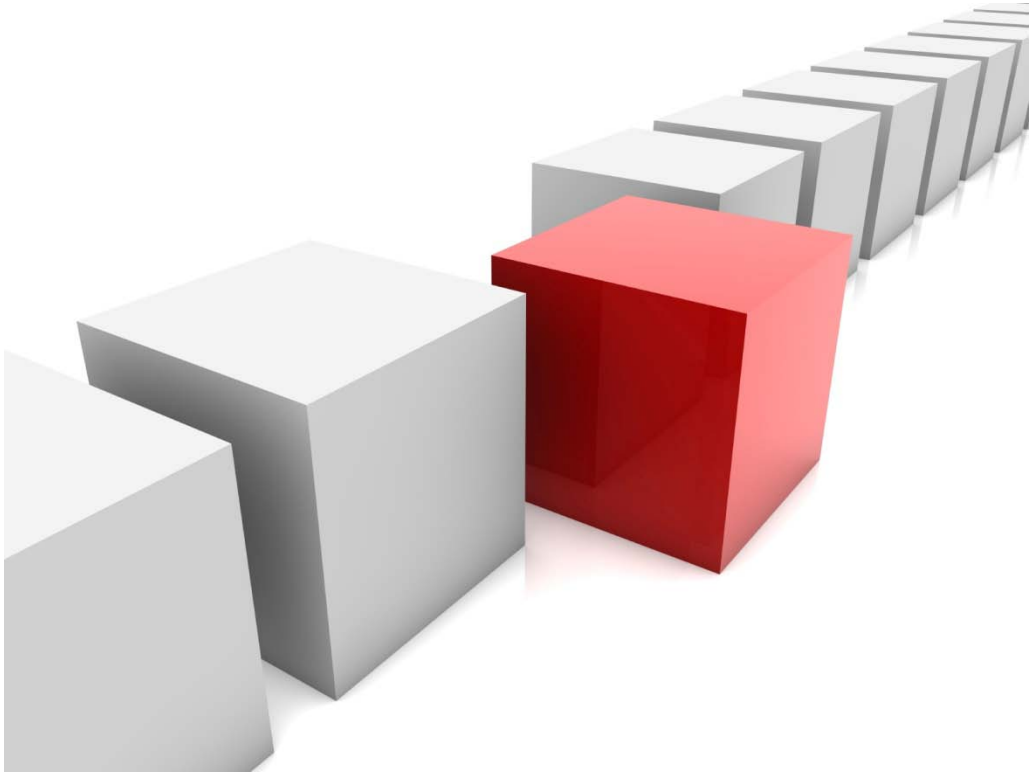
Annual Report

fiscal year 2010



Office of Technology Transfer

National Institutes of Health

U.S. Department of Health and Human Services

Message from the Director

Dear colleagues and commercialization partners:

The NIH Office of Technology Transfer (OTT) report for fiscal year 2010 illustrates the vitality of a program that celebrated its 20th anniversary year last January. I am still amazed by the foresight of people like Dr. Philip Chen who helped organize the NIH technology transfer functions in the 1980s. The principles and basic mechanisms established at that time still serve us well as evidenced by the significant contributions NIH technology transfer has made to new drugs and therapeutics brought to market by the private sector.* Today, however, we are faced with new challenges such as the economy, health care, revolutionary technologies like genomics, and the opportunities offered by 21st century IT tools. Technology transfer can help address these challenges by "add[ing] the fuel of interest to the fire of genius." (–Abraham Lincoln, the only President who is an inventor on a patent.)

More than ever, public and private sectors need to work together to enhance collaboration, taking full advantage of their complementary skill sets, facilities, and missions.

OTT has begun using new IT tools, like RSS feeds and full-text data mining, to better assess its technologies and more effectively communicate opportunities for collaboration and licensing. There is more we can do to utilize social networking tools in collaboration with other federal, state, and private research institutions to improve access to information on technology licensing and partnering opportunities.

We need to further reduce transactional barriers to technology transfer. This past year, OTT launched a new electronic means of payment using ACH transfers. We will launch in 2011 a web-based biological material licensing module that will significantly speed up our ability to transfer critical research materials to companies. We hope to develop in time a web-based portal to give companies better access to technologies available for licensing and electronic means of negotiating and executing licenses.

One huge challenge, however, remains the gap between early-stage technologies arising from the public sector laboratories and more proven technologies with a risk profile acceptable to companies and their investors. It will take partnering between research institutions at the federal and state level, investors, regional partners, and companies to find better means to bridge the product development pipeline gap. When (not if) we do so, the public will enjoy new products utilizing new technologies, such as genomics, to prevent and treat disease, and in doing so create new jobs that to grow our economy.

I hope you will join me in meeting these challenges.

Sincerely,

Mark L. Rohrbaugh, Ph.D., J.D.
Director, Office of Technology Transfer

*See for example, Stevens et al., "The Role of Public-Sector Research in the Discovery of Drugs and Vaccines", NEJM 364: 6, pp. 535-541 (2011), showing that OTT licensed technologies represented 22 (14%) of the 153 FDA-approved drugs and therapeutics reaching the market in the last 40 years based on licenses from all US public-sector research institutions.

Table of Contents

Mission Statement

The mission of OTT is to improve public health through the management of National Institutes of Health (NIH) and Food and Drug Administration (FDA) inventions and in doing so serve a leading role in public sector biomedical technology transfer policy and practice.

NIH and FDA are agencies of the Department of Health and Human Services (HHS).

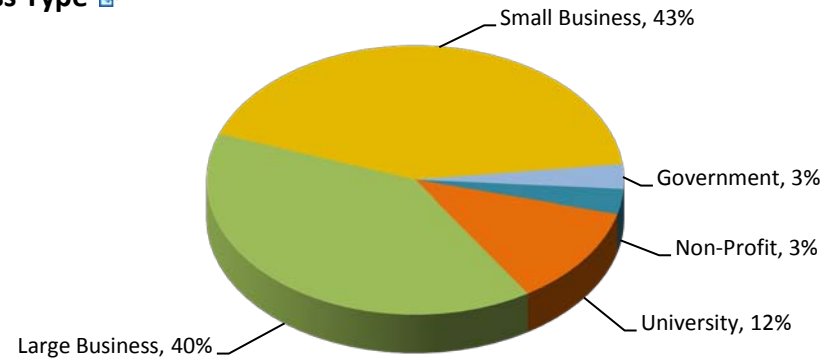
Purpose

OTT serves as a bridge that connects the inventive discoveries made in the NIH and FDA intramural research programs to commercial partners that develop these technologies into products and services to benefit public health. Without this bridge, the public would not benefit from the full potential of these biomedical discoveries. In carrying out its mission and purpose, OTT applies its policies and practices to the management of NIH's and FDA's inventions, including: the appropriate use of the patent system; marketing NIH and FDA technologies to identify appropriate commercial partners; negotiating licenses to ensure the timely development of technologies; and monitoring the progress of the development of the technology to ensure commercialization milestones are reached and royalties are paid.

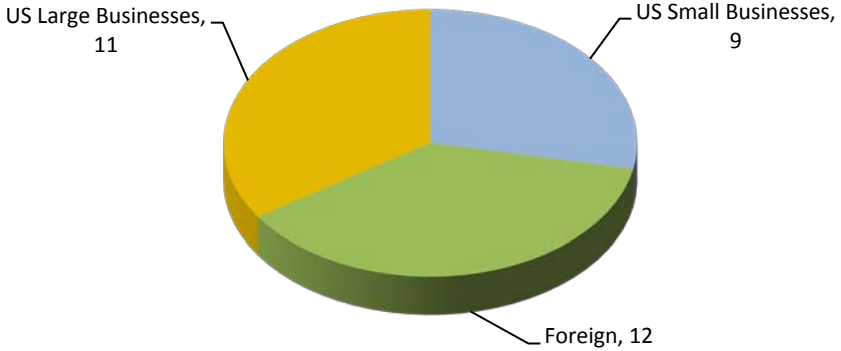
Licensing and Patenting

The ultimate goal of any technology transfer office is effective and responsible licensing to facilitate the development of technologies. NIH and FDA have maintained a strong patent and license portfolio, in an otherwise slow economy, and in doing so has made a positive impact on public health and jobs. Over the years, these efforts have helped stimulate the economy through small entrepreneurial companies created to commercialize a technology licensed from OTT as well as large companies developing high-growth technologies. In FY10, OTT executed 226 license agreements — 79% with US companies of which 42% were small businesses. Nearly 49% of the first-time licensees were US companies and about 78% of these were small US businesses. About one quarter of the new licenses were to companies licensing from NIH and FDA for the first time.

Licensee by Business Type



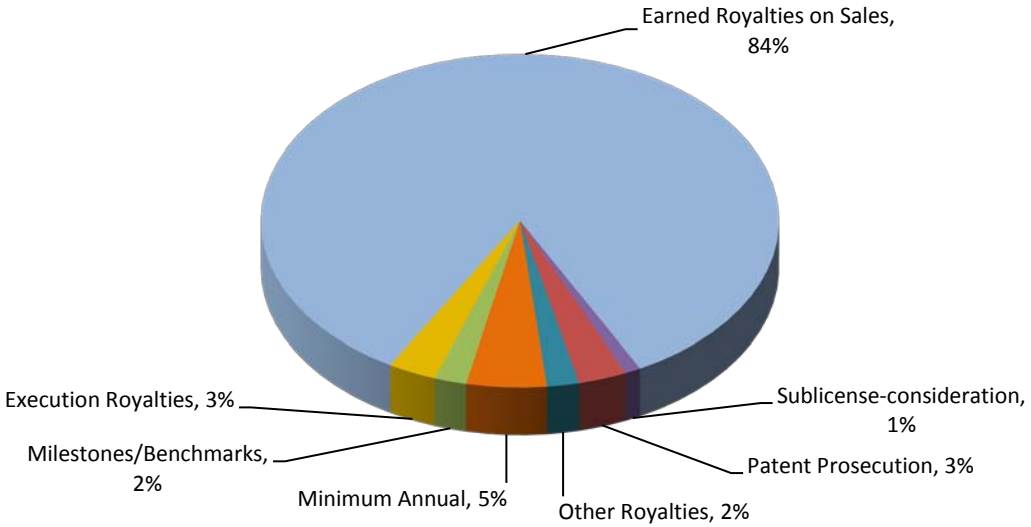
First Time Licensee by Business Type



Licensing and Patenting (cont)

Sales of products built around NIH and FDA licensed products remain strong with licensees reporting nearly $6B in sales of products licensed from the NIH. In FY10, OTT had 377 licenses reporting products on the market. Royalties on sales of these commercial products and services account for 84% of the $91.6M in royalties collected in FY10, with that percentage staying fairly steady for the last few years.

Royalty Income by Type



The top 20 products generating royalty income account for 82% of the total royalty income. Thus, sales of a limited number of products generate the vast majority of the royalty income.

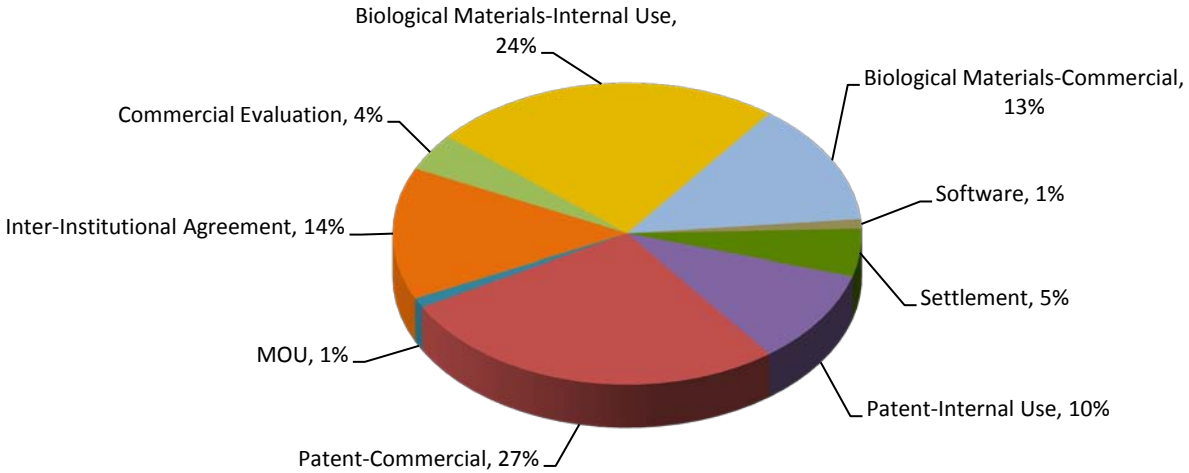
The FY10 technology transfer outcomes follow a long trend of successful licensing of biomedical inventions by the NIH and FDA and also reflect HHS's dedication to technology transfer - the broader economic impact of which becomes especially important during difficult economic times. OTT has used novel and flexible licensing practices to mitigate economic stressors affecting the pharmaceutical and biotechnology industries. Through these efforts, OTT continues to build strong partnerships with both public and private entities to support the NIH mission of improving public health. While most of the royalty income collected by OTT is based on sales of pharmaceutical and biotechnological products and services, most of the products and services on the market under OTT licenses are research tools and reagents. Although the sales of research

Licensing and Patenting (cont)

tools cannot compete in volume or financial return with sales of FDA-approved products, they make a considerable impact in advancing both private and public sector research.

Some of these best selling products include Prezista®, a novel protease inhibitor for treatment of drug-resistant HIV-1, and Gardasil® and Cervarix®, HPV vaccines based upon recombinant Papillomavirus Capsid proteins.

Licenses by Type of Agreement



The success of OTT's licensing program and its overall mission of serving global public health is reflected in the following:

1. Gardasil®, Merck's human papillomavirus (HPV) vaccine, helps protect against two types of HPV that cause about 75% of cervical cancer cases and two more types that cause 90% of genital warts cases. Under a license from OTT, the vaccine includes technology invented by NCI scientists who showed that the HPV L1 protein can self assemble into virus-like particles that elicit an immune response. OTT and Merck worked together to consider access to this vaccine in developing countries. In support of the NIH's public health mission, OTT agreed not to charge royalties on Merck's sale of products at-cost or less in developing world countries. This is just one approach that OTT uses under its license agreements to provide incentives to broaden access to NIH technologies. NIH has also developed an alternative HPV vaccine technology involving the L2 protein, which OTT licensed on a non-exclusive basis to an Indian company.

Licensing and Patenting (cont)

2. Launch of meningitis vaccine, MenAfriVac, in sub-Saharan Africa based on technology from the FDA. MenAfriVac is the first vaccine developed specifically for Africa. Meningitis A, which MenAfriVac targets, accounts for about 85% of the meningitis epidemic in Africa and is expected to reduce endemic meningitis by 50%. The vaccine utilizes a conjugation technology developed by FDA scientists that enhances the immune response to the viral protein.

3. Fluorouracil (5-FU) is a commonly used anti-cancer drug. Yet, this therapeutic molecule can result in a toxic reaction leading to death in certain patients with a mutation in the dihydropyrimidine dehydrogenase (DPD) gene. Scientists at the NCI have discovered a method to detect DPD splicing mutations that interfere with the RNA processing. This method can identify patients with such mutations and thereby alert the healthcare provider that the patient will have an adverse reaction to 5-FU. Physicians can then develop alternative, safer treatment regimens for such patients. The DPD mutation detection method was licensed to multiple companies, including two US companies, on a non-exclusive basis, and has been developed into diagnostic products. The wide dissemination of this life saving diagnostic test promotes the NIH mission of improving public health and demonstrates the commercial viability of one of NIH's licensing principles — non-exclusive licensing of diagnostic tests whenever possible.

4. The OTT licensed its US government-owned patents for methods of using darunavir, an HIV anti-retroviral drug (ARV), to the Medicines Patent Pool (MPP). The NIH license marks the first contribution to the Medicines Patent Pool. This voluntary patent pool for ARV patents is designed to facilitate access to HIV treatments in developing countries by reducing any patent licensing barriers for developers of new combinations of ARVs and adapted formulations for developing countries. The licensed patents resulted from research undertaken by the NIH and the University of Illinois at Chicago. The OTT and the MPP are exploring other patented technologies that might be added to the pool.

Trans-NIH Initiatives

SBIR-TT Initiative

Small Business Innovation Research-Technology Transfer (SBIR-TT) is a new paradigm at NIH that advances the commercial development of intramural NIH inventions. It can be viewed as a way for NIH to "spin-off" inventions using the statutory authorities available. Inventions from the NIH Intramural Research Program are licensed to qualified small businesses which have been awarded an SBIR contract to develop the technology into commercial products that benefit the public. These inventions would be commercially promising but for identifiable research gaps that have delayed their commercialization. Using SBIR funding to develop the technology, the contractor will work closely with the inventor(s) to address the research gaps.

The SBIR Program is a federally mandated program that requires federal agencies expending over $100,000,000 annually in extramural research and development to set aside 2.5% of that budget for awards to for-profit, small U.S. businesses. Traditionally, SBIR funds have been granted to small businesses in order to develop a commercial product of utility to the awarding agency's internal research program(s) and/or a commercial product that supports the agency's stated mission.

The pilot program was developed in cooperation with OTT, the National Cancer Institute's (NCI) Center for Cancer Research (CCR), NCI SBIR Program Office, and the NCI Technology Transfer Center. The first SBIR-TT Topic chosen was "Low-Field Electron Paramagnetic Resonance Imaging Device to Optimize Development of Anti-Angiogenic Therapeutics in Cancer Animal Models" based on inventions by Dr. Murali Krishna Cherukuri and Dr. Sankaran Subramanian. The second topic was "A New Type of Vaccine for Prevention of HIV Infection and HIV-Associated Cancers" based on an invention by Dr. Dimiter Dimitrov.

Contract awards are expected in September 2011.

Marketing

OTT reaches out to maintain close communication with its existing and potential licensees to better meet their needs. OTT staff meet with interested parties to discuss scientific, business, and legal issues in support of the transfer of NIH/FDA technologies. During this last year, a number of separate meetings with companies led to executed licenses.

OTT joined with sister offices in other federal agencies to increase access to information on publicly-funded technologies that are available for license and on opportunities for collaborations with federal laboratory scientists. By making information from multiple agencies available in RSS feeds on Data.gov, a business can go to one website, find the information easily and efficiently, download the information, and receive real time updates with no effort. OTT provided Data.gov with RSS feeds for technologies available for licensing and CRADA opportunities as well as a widget for its Product Showcase. These RSS feeds and widget are also available on the OTT website home page.

To better underscore the lengthy process of bringing a biomedical product to the market, OTT developed its Product Development Pipeline. Many inventions from the NIH and FDA Intramural Research Programs have been licensed and are now in clinical development with the hope of eventually reaching the market. These inventions are shown as a development pipeline and illustrate the valuable synergy between NIH/FDA and industry as well as the depth and richness of the science conducted in these labs. In FY10, there were seven inventions in Phase III clinical development, 28 in Phase II, and 17 in Phase I.

OTT licenses NIH intramural inventions to companies across the globe. To illustrate the global impact OTT created "NIH Lights Up the World," a website using Google map where the stars on the map represent locations where a commercial entity has completed a license for an NIH intramural invention. The licenses can be filtered by country of licensee, NIH Institute, and fiscal year the license was executed.

OTT continued to add new products to the Product Showcase, a website that displays products developed by commercial partners from NIH intramural inventions. The Showcase now includes 195 products from a variety of NIH Institutes.

Developing performance metrics is an important measure of an organization's activities and performance. OTT designed an interactive website that allows the user to view commonly tracked metrics in a variety of formats.

OTT continues to develop an electronic website for Research Materials (eRMa) that will serve as a marketplace for many hundreds of research materials available for licensing from the NIH and FDA intramural research programs. The objective in developing this website is to ensure the efficient transfer of research materials to the private sector. The interactive website will provide a marketing and licensing option that is designed to expedite the licensing process, decrease transaction costs, and facilitate greater dissemination of research materials to companies. The expected launch date is early 2011.

Royalty Administration

While the essential purpose of the technology transfer process is to improve public health, the collection of royalties is an important by-product. Royalties collected from licensees of NIH and FDA intramural program inventions are distributed to the inventors, the Institutes/Centers (ICs) that developed the inventions, and, when relevant, extramural institutional co-owners of the inventions. There are various payments collected as royalties under licenses, including upfront license fees, annual minimum payments to maintain a license, payments associated with the achievement of commercial development milestones and "running royalties" as a percentage of the sales of products. By far, the largest amount of royalty funds is received on sales of products. Royalty collections fluctuate from year to year and are impacted by a variety of factors, including rise and fall in sales, FDA licensing approval, license termination when patents expire, etc. Royalty funds support activities that might otherwise remain unfunded. The ICs use the income to pay technology transfer expenses (such as patent expenses and OTT costs) and to support research and training programs, including the purchase of expensive laboratory instrumentation or pharmaceuticals for clinical trials.

Just as the fiscal year was coming to a close, NIH launched a new electronic web-based royalty payment site to make it easier for companies to make their royalty payments. The site is located at www.pay.gov, a multifaceted web-based application allowing anyone to make Automated Clearing House (ACH) payments to government agencies by debit from a checking or savings account. Pay.gov was launched in 2000 and is maintained by the U.S. Department of the Treasury. By eliminating the need for bank checks, this bank-to-bank transfer system can shorten the processing time from several weeks down to a day or less and also reduce the OTT's administrative costs. Benefits to the licensees are immediate confirmation of payment receipt and expedited shipment of materials. The project was led by the OTT and the NIH Office of Financial Management.

The OTT administered $91.6M in royalties in FY10 with 80% of the total going to the ICs and 9% to the inventors. The remainder was distributed under Inter-Institutional Agreements (IIAs) to our extramural partners that are co-owners of licensed inventions.

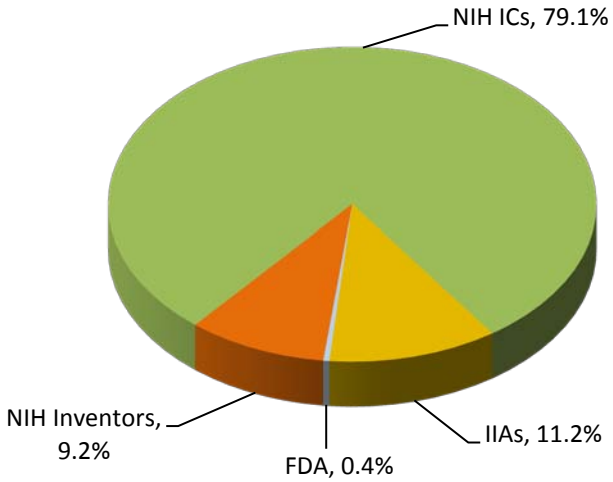
This income was received under 859 license agreements from 428 companies, or their subsidiaries, three-quarters of which are US based. Royalty levels have remained relatively stable in the last few years with almost a 1% increase over 2009.

In accordance with statutory requirements, inventors under a given license receive annually the first $2,000 received by the NIH; 15 percent of royalties above $2,000 and up to $50,000; and 25 percent of royalties in excess of the first $50,000 up to a cap of $150,000 per year per inventor. In FY10, 1,097 inventors received royalty payments amounting to $8.4M. Of these, 68 were first-time recipients, and 22 received the statutory cap.

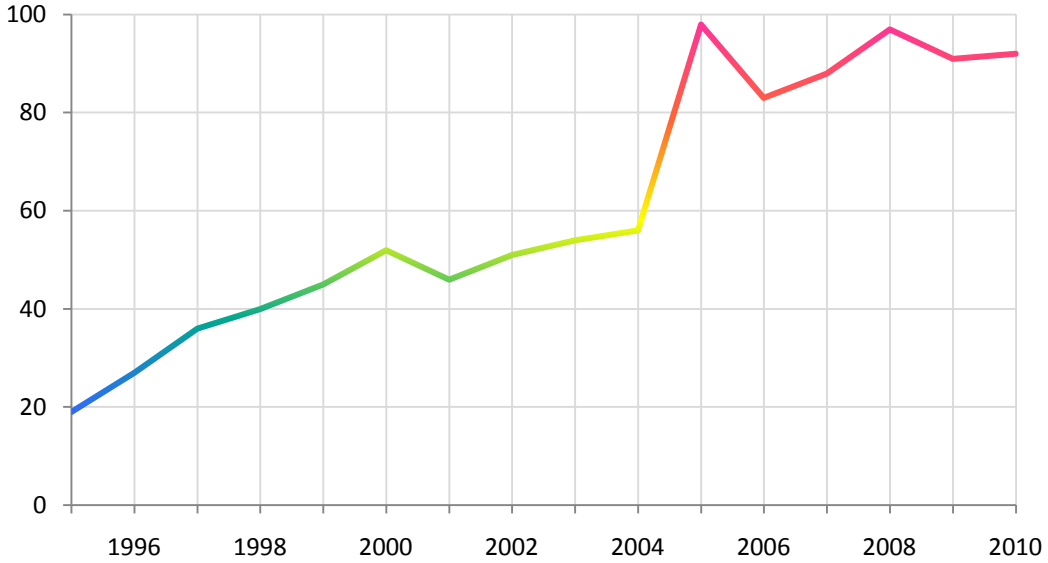
During this fiscal year, the Office continued to improve the process to identify licensees that are required to reimburse the ICs' patent prosecution costs. As a result of this effort, $2.87M was recovered in fiscal year 2010.

Royalty Administration (cont)

Royalty Distribution



Royalty Income



Monitoring and Enforcement

To ensure compliance with license obligations and development of technologies licensed from NIH and the FDA, OTT maintains a monitoring and enforcement program for its portfolio of more than 1,318 active license agreements. During FY10, 53 licenses were terminated and 83 licenses expired. Sixteen cases of alleged infringement of NIH/FDA patents were investigated and closed either through licensing or by the company's voluntary withdrawal of the infringing product. At no time, however, did NIH ask for product to be withdrawn or seek an injunction. OTT conducted internal audits of all licenses for administration and royalty compliance, resulting in an overall collection rate of 95% of royalties due in fiscal year 2010. OTT terminated four NIH licenses for non-compliance during the year. Additionally, OTT contracted with firms to conduct audits of three licensees with higher licensed product sales to verify proper payment under the terms of the license. OTT's enforcement activities resulted in the collection of over $6.92 million in overdue royalties during the year.

Trends

OTT has weathered the economic downturn extremely well. In fact, the amount of royalties received by OTT rose by almost 1%, the number of license applications received actually increased by 3% from the previous year, and 34% fewer licenses were terminated as compared to FY09. Most importantly, not only did the number of executed licenses increase by 5%, but the increase can be attributed to a 21% increase in patent commercial licenses versus internal use or research material licenses. The increase in patent commercial licenses reflects a positive trend by companies looking to NIH for innovative technologies for commercial product development.

While the number of executed licenses has increased, they have not yet rebounded to the level attained in FY07 and FY08. Royalties remain stable but are less than the $97.2M achieved in FY08, primarily due to changes in earned royalties on sales from two products. Although royalties on one product decreased by nearly a third in FY09, another one has been steadily increasing since FY08.

Policy Activities

The scope of OTT's formal and informal policy activities is broad, including health related technology transfer and intellectual property matters and support of legislative affairs. Leveraging the experience of NIH and U.S. universities in technology transfer, OTT drafted and communicated policies and procedures to enhance the translation of early-stage technologies into practical applications for the benefit of public health. OTT, working through the NIH Office of Legislative Policy and Analysis, serves as a resource for the development of NIH input on a variety of legislative initiatives directed to technology transfer, intellectual property policy, and associated operational issues. Additionally, OTT provided support for training activities and expert advice to programs both internally within the HHS and externally across the U.S. Government. OTT, by designation of HHS, served as the lead office to evaluate a request to exercise "march-in" authority under 35 U.S.C. § 203(a)(2) in connection with certain NIH-funded inventions associated with the drug Fabrazyme®. NIH issued its decision on December 1, 2011 (see http://www.ott.nih.gov/policy/March-in-Fabrazyme.pdf).

Among its administrative duties, OTT provides the agency determination for requests by the extramural and intramural communities for waivers. In FY10, OTT reviewed two requests to waive title to intramural inventors and 71 extramural waiver requests, comprising 56 requests to waive title to inventors, seven requests to waive the U.S. manufacturing requirement, and eight requests to waive rights to a third party.

OTT has led a variety of initiatives directed to NIH-wide technology transfer policies and procedures. OTT representatives serve as Vice-Chair and Executive Secretary of the Public Health Service (PHS) Technology Transfer Policy Board (TTPB). The TTPB serves as the principal advisory board to NIH, the Centers for Disease Control and Prevention, and the Food and Drug Administration in establishing and modifying, as appropriate, PHS technology transfer policies. In that capacity, OTT led the ongoing comprehensive review of policies and procedures related to patenting, licensing, Cooperative Research and Development Agreements (CRADAs), material transfer agreements (MTAs), royalty disbursement, and extramural activities.

Additionally, OTT, together with the NIH technology transfer community, the NIH Office of Human Subjects Research, and other NIH stakeholders, contributed to the implementation of the Policy for the Transfer of Materials from NIH Intramural Laboratories and the development of a model MTA to transfer materials obtained from humans. OTT also hosted the NIH CRADA Policy Advisory Group, a forum for identifying and providing recommendations to the NIH CRADA Subcommittee with respect to NIH-wide CRADA policy issues.

Members of OTT actively participate in a wide array of NIH-wide and Government-wide projects that address programmatic components of technology transfer. Within NIH, OTT policy staff serves on the Trans-NIH Task Force on Nanotechnology, the Data/Resources Sharing Interest Groups, the NIH Biomarkers Consortium, and the Cancer Human Biobank. Members of OTT policy staff represent HHS and NIH in interagency and intergovernmental fora, such as the Inter-Agency Working Group on Technology Transfer, Global Issues in Nanotechnology Working Group

Policy Activities (cont)

in the U.S. Government's National Nanotechnology Initiative, and the Interagency Working Group for the Working Party on Biotechnology in the Organisation for Economic Cooperation and Development. OTT also served as a technical advisor to the Secretary's Advisory Committee on Genetics, Health and Society.

OTT policy staff served as advisor to NIH and HHS on many *ad hoc* issues related to technology transfer and intellectual property, including gene diagnostic technologies, stem cells, and the transfer of materials from human subjects. OTT policy staff proposed, coordinated, and served as a facilitator of a debate forum on patenting of genomic inventions at the Association of University Technology Managers (AUTM) 2010 Annual Meeting.

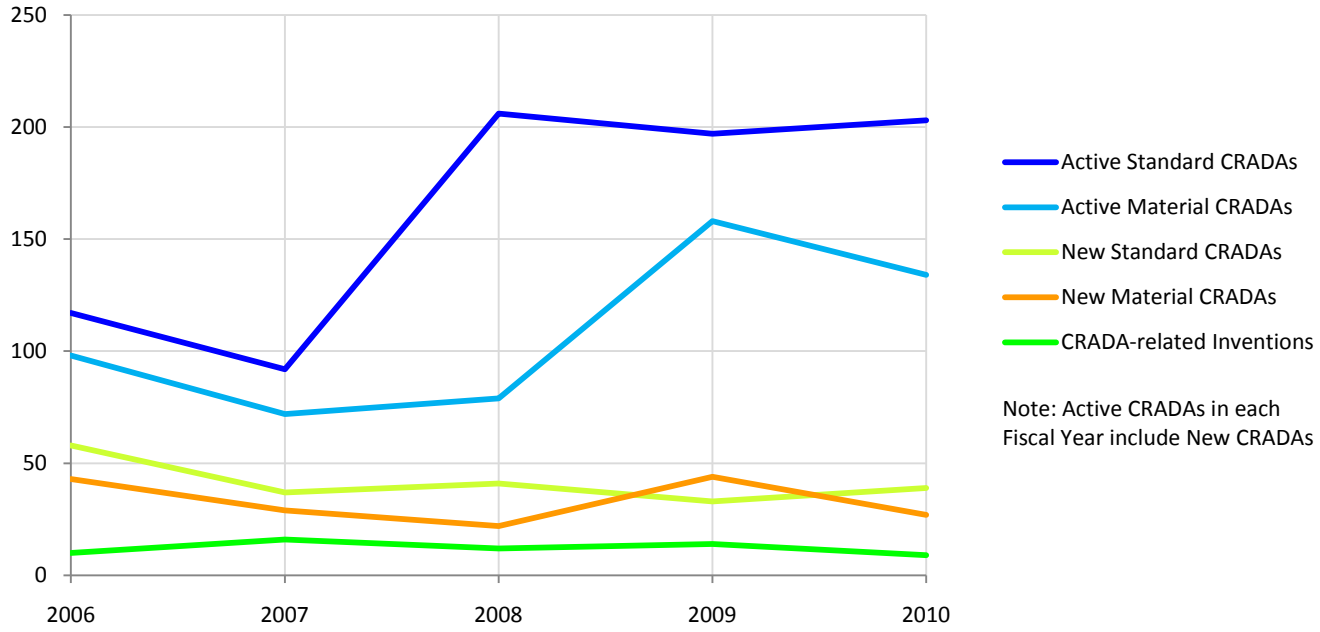
In support of OTT's negotiations of inter-institutional agreements between NIH and university collaborators, OTT policy staff spearheaded efforts to encourage and enhance dialogue between NIH and university technology transfer offices. OTT advanced discussions among representatives from NIH's extramural grantees, the Council on Governmental Relations, AUTM, and NIH IC technology transfer offices. These discussions have been directed to facilitating efforts to update the various material transfer agreement models and to draft new models. Through these activities, OTT policy staff supported the transfer of materials among researchers and non-profit entities in a direct and expeditious manner.

Cooperative Research and Development Agreements (CRADAs)

Cooperative Research and Development Agreements (CRADAs) provide an opportunity for NIH investigators to join with their colleagues from industry and academia in the joint pursuit of common research goals. CRADAs are negotiated by technology transfer staff in the ICs, while OTT collates and administers CRADA data and serves as a member of the NIH CRADA Subcommittee. While there are various mechanisms that support collaboration between companies and intramural scientists, CRADA are the only mechanism that permits the NIH to offer an exclusive option to license inventions made within the scope of the collaboration agreement and to receive funds from the company collaborator.

In FY10, there were 337 active CRADAs; 203 were standard CRADAs and 134 were Materials-CRADAs. During the year, NIH executed 66 new CRADAs; 39 of which were standard and 27 were Material-CRADAs. Seventy-two percent of these were with US companies, and 47% of the US companies are small businesses. The number of new CRADAs executed in FY10 was about 10% less than FY09 or FY08 but the percentage of new CRADAs with small US companies continued to climb. This last year, nine CRADAs led to inventions reported by NIH researchers at eight different Institutes.

Multi-year CRADA Metrics



The Green Initiative

Through the increased the use of digital media, OTT has made significant strides to facilitate communication with outside entities and decrease use of consumables. The Office purchased a multi-feed, high volume scanner to enable it to perform in-house scanning of 3,500 files. All the files were then attached to OTT's data management system allowing users to work offsite and still have access to the necessary files. By doing the work in-house, this effort saved OTT approximately $250,000. In recognition of these and other efforts, OTT received the HHS Green Champions Award for Environmental Stewardship.

Other Accomplishments

Members of the Office were recognized with awards for their significant contributions to technology transfer as well as the overall mission of NIH. These included seven group and two individual NIH Office of the Director Merit Awards, and the Licensing Executive Society "Deal of Distinction Award™."

Members of the OTT staff were invited to give presentations at many domestic and international meetings. These outreach efforts help communicate NIH's technology transfer policies, increase opportunities for licensing technologies, learn from others engaged in technology transfer, engage in cooperative technology transfer with governmental and non-profit institutions, and provide training to institutions implementing technology transfer mechanisms. The major meetings included: Federal Laboratory Consortium (FLC) Annual Meeting, Biotechnology Industry Organization (BIO) Annual Meeting, Association of University Licensing Managers (AUTM) Annual Meeting, HHS International Vaccine Technology Workshop, Technology Transfer Summit, Technology Transfer Society Annual Meeting, University Startups Conference, and Gates Foundation Product Development Partnerships Conference.

Additionally, OTT staff published two articles:

- Keller, George H. and Ferguson, Steven M., "Commercial Licensing of HIV-1 Protease: Applications of the NIH Research Tools Policy," published in *The Journal of Biolaw and Business, Volume 12 No. 4 pp.1-5, (2009).*
- Vensko, Nancy W. and Ferguson, Steven M., "Research Discoveries after *Kubin*", published in *Tomorrow's Technology Transfer, Volume 2 No. 1 pp. 48-58 (Winter/Spring 2010).*

In FY10, Mark Rohrbaugh served as an Expert to the World Health Organization's Working Group on R&D Financing [for diseases that disproportionally affect developing countries].

A number of OTT staff members served as organizers, instructors, and speakers for several local technology transfer educational programs including the Foundation for Advanced Education in the Sciences (FAES). These programs allow OTT to share its experience and expertise in technology transfer and provide training opportunities in the field for scientists, other members of the NIH, and the regional community.

Summary

Overall, the transfer of inventions from NIH and FDA intramural laboratories and the role of OTT in informing technology transfer policy considerations remain strong. With 377 licenses reporting products on the market in FY10 and combined projected sales of nearly $6B, the NIH through its technology transfer program continues to have an important public health and economic impact. From the technology transfer perspective, the American public is receiving a strong return on its investment in the NIH and FDA intramural biomedical research programs. OTT remains committed to finding new and innovative ways to streamline its processes, whether by utilizing new IT tools or developing more effective systems. As always, we welcome your suggestions and inquiries.