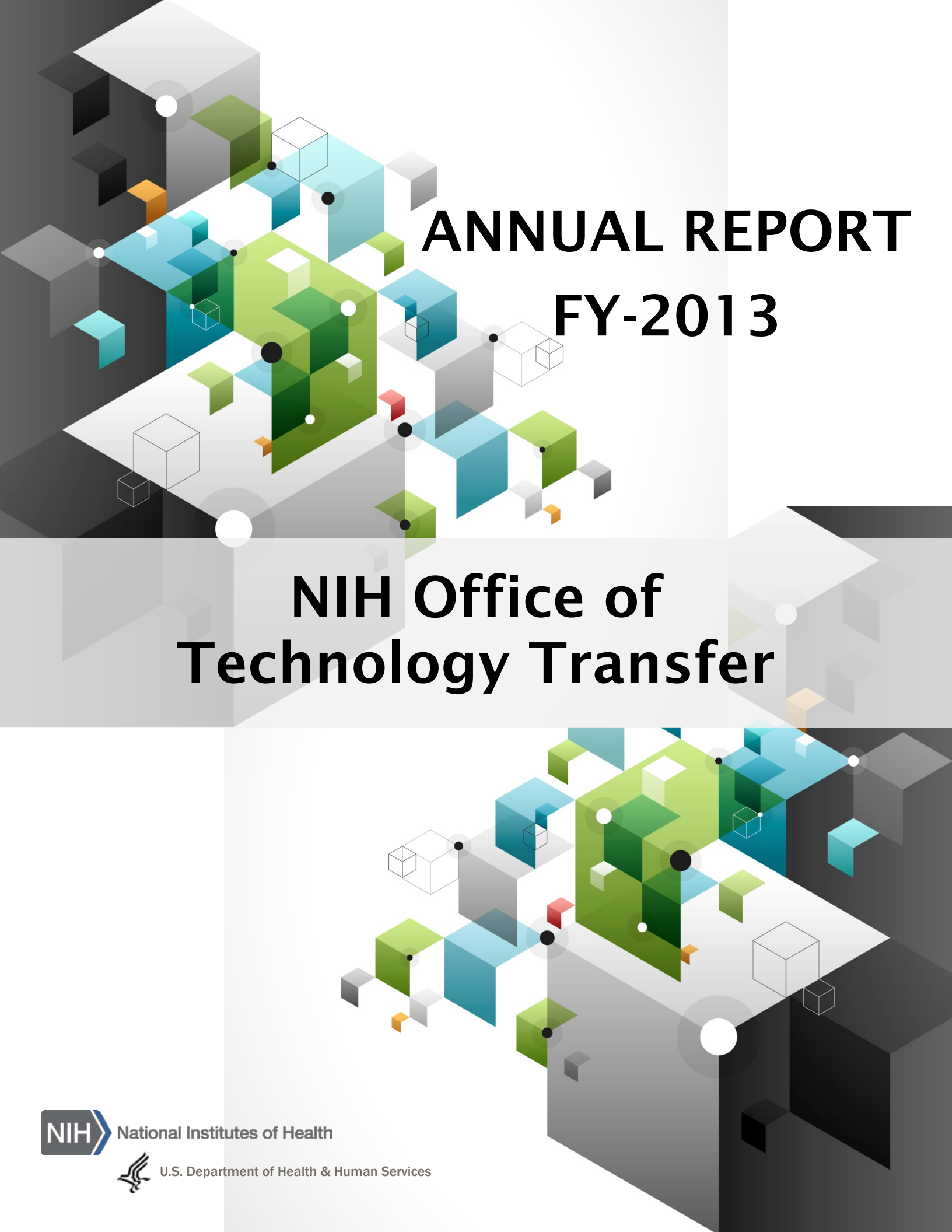
ANNUAL REPORT FY-2013

NIH Office of Technology Transfer



National Institutes of Health

U.S. Department of Health & Human Services

Contents

Message from the Director

Dear colleagues and partners in commercialization:

In Fiscal Year 2013, the NIH Office of Technology Transfer (OTT) responded to new opportunities and challenges in a manner that should improve the technology transfer program at the NIH and the Department of Health and Human Services at large.

A significant restructure this year resulted from the decision by the CDC to transfer the management of its patenting and licensing portfolio to the OTT. We welcomed this opportunity to work more closely with our CDC colleagues. The CDC technology transfer program will now operate similar to that of the FDA and the NIH Institutes and Centers (ICs) with respect to forwarding employee invention reports to the OTT for patenting, licensing, and royalty administration, while retaining at the agency and center level the management of agreements associated with the ongoing scientific activities, such as CRADAs, Material Transfer Agreements (MTAs), and other collaborative research agreements. Coordinated management of inventions made by researchers at the three major intramural research components of HHS promotes efficiency, allows companies to review the entire HHS portfolio in one location, either physical or virtual, and permits complementary technologies from multiple agencies to be marketed and packaged for licensing together.

A significant amount of work has been accomplished by both the CDC and OTT in hiring people to manage the CDC portfolio (at CDC's expense) and in bringing the portfolio under OTT's management umbrella. OTT verified and entered into its data management system 576 invention disclosures, 3,088 patent records, 312 licenses, 49 CRADAs, 176 royalty records, and 126 monitoring records, and wrote 31 invention abstracts. CDC and NIH expect initial benefits of this reorganization to be realized in FY14.

Another significant activity involved the review of OTT activities by the newly established Advisory Committee to the Deputy Director for Intramural Research (ACDDIR). An ad hoc subcommittee chaired by Marvin Parnes of the University of Michigan and Katherine Ku of Stanford University heard from senior staff at OTT and members of the IC technology transfer community. The committee submitted a report to Dr. Michael Gottesman, the DDIR, which recognized the substantial accomplishments of the program but urged NIH to make changes in the operations of NIH technology transfer to improve interactions between OTT and the ICs. The Advisory Committee suggested a range of options that are being considered by the NIH leadership. We look forward to their final recommendations and the opportunity to improve technology transfer at NIH.

Sincerely,

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

Mission Statement

The mission of the Office of Technology Transfer (OTT) is to improve public health and safety through the management of National Institutes of Health (NIH), Food and Drug Administration (FDA), and the Centers for Disease Control and Prevention (CDC) inventions and in doing so serve a leading role in public sector biomedical technology transfer policy and practice.

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

PURPOSE

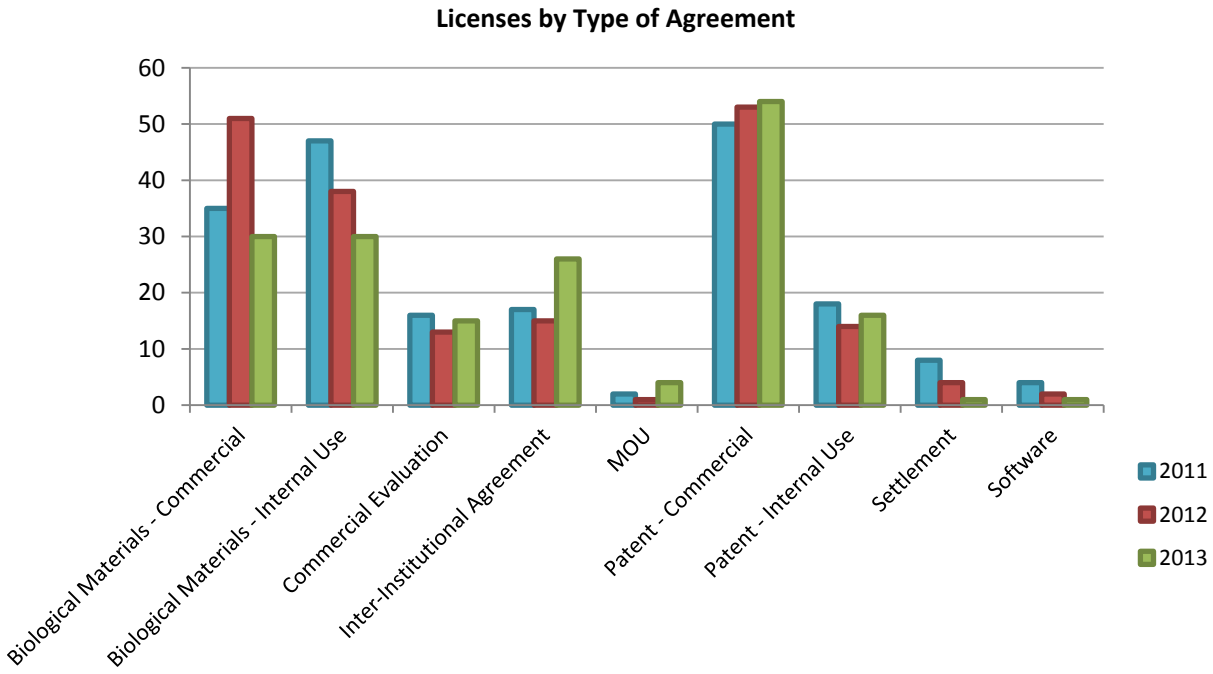
OTT serves as a bridge that connects the inventive discoveries made by scientists in the NIH, FDA, and CDC (beginning in FY13) intramural research programs to commercial partners that develop these technologies into products and services to benefit public health. Without this bridge, the public would not benefit from the full potential of these biomedical discoveries. OTT also serves as the lead technology transfer office for HHS. In carrying out its mission and purpose, OTT applies its policies and practices to the management of HHS'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 in the development of the technology to ensure commercialization milestones are reached, products are brought to the market, and royalty fees are paid. In addition, OTT makes agency determinations for requests from both intramural scientists and extramural institutions to assign invention rights to inventors or to third parties, and requests for waivers of US manufacturing requirement for products sold in the US under licenses of NIH funded inventions.

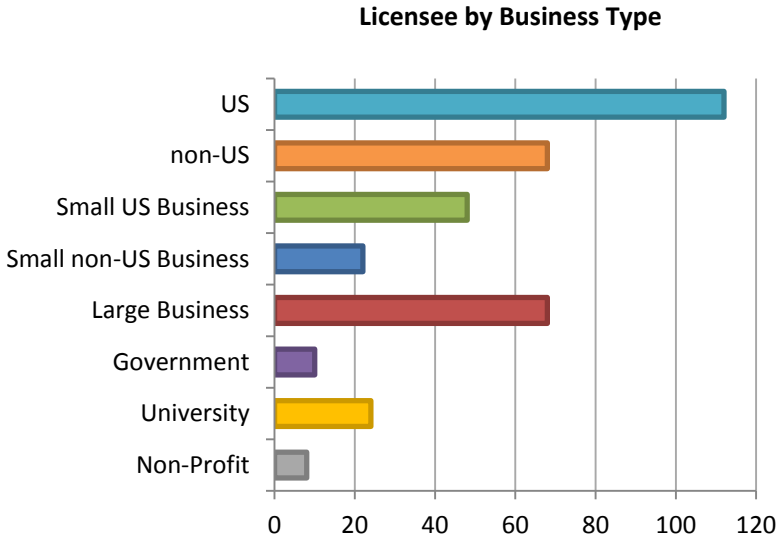
Licensing and Patenting

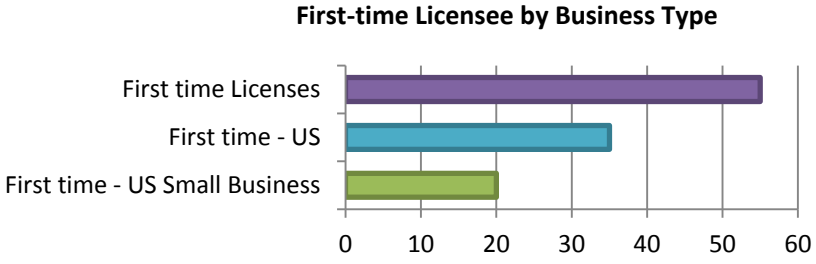
The ultimate goal of any technology transfer office is effective and responsible licensing to facilitate the development of early stage technologies. Inventions made by scientists in the NIH Institutes and Centers (ICs), the FDA, and most recently by the Centers for Disease Control and Prevention (CDC are reported to the NIH OTT through their respective Technology Development Coordinators (TDCs) who provide important input to OTT for its assessment of patenting and licensing decisions. OTT has continued its efforts to work ever more cooperatively with companies to facilitate the licensing of inventions, which at times is enhanced by collaborations with scientists in the ICs to support commercial development of the technologies. The goal for all involved is to enhance the likelihood that these efforts will lead to products to improve public health. In addition, these licensing activities help stimulate the economy when the Government's high-growth technologies are developed into products by small entrepreneurial companies as well as by large biotechnology and pharmaceutical companies. Charts of our metrics involving NIH and FDA inventions can be found at http://www.ott.nih.gov/erma/tt-metrics. Those for CDC will be included beginning next fiscal year.

In FY13, OTT executed 180 license agreements — 62% with US companies of which 43% were small businesses. Of the new licenses executed, 55 (31%) were with companies licensing from NIH for the first time; 64% of those first-time licensees were US companies and about 57% of those were small US businesses. Over the last seven years there has been a decline in the total number of licenses, more from small than large US businesses, with a slight increase in the number of licenses to non-US businesses.

Over the last two years, however, the largest increase in agreement type has been in the number of Start-Up Licenses. In FY13, the number of patent commercial licenses stayed consistent but still accounted for 30% of the total licenses executed. The most significant decline was in the number of biological material licenses, both commercial and internal use.


Licenses by Type of Agreement
60
50
40
30
20
10
0
Biological Materials - Commercial
Biological Materials - Internal Use
Commercial Evaluation
Inter-Institutional Agreement
MOU
Patent - Commercial
Patent - Internal Use
Settlement
Software
2011
2012
2013


Licensee by Business Type
US
non-US
Small US Business
Small non-US Business
Large Business
Government
University
Non-Profit
0
20
40
60
80
100
120


First-time Licensee by Business Type
First time Licenses
First time - US
First time - US Small Business
0
10
20
30
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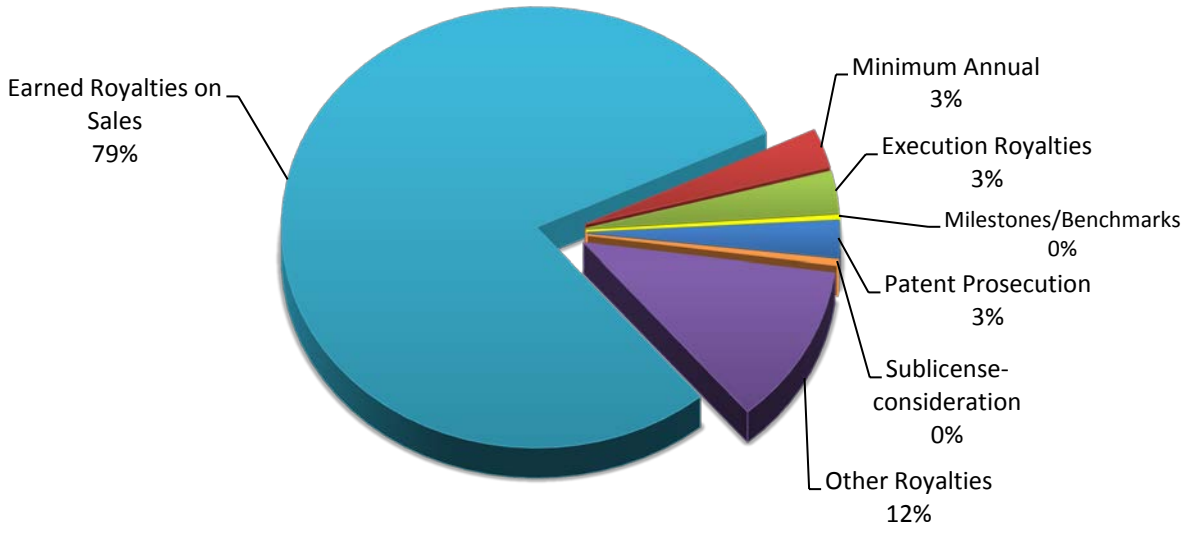
50
60

Sales of products built around licensed NIH and FDA inventions remain strong with 358 licensees reporting a total of $7B in sales of these products. While the total products sales by licensees increased 8% over FY12, the actual number of licensees reporting sales decreased 18%. This is in line with the increasing royalties from the top products. The license product pipeline has strengthened with 87 drug, vaccine, and device candidates undergoing clinical trials, an increase of 67% over last year.

Royalties collected on product sales account for 79%, primarily drugs and biologics, of the $116M in royalties collected in FY13 (see the chart below), with that percentage decreasing for the last two years. The top 20 products generating royalty income account for nearly 88% of the total royalty income. Thus, sales of a limited number of products generate the vast majority of the royalty income.

Royalty Income by Type



The FY13 technology transfer outcomes follow a long trend of successful licensing of biomedical inventions made by NIH and FDA scientists and reflect HHS's dedication to technology transfer — the broader economic impact of which becomes especially important during difficult economic times. While most of the royalty income collected by OTT is based on sales of pharmaceutical and biotechnological products and services, most of the actual products and services on the market under OTT licenses are research tools and reagents. Although the sales of research 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.

The three best-selling products utilizing technology licensed from NIH are Prezista™, a novel protease inhibitor for the treatment of HIV-1 in patients who are non-responsive to existing antiretroviral therapies, Gardasil®, a vaccine to protect against cervical

cancer, and Synagis®, a monoclonal antibody for the treatment of Respiratory Syncytial Virus in infants.

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

OTT successfully licensed rights in biological materials to PATH Vaccine Solutions for the development of *in vitro* diagnostics for onchocerciasis, lymphatic filariasis, and loa loa infection in humans. PATH originally received recombinant glutathione-S-transferase-OV16 fusion protein and an expression plasmid under a material transfer agreement (MTA) from the NIH National Institute of Allergy and Infectious Diseases. The interest was to develop a diagnostic for monitoring post-control areas for recrudescence and detection. PATH had a single-plex diagnostic that they sought to expand to multi-plex through incorporation of the GSV-OV16 protein. Under the MTA, PATH had successfully advanced their development of a diagnostic using these materials to the point that commercial application was possible and desired. However, the MTA limited PATH's use of the materials to non-commercial applications. Thus, PATH contacted OTT regarding negotiation of an appropriate license agreement. Given that PATH is a non-profit organization and the technology falls within the neglected tropical diseases (NTD) category, OTT used its non-profit license term sheet for NTDs that had been developed by OTT with advice from the major non-profits and NGOs working in this field. This term sheet provided a financial structure based on realizing product introduction to low- and low-middle income countries where the need is greatest. Although PATH's primary market was envisioned as being NTDs countries, they desired a worldwide license to allow the diagnostic to be widely offered as needed. Therefore, the non-profit term sheet had to be adjusted to reflect the change. The agreement itself addressed many aspects, including sublicensing, to enable PATH to accomplish their goals and ensure the public health and the NIH's interests would be best served through the agreement. As provided for under their agreement, PATH has sublicensed the NIH rights to Standard Diagnostics, Inc., a Korean-based company, for the diagnostics' manufacturing and distribution. PATH has publicized its plans to further partner with the African Programme for Onchocerciasis Control and other researchers to identify study sites for field evaluations beginning in Q1 2014. This license agreement forms the cornerstone of a Government-Non-Profit-Industry arrangement that represents a major step contributing to elimination of river blindness worldwide.

OTT executed an exclusive license agreement with PregLem, S.A., a Switzerland-based company focused on women's health. The license permits PregLem to develop ulipristal acetate, a selective progesterone receptor modulator derived from 19-norprogesterone, as the first non-surgical treatment of symptomatic uterine fibroid tumors that often cause infertility and uterine bleeding in women of all ages. The license is notable in that it highlights and recognizes for the first time the central role of the NIH National Institute for Child and Human Development and clinicians Dr. Lynnette Nieman and Dr. Diana Blithe in the development of this therapeutic agent. PregLem, S.A. has exclusively licensed the rights to ulipristal acetate from the NIH and its collaborator HRA Pharma and is marketing the compound as Esmya® in North America through the generic prescription drug manufacturer, Actavis plc (formerly known as Watson Pharmaceuticals).

In August 2013, OTT granted a Start-up Exclusive Patent License Agreement aimed at developing an anti-cancer drug for human use. The licensed technologies originated in the laboratories of NIH National Cancer Institute scientists, Joseph E. Saavedra, Larry Keefer, and Aloka Srinivasan. The underlying technologies are O^2-arylated, O^2-glycosylated, and O^2-substituted 1-[(2-carboxylato) pyrrolidin-1-yl] diazeniumdiolates. These compounds contain an N_2O_2 functional group and generate nitric oxide upon degradation. These derivatives are stable in neutral to acidic environments and are potentially suited to deliver nitric oxide to basic or nucleophilic compartments of the body. These compounds may be useful for inactivating proteins to prevent detoxification of chemotherapeutic agents or disruption of proteins active in tumor formation, infection, or regulatory activities. Overall, these compounds may be applicable toward a wide variety of processes involving nitric oxide. These technologies have been licensed to JSK Therapeutics, Inc. (JSKT) of Salt Lake City, Utah, a start-up pharmaceutical company with a focus in cancer treatment spun off from the University of Utah. JSKT plans to pursue Acute Myeloid Leukemia (AML) as its first oncology indication. Current therapies for AML are particularly cytotoxic and difficult for older individuals who constitute the majority of subjects presenting with AML. Development of a new agent that works synergistically with current chemotherapy drugs and prevents bone marrow suppression could benefit older patients with this rapidly debilitating bone marrow malignancy that is fatal in the vast majority of cases.

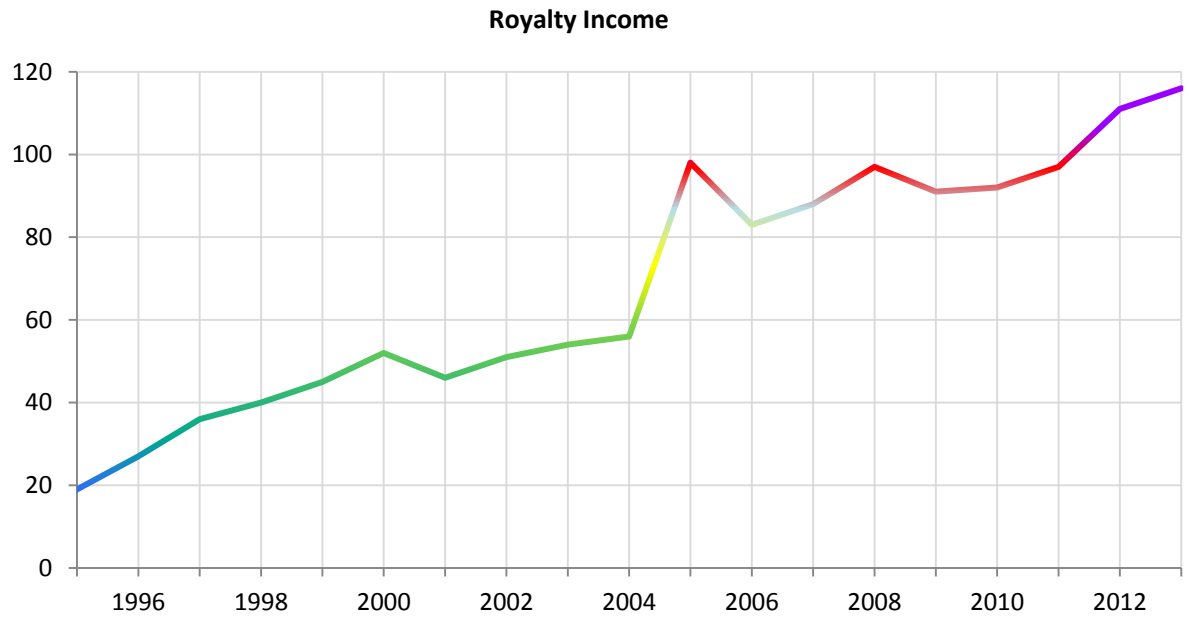
Royalty Administration

While the essential purpose of the technology transfer process is to improve public health and safety, the collection of royalties is an important by-product. Royalties collected from licensees of intramural research program inventions are distributed to the inventors, the Institutes and 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 payments, patent reimbursement costs, 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 or services. By far, the largest amount of royalty funds is received on sales of products. Royalty collections fluctuate from year to year as a result of factors such as sales volume, FDA approvals (when needed), competitive market forces, changes in standard of patient care, license termination when patents expire, etc. The intramural laboratories use the income to pay technology transfer expenses (such as patent expenses and technology transfer administrative costs) and to support research and training programs, including the purchase of expensive laboratory instrumentation or pharmaceuticals for clinical trials. Royalty funds thus support biomedical research and development activities that might otherwise remain unfunded.

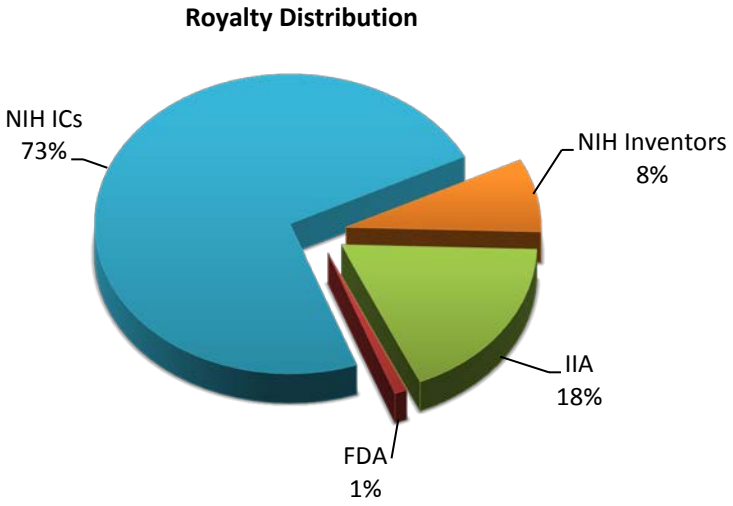
In FY 13 OTT licensees continued to have the option of paying royalties directly through Pay.Gov, a web-based royalty payment application that allows companies to make Automated Clearing House (ACH) payments by debit from a checking or savings account. It has been integrated into the new electronic Research Materials (eRMa) website. Previously, companies had to use systems falling into historical disuse, such as wires to lock boxes and paper checks. Since its launch, OTT licensees have used the system with ease and significant speed of payment over conventional check payment systems. With respect to research materials, where ready access is needed for important research programs, rapid processing by the system permits NIH to expedite the release of these vital materials. For these reasons, Pay.Gov was also integrated into the new electronic Research Materials (eRMa) website.

OTT administered $116M in royalties in FY13 with 74% of the total going to the NIH ICs and the FDA and 8.2% to inventors. NIH distributed 17.9% of the royalties under Inter-Institutional Agreements (IIAs) to our extramural partners that co-owner some of the licensed inventions.

This royalty income was received under 782 license agreements from 483 companies, or their subsidiaries, 76% of which are based in the US. Royalty levels continued an upward trend with almost a 5% increase over FY12, setting a record high. Although royalties on some products decreased in FY13, others have been steadily increasing over the last few years with about three-quarters of all royalty income now coming from product sales of five technologies. This also means that future royalty income will be highly sensitive to changes in sales of these products and expiration of patent licenses until major new products in the pipeline reach the market.



In accordance with statutory requirements and NIH policy, inventors under a given license receive annually the first $2,000 in royalties; 15% of royalties above $2,000 and up to $50,000; and 25% of royalties in excess of the first $50,000 up to a cap of $150,000 per year per inventor. Inventors who have assigned their inventions to the US Government receive royalty payments even when they retire or move to other institutions. In FY13, 1,039 inventors received royalty payments amounting to $9.6M. Of these, 101 were first-time recipients, a 17% increase over last year, and 25 received the statutory cap, a decline of 8%.



During this fiscal year, OTT identified patent prosecution costs amounting to $3.2M.

Monitoring and Enforcement

To ensure compliance with license obligations and development of licensed technologies, OTT maintains a monitoring and enforcement program for its portfolio of 1,315 active license agreements. During FY13, 69 licenses expired and 66 licenses were terminated, seven of which were "for cause" and the remainder at the request of the licensees. OTT identified and investigated four cases of alleged infringement of NIH and FDA patents (10 less than last year). These cases were closed either through licensing, lack of sufficient evidence, or by the company's voluntary withdrawal of the infringing product. At no time, however, did NIH ask for a 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 98.6% of royalties due. OTT terminated seven licenses for non-compliance during the year, slightly higher than FY12. Additionally, OTT contracted with firms to conduct external audits of two licensees with significant licensed product sales to verify proper payment under the terms of the license. Overall, OTT's enforcement activities ensured proper payments by licensees and resulted in the collection of over $3.1 million in overdue royalties.

Policy Activities

The scope of OTT's formal and informal policy activities is broad, including biomedical technology transfer and intellectual property matters and support of legislative affairs. Leveraging the experience of NIH and US universities in technology transfer, OTT drafts and communicates policies and procedures to enhance the translation of early-stage technologies into practical application for the benefit of public health. OTT, working through the NIH Office of Legislative Policy and Analysis, serves as a resource for NIH review of 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 within HHS as well as across the Federal Government.

Among its administrative duties, OTT provides the agency determination for requests by the extramural and intramural communities for waivers of rights in inventions. In FY13, OTT reviewed five extramural waiver requests, comprising one request to waive title to inventors and four requests to waive the US manufacturing requirement. OTT also reviewed six requests to waive title to intramural inventors.

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 CDC, and the FDA in establishing and modifying, as appropriate, PHS technology transfer policies. In that capacity, OTT led work groups, which included representatives from the PHS technology transfer community, to complete the comprehensive review of policies and procedures related to patenting, licensing, Cooperative Research and Development Agreements, material transfer agreements, royalty disbursement, and extramural activities.

Members of OTT actively participate in a wide array of NIH and US Government projects that address programmatic components of technology transfer. Within the NIH, OTT 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 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 within 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 is actively involved with the HHS Innovation Council and other intra-governmental efforts to apply innovative tools to enhance technology development and transfer.

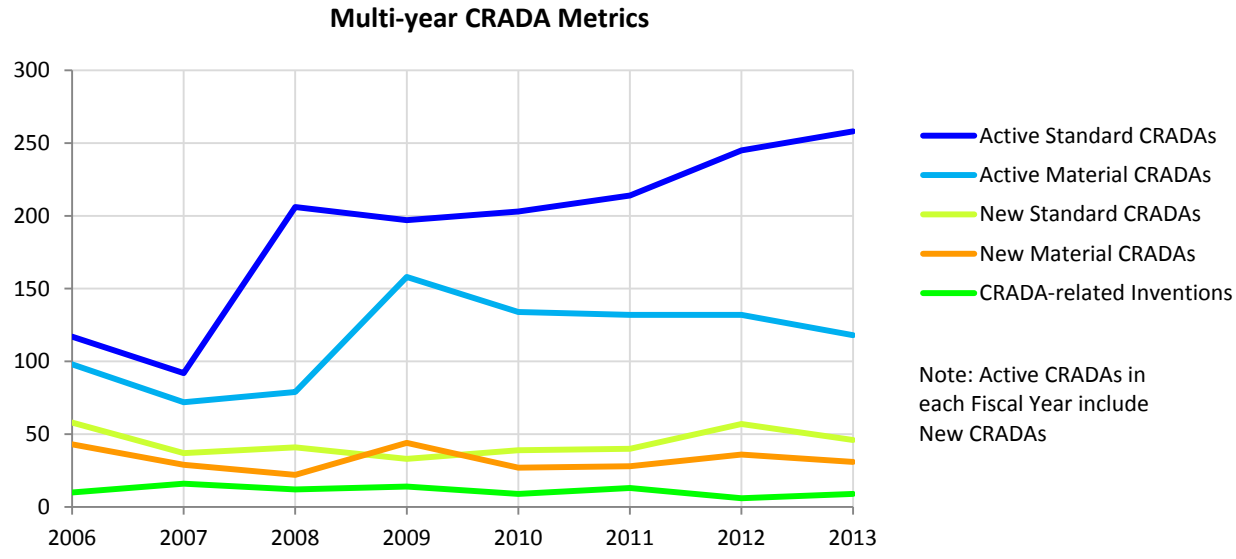
OTT staff served as advisors to NIH and HHS on many *ad hoc* issues related to technology transfer and intellectual property, including gene diagnostic technologies, stem cells, biotechnology patenting, patent reform, mouse model access, and NIH's drug rescue and repurposing program.

In support of negotiations of inter-institutional agreements between NIH and university collaborators, OTT 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 facilitated efforts to update the various material transfer agreement models and 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 pursuit of common goals. CRADAs are negotiated by technology transfer staff in the ICs. OTT collates and administers CRADA data and serves as a member of the NIH CRADA Subcommittee, which reviews all NIH CRADAs. While there are various mechanisms that support collaboration between companies and NIH scientists, the CRADA is the only mechanism that permits the NIH to offer an exclusive option to license inventions that could be made within the scope of the collaboration agreement and, to the extent contemplated, allows laboratories to receive funds from the company collaborator. NIH is not legally permitted to transfer funds to the collaborator under a CRADA but can collaborate with companies receiving funds under separate awards, such as SBIR or STTR.

During FY13, there were 377 active CRADAs; 258 were standard CRADAs and 118 were Materials-CRADAs (a way to transfer a company's proprietary materials to the NIH for research purposes). During the year, NIH executed 77 new CRADAs; 46 of which were standard and 31 were Material-CRADAs. Eighty eight percent of these were with US companies and 38% of these are small businesses. The number of new CRADAs executed in FY13 decreased 17% compared to FY12, and the percentage of new CRADAs with small US companies dropped significantly. This last year, nine CRADAs led to inventions reported by NIH or FDA researchers at nine different NIH Institutes.



CRADAs are complex documents, due in large part to the wide variety of statutory and policy requirements involved. CRADAs negotiations can thus be a time-consuming activity, delaying promising science until the terms of the agreement can be agreed upon. This year the technology transfer offices in the NIH ICs and the OTT finished a comprehensive review of CRADAs with the intent of moving the document away from a "model" approach to a "term sheet" approach. As part of this process, NIH is designing an online system, named CRADA Builder, which would allow NIH, CDC, and the FDA to generate agreements using a series of guided questions to tailor the terms to the specific needs of the collaboration. The new system should be available by the spring of 2014.

Other Initiatives

ENTREPRENEURSHIP AND ECONOMIC DEVELOPMENT

In FY13, OTT continued its active participation in entrepreneurship and economic development activities that support the development of new innovative biomedical products.

One of the highlights of the year relating to entrepreneurship and economic development was activities that OTT undertook again with BioHealth Innovation (BHI) under a Partnership Intermediary Agreement (PIA). BHI is a regional private-public partnership in Maryland focusing on commercializing market-relevant health innovations and increasing small company access to early-stage funding. In expanding one of the first projects under the PIA, BHI employed and placed a second Entrepreneur-in-Residence (EIR) within OTT to help evaluate and identify licensing opportunities from the intramural research programs in the area of diagnostics and medical devices and thus expand upon the existing EIR's focus on therapeutics. An OTT EIR is an industry expert with scientific, entrepreneurial/managerial, and financial experience who works with NIH to identify, evaluate, and support the development of new start-up companies based upon technology license agreements from OTT. EIRs do not have access to proprietary information OTT receives from companies seeking or obtaining licenses. During the past year NIH benefited from BHI's assistance in evaluating the commercial potential of technologies via BHI's mentoring of the NIH Entrepreneur and Commercialization Club, which invites scientists from the post-doctoral community to explore the commercialization potential of intramural technologies as an educational exercise.

A second major effort for the year was the expanded project with the Carey Business School at Johns Hopkins University in Baltimore, which conducts graduate level business educational programs with a specific focus on healthcare and health technology development. Operating under a Memorandum of Understanding Agreement, OTT staff worked with MBA students and faculty in their "Discovery 2 Market" classes for feasibility analysis and recommendations regarding technologies from the portfolio of NIH and FDA intramural inventions. In FY13, this program was expanded to include MBA students in classes at both the Baltimore, MD, and Washington, DC, campuses of the university. By providing actual current healthcare-related inventions for student analysis, OTT licensing and patenting managers receive additional feedback and insight into the market dynamics and commercial potential associated with inventions in their portfolios. As a result, NIH technology managers received several promising leads for both licensing and research collaborations with industry.

EDUCATIONAL AND TRAINING PROGRAMS FOR SCIENTISTS

FY13 was also very busy year in terms of educational and training activities conducted by OTT staff in the areas of technology transfer and entrepreneurship.

One of the most popular programs were the courses organized or delivered by OTT staff members for the "Advanced Studies in Technology Transfer" certificate program hosted by the Foundation for Advanced Education in the Sciences (FAES) Graduate School at NIH. Interest in technology transfer training remained strong with this non-degree program receiving the largest enrollment of any at the FAES Graduate School at NIH. Class offerings grew to more than 20 different courses, ranging from "Introduction to Technology Transfer" to "Translational Medical Product Development."

OTT staff members were again co-organizers and speakers for several programs with the National Council for Entrepreneurial Tech Transfer (NCET2). These included the "Research Commercialization Webinar Course," an introductory course given via the web during the spring and fall semesters, as well as the "University Start-Ups Conference" annual meeting and workshop at the Washington Convention Center.

Staff members also organized and participated in the "Chief Science Officer Boot Camp" Program in conjunction with Montgomery College, Montgomery County Department of Economic Development, FAES Graduate School at NIH, and Human Work Flows, LLC. This program is designed to prepare academic and federal scientists for research jobs in industry.

For the NIH Research Festival this year, OTT organized and moderated a symposium entitled "Commercial Development of My Own Research Discoveries: Personal Stories of Former NIH Scientists" and presented two posters – one on "Careers in Technology Transfer & Business Development for Scientists" and another on "Technology Transfer Education Opportunities."

Other Accomplishments

NATIONAL & REGIONAL AWARDS

Members of the Office were recognized with regional and NIH awards for their significant contributions to technology transfer as well as the overall mission of NIH. These included three group and two individual NIH Office of the Director Honor Awards, three Federal Laboratory Consortium (FLC) National Awards, four FLC Mid-Atlantic Region Awards and the "Deal of Distinction Award" from the Licensing Executives Society.

PUBLICATION

"If the Sky Were the Limit, What Would You Do In Technology Transfer?"*Gary Keller, Fizie Haleem, Steven Ferguson, Al Jordan and Cheryl Cejka, les Nouvelles, Volume XLVIII No. 1 pp 66-70 (March 2013).*