency often hires these fellows into permanent positions after their fellowships end, which enables FDA to enhance its staff with additional individuals who are cross-trained in devices and biologics—a helpful skill set for reviewing regenerative medicine products. FDA officials also noted that fellows who have gone on to scientific careers outside of the FDA add value to the field of regenerative medicine because of their familiarity with FDA regulatory processes and the interdisciplinary training their fellowships provided. One official noted he was encouraged by a growing recognition among universities and industry of the importance of interdisciplinary approaches and training for this field.

Regulatory review process. Some nonfederal stakeholders and officials from one agency we spoke with said that, because regenerative medicine products may be highly individualized treatments and do not conform to a single type of therapy, obtaining FDA approval for them may be challenging. FDA maintains discrete pathways for each product type—drugs, devices, biological products, and combination products—that sponsors of new medical products, including regenerative medicine products, must follow to obtain FDA approval.[17] According to FDA, some stakeholders advocate for a separate FDA approval pathway for regenerative medicine products, noting that, for one thing, they are different from drugs because they typically are not distributed throughout the entire body and are also different from devices. One stakeholder we interviewed noted that the combination product pathway is difficult to navigate for regenerative medicine products because it requires meeting the criteria and requirements for multiple review pathways, for example, for both drugs and devices, instead of just one. In addition, nonfederal stakeholders identified as a challenge the time and expense of successfully shepherding a product through the review process and gaining approval for it. They raised concerns that these characteristics of the current regulatory system may create a disincentive for product sponsors to bring regenerative medicine products to market in the United States. Stakeholders noted that this particular challenge is significant; however, it is not unique to regenerative medicine. For example, we previously reported that, on average, drug sponsors can spend over 13 years studying the benefits and risks of a new compound and several hundred million dollars completing these studies before seeking FDA's approval of a new drug application.[18] Only about 1 out of every 10,000 chemical compounds initially tested for their potential as new medicines is found safe and effective, and eventually approved by FDA, making the drug discovery and development process complex, time consuming, and costly.

[17]Among other things, a combination product is one that comprises two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity.

[18]See GAO, *New Drug Development: Science, Business, Regulatory, and Intellectual Property Issues Cited as Hampering Drug Development Efforts*, GAO-07-49 (Washington, D.C.: Nov. 17, 2006).

FDA officials counter that developing a new regulatory review pathway for regenerative medicine products would require that a legal definition for regenerative medicine be established. However, these officials added that development of such a pathway is unnecessary because the agency has an adequate understanding of the science behind regenerative medicine and has instituted a sound process for reviewing product applications and regulating these products through existing pathways. FDA officials said that, as of April 2015, the agency had approved 14 regenerative medicine products, for uses including the repair or regeneration of skin and cartilage.[19] They explained that these products were approved through the existing pathways for biological products or devices, with some approved by both pathways as combination products. In addition, they said there are many more regenerative medicine products in earlier phases of FDA's review process. FDA officials said that one way they plan for the review of new regenerative medicine products is by meeting with potential product sponsors before an application is submitted. Such sponsor-initiated meetings can be as informal as a sponsor calling FDA to discuss ideas and seek advice for future applications, or through more formal, documented meetings, sometimes years before they intend to submit an application. FDA officials said they archive general information from these meetings, such as the type of product and a sponsor's anticipated time frame for submitting an application for review, which can be helpful for the agency when determining its needs for staff and scientific expertise.

Related to FDA's review process, officials from two agencies cited as a challenge FDA's restrictions on sharing certain information gained from its product reviews about the fruitfulness of particular avenues of research. Officials from these two agencies said that finding mechanisms by which FDA can share its knowledge of sponsors' challenges without disclosing proprietary information would be helpful. Further, they noted that this information may be valuable for other agencies for prioritizing and funding research. For example, officials at NIST said they would like to help develop measurement standards for regenerative medicine products, and FDA is in a unique position to identify trends seen across similar types of

[19]FDA officials noted that there are perhaps hundreds more that could be considered regenerative medicine products if one expanded the definition to include products regulated as tissues and certain types of devices. In terms of its regulation of biologics products, FDA makes a distinction between cellular therapy products, such as cellular immunotherapies, and tissue products, such as bone and ligaments.

products that may help suggest what standards should be priorities for development. However, FDA officials stated that FDA cannot disclose measurement information to NIST if it constitutes a trade secret or confidential commercial information—for example, a measurement protocol that may offer a competitive advantage.[20] FDA generally does not disclose any information about the status or contents of an application submitted to the agency until the product has been approved. FDA may share some limited information with other federal agencies when an established memorandum of understanding specifies the information to be shared. FDA officials said that limitations on sharing information with other agencies and stakeholders are always an issue for FDA and that this is not a challenge unique to regenerative medicine. Officials from FDA said that, although they limit the information they share on specific product applications, sponsors of products in review at FDA are free to invite others to the meetings and discussions they hold with FDA.

Setting payment policies for regenerative medicine products. Officials from one agency and other stakeholders raised concerns that the Centers for Medicare & Medicaid Services (CMS) is not planning sufficiently for the availability of future regenerative medicine products following FDA approval, when CMS will need to consider setting Medicare payment policies.[21] Officials from one agency cited CMS's lack of involvement in MATES and engagement in the field of regenerative medicine in general as a reason for concern that CMS may not have a good sense of the types of regenerative medicine products being developed and the time frames for when those products might arrive on the market.

CMS officials countered this criticism by pointing out that although the agency does not have any unique policies or procedures for making coverage determinations for regenerative medicine products overall, it has made national coverage determinations on regenerative medicine products, such as stem cell transplants.[22] CMS officials explained that for

[20]See 18 U.S.C. § 1905, 21 U.S.C. § 331(j).

[21]The proceedings from GAO's 2007 forum on the future of the U.S. health care system note that federal payment models have had a strong influence on private payers. See GAO, *Highlights of a Forum: Health Care 20 Years From Now—Taking Steps Today to Meet Tomorrow's Challenges,* GAO-07-1155SP (Washington, D.C.: September 2007).

[22]National coverage determinations stipulate coverage rules for the items and services that are reasonable and necessary for the diagnosis or treatment of an illness or injury.

all coverage decisions, CMS follows the same process: a company requests a coverage decision for an FDA-approved device or product; CMS reviews documentation, including materials associated with FDA's review and decision making; and CMS determines if the product or device is "reasonable and necessary" and, therefore, whether it should be approved for coverage by Medicare. CMS officials said that because the agency's role is also to decide how much to pay for a new product, officials will not make such decisions unless CMS has determined, in fact, that Medicare will cover the device or product. In response to concerns about a perceived lack of planning by CMS, officials from CMS told us they stay informed about new products—including those related to regenerative medicine—through communications directly with drug sponsors and manufacturers who may engage with CMS while a product is moving through the regulatory review process at FDA. CMS officials said that although they do not take steps to proactively reach out to the regenerative medicine research community, they welcome product sponsors to contact them about the status of potential new products. CMS officials said if they encounter an area where they need additional scientific expertise to help establish payment policy, they may consult with their colleagues at NIH or obtain advice from the Institute of Medicine. Officials from DOD—which has its own system for determining payment policies for the products that are covered by its TRICARE program—emphasized the importance of planning for coverage decisions particularly because these types of treatments are new and do not have precedents for how to structure payments.[23] These DOD officials noted that they have been working with the Military Health System and TRICARE administrators to plan for payment issues as new regenerative medicine products become available.

Agency Comments

We provided a draft of this report to the Department of Commerce, DOD, the Department of Energy, HHS, NSF, and VA for review and comment. We received technical comments from the Department of Commerce, DOD, HHS, NSF, and VA which we incorporated, as appropriate. In its technical comments, VA also indicated its agreement with our conclusions. The Department of Energy did not provide any comments.

[23]TRICARE is the health care program for military servicemembers (active duty, Guard/Reserve, retired) and their families and is a component of the Military Health System.

As agreed with your offices, unless you publicly announce the contents of this report earlier, we plan no further distribution until 30 days from the report date. At that time, we will send copies of this report to the Secretaries of Commerce, Defense, Energy, Health and Human Services, and Veterans Affairs, as well as to the Director of the National Science Foundation. In addition, the report will be available on the GAO website at http://www.gao.gov.

If you or your staff have any questions about this report, please contact me at (202) 512-7114 or crossem@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report. GAO staff who made major contributions to this report are listed in appendix II.

Marcia Crosse
Director, Health Care

List of Requesters

The Honorable Lamar Alexander
Chairman
The Honorable Patty Murray
Ranking Member
Committee on Health, Education, Labor, and Pensions
United States Senate

The Honorable Orrin G. Hatch
Chairman
Committee on Finance
United States Senate

The Honorable Johnny Isakson
Chairman
Committee on Veterans' Affairs
United States Senate

The Honorable Barbara Boxer
United States Senate

Appendix I: Funding for Regenerative Medicine Research by National Institutes of Health (NIH) by Institute, Center, or Program

NIH was the largest federal funder of regenerative medicine research in fiscal years 2012 through 2014, having invested more than $2.54 billion into research in this field. Of NIH's 27 institutes and centers, 22 funded some regenerative medicine research during the time period of our review. Two other entities within NIH—the Office of the Director and the NIH Common Fund—also funded regenerative medicine research during this time period. Table 2 shows the level of investment by each funding entity at NIH.

Table 2: Funding for Regenerative Medicine Research by the National Institutes of Health (NIH) by Individual Institute, Center, or Program, Fiscal Years 2012-2014

	2012		2013		2014			
Institute, center, or program	Funded amount ($)	Number of awards	Funded amount ($)	Number of awards	Funded amount ($)	Number of awards	Total amount funded ($) [Note A]	Percentage of total funding
National Heart, Lung and Blood Institute	212,869,528	532	208,251,404	500	196,051,892	459	617,172,824	24.26
National Institute of Diabetes and Digestive and Kidney Diseases [Note B]	90,073,024	274	81,142,224	274	93,233,038	258	264,448,286	10.39
National Cancer Institute	81,631,471	227	80,376,050	226	77,256,469	209	239,263,990	9.40
National Institute of Neurological Disorders and Stroke	73,812,668	253	72,285,570	249	72,913,912	248	219,012,150	8.61
National Institute of General Medical Sciences	69,145,159	161	64,132,487	173	59,256,816	174	192,534,462	7.57
National Institute of Arthritis and Musculoskeletal and Skin Diseases	62,726,547	215	62,533,204	233	65,809,026	239	191,068,777	7.51
National Institute of Dental & Craniofacial Research	41,946,674	123	40,335,711	121	36,798,976	116	119,081,361	4.68
National Institute on Aging	30,543,698	118	29,411,199	124	30,090,503	116	90,045,400	3.54
National Eye Institute	26,149,555	69	27,408,283	73	33,930,305	95	87,488,143	3.44

Institute, center, or program	2012 Funded amount ($)	2012 Number of awards	2013 Funded amount ($)	2013 Number of awards	2014 Funded amount ($)	2014 Number of awards	Total amount funded ($) [Note A]	Percentage of total funding
National Institute of Allergy and Infectious Diseases	31,038,642	79	26,926,178	79	28,919,209	80	86,884,029	3.41
NIH Common Fund [Note C]	32,645,867	33	24,987,560	35	27,403,675	35	85,037,102	3.34
National Institute of Child Health and Human Development	27,766,968	104	24,987,273	100	24,604,887	96	77,359,128	3.04
National Institute of Biomedical Imaging and Bioengineering	25,266,650	83	21,688,945	70	23,735,698	73	70,691,293	2.78
National Institute on Deafness and Other Communication Disorders	19,198,575	63	15,653,688	61	18,656,713	63	53,508,976	2.10
Office of the Director [Note D]	14,907,260	36	15,530,283	45	12,559,782	33	42,997,325	1.69
National Institute of Environmental Health Sciences	12,400,682	26	14,897,373	31	11,611,414	24	38,909,469	1.53
National Institute on Alcohol Abuse and Alcoholism	5,532,702	21	6,708,626	21	5,691,276	19	17,932,604	0.70
National Institute of Mental Health	7,059,618	20	4,024,101	13	5,137,875	17	16,221,594	0.64
National Human Genome Research Institute	4,709,383	8	4,627,132	8	4,144,462	8	13,480,977	0.53
National Center for Advancing translational Sciences	2,442,338	5	2,650,712	7	5,044,348	14	10,137,398	0.40
National Institute on Drug Abuse	4,504,775	11	2,251,541	6	3,327,704	10	10,084,020	0.40
National Institute of Nursing Research	192,032	2	217,566	1			409,598	0.02
National Institute on Minority Health and Health Disparities	170,541	1	129,281	1			299,822	0.01

	2012		2013		2014			
Institute, center, or program	Funded amount ($)	Number of awards	Funded amount ($)	Number of awards	Funded amount ($)	Number of awards	Total amount funded ($) [Note A]	Percentage of total funding
Fogarty International Center [Note E]	107,411	2	102,040	2			209,451	0.01
Total	**876,841,768**	**2,466**	**831,258,431**	**2,453**	**836,177,980**	**2,386**	**2,544,278,179**	**100.00**

Source: GAO analysis of NIH funding data. | GAO-15-553

Note A: For purposes of this report, we use the term “funding” to refer to obligations. An obligation is a definite commitment that creates a legal liability of the federal government for payment of goods and services ordered or received. A federal agency incurs an obligation, for example, when it awards a grant.

Note B: Data for the National Institute of Diabetes and Digestive and Kidney Diseases includes regenerative medicine projects funded through the Special Statutory Funding Program for Type 1 Diabetes Research, which is administered by the National Institute of Diabetes and Digestive and Kidney Diseases.

Note C: NIH Common Fund, formerly the NIH Roadmap for Medical Research, is a series of initiatives designed to speed the movement of scientific discoveries. It provides a framework of the priorities the NIH must address in order to optimize its entire research portfolio and lays out a vision for a more efficient and productive system of medical research.

Note D: The Office of the Director is responsible for coordinating some programs and activities that span NIH components, particularly research initiatives and issues involving more than one of the institutes or centers.

Note E: The Fogarty International Center supports and facilitates global health research conducted by U.S. and international investigators.

Appendix II: GAO Contact and Staff Acknowledgments

GAO Contact

Marcia Crosse, (202) 512-7114 or crossem@gao.gov

Staff Acknowledgments

In addition to the contact named above, Geri Redican-Bigott, Assistant Director; Jill K. Center; Cathleen J. Hamann; Erin C. Henderson; and Jennifer Whitworth made key contributions to this report.

Appendix III: Accessible Data

Data Tables

Data Table for Highlights Figure and Figure 1: Federal Funding for Regenerative Medicine Research, Fiscal Years 2012 through 2014

Agency	Total funded (in millions)
National Institutes of Health	$2,544.28
Department of Defense	$252.63
Department of Veterans Affairs	$40.95
National Science Foundation	$40.23
Food and Drug Administration	$8.63
National Nuclear Security Administration	$4.81
National Institute of Standards and Technology	$2.39

Source: GAO analysis of agency funding on regenerative medicine research. | GAO-15-553

Note: For purposes of this report, we use the term “funding” to refer to obligations. An obligation is a definite commitment that creates a legal liability of the federal government for payment of goods and services ordered or received. A federal agency incurs an obligation, for example, when it awards a grant.

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