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STATEMENT OF

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INTRODUCTION

Good afternoon, Chairman Smith, Ranking Member Bass, and Members of the Subcommittee. I am Dr. Jesse L. Goodman, Chief Scientist at the Food and Drug Administration (FDA or the Agency), which is part of the Department of Health and Human Services. I appreciate the opportunity to be here today to discuss FDA's role with respect to rare and neglected diseases.

There are approximately 7,000 rare diseases, generally defined by the Orphan Drug Act (ODA) as diseases affecting fewer than 200,000 people in the United States, and numerous neglected diseases that predominantly affect impoverished or disenfranchised populations of the developing world. In addition, the World Health Organization (WHO) has identified 17 neglected tropical diseases globally. While the number of people affected with each rare disease is small, collectively, rare diseases affect approximately 1 in 10 people in the United States (around 30 million Americans), and around the world, more than 1 billion people are affected by at least one neglected disease. For these reasons, rare and neglected diseases are a major public health concern. As a practicing physician and researcher specializing in infectious diseases and also trained in oncology, I have personally witnessed the devastating human face of diseases like these.

Infectious diseases know no boundaries. Threats to health anywhere are threats to everyone. For example, in recent months, outbreaks of avian influenza in China and of Middle East Respiratory Syndrome coronavirus have captured global attention and spurred preparedness efforts in the United States. Witness the risks to the United States from extensively drug-resistant TB and the disruption that a single infected traveler caused in 2007. In May 2010, the Centers for Disease Control and Prevention (CDC) reported that, for the first time, cases of dengue, the most

common mosquito-borne viral disease causing 50 to 100 million infections and 25,000 deaths each year around the world, were identified in Florida residents who had not traveled overseas.[1] These compelling global humanitarian needs, as well as our desire to do all we can to protect our own nation's health and national security, require us to bring the best possible science to bear against rare and neglected diseases. For all of these reasons, the needs and opportunities are enormous and FDA, working with government partners, industry, and non-governmental organizations, can help make a real difference.

I appreciate the opportunity to briefly highlight some of FDA's many activities in encouraging and speeding the development of drugs, vaccines, devices, and diagnostic tests for rare and neglected diseases.

The Orphan Drug Act (ODA)

ODA, passed in 1983, created financial incentives, including grants, to support the development of new drugs for people with rare diseases. Under this system, developers of promising drugs, including biologics, can apply to receive "orphan designation." Orphan designation provides three main financial incentives for the development of products for qualifying rare diseases. First, the sponsor can receive tax credits of up to 50 percent on clinical trial costs associated with studying the designated drug for that rare disease. Second, the sponsor is eligible for a waiver of the user fee associated with that marketing application. Third, if a designated drug is subsequently shown to be safe and effective and receives marketing approval, the sponsor may be eligible to receive market exclusivity for seven years. This program also benefits those affected by neglected diseases, as drugs for the treatment of the neglected diseases of the

[1] *http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5919a1.htm*

developing world often also qualify as orphan drugs because they affect fewer than 200,000 people in the United States.

Since its passage 30 years ago, ODA has been extremely successful. In the decade prior to passage of ODA, there were fewer than 10 drug approvals for orphan diseases that were sponsored by industry, but since passage, more than 2,800 drugs and biologics have been officially designated as "orphans," and approximately 440 have gone on to full marketing approval.

ODA also established the Orphan Products Grant Program to encourage clinical development of products for use in rare diseases. Since the grant program's inception 30 years ago, over $290 million has been used to fund over 530 clinical trials. Approximately 10 percent of all approvals of products for rare diseases have been supported, in part, by the Orphan Products Grants Program. This program also can help support important work on diseases that predominantly affect impoverished populations of the developing world. Currently, for example, we are funding a study of rifapentine for pulmonary tuberculosis and a study of AQ-13 for the treatment of drug-resistant malaria.

ODA's fundamental principles have been adopted by many other countries, most notably by the European Medicines Agency (EMA) in 1999. While FDA remains a world leader in orphan drug regulation, this international attention to orphan drugs, combined with Internet linkages among patient groups and a pharmaceutical industry without borders, has made global harmonization an important component of the work at FDA. EMA and FDA now have a joint application form for orphan designation.

FDA's Office of Orphan Products Development (OOPD) serves as a focal point for FDA's efforts to address rare diseases, including efforts on global harmonization for orphan drugs. OOPD was created shortly before the passage of ODA, and it administers the orphan drug designation program, among others. OOPD also fosters inter-agency collaboration to further the development of medical products for rare diseases and to help address the needs of rare disease patients. To facilitate this interaction, in 2012, OOPD spearheaded the creation of the FDA Rare Disease Council. This Council, which consists of representatives from all of the Centers and Offices within the Agency who work on rare disease issues, meets regularly to ensure appropriate communication, coordination, and collaboration on rare disease issues.

Generating Antibiotics Incentives Now (GAIN)

There is now also new support for stimulating the development of new antibiotics, which are often important for neglected diseases. FDA is implementing Title VIII of the Food and Drug Administration Safety and Innovation Act (FDASIA) entitled "Generating Antibiotics Incentives Now" or GAIN. The new law provides an additional five years of exclusivity to be added to certain exclusivity periods already provided by the Federal Food, Drug, and Cosmetic Act for certain antibacterial and antifungal drugs intended to treat serious or life-threatening infections, including serious or life-threatening infections caused by antibacterial- or antifungal-resistant pathogens (including new or emerging pathogens), and serious or life-threatening infections caused by qualifying pathogens; these drugs are designated as "qualified infectious disease products." Under GAIN, an application for a qualified infectious disease product is eligible for both Priority Review and Fast Track designation, programs for expediting drug development that are described below. As of the beginning of the month, FDA had designated 17 products (12 distinct active moieties) as qualified infectious disease products under GAIN.

The list of qualifying pathogens will be listed and revised by FDA through regulation; the proposed list of qualifying pathogens published recently and includes *Mycobacterium tuberculosis.*

Expediting Drug Development for Serious or Life-threatening Conditions

FDA has a number of programs intended to facilitate and expedite development and review of new drugs, including biologics, to address unmet medical needs in the treatment of serious or life-threatening conditions. These expedited programs help ensure that therapies for serious conditions are available as soon as it can be concluded that the therapies' benefits justify the risks, taking into account the seriousness of the condition and the availability of alternative treatment.

Fast Track designation is intended to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need. Designation may be granted on the basis of preclinical or clinical data. Fast Track designation typically supports both early and more frequent interactions with FDA during drug development. In addition, sponsors can submit portions of a Fast Track marketing application as they are ready and before submitting the complete application, using a practice that is known as rolling review.

The Accelerated Approval pathway can be used to expedite the development and approval of promising therapies that treat a serious or life-threatening condition and provide meaningful therapeutic benefit over available therapies. Accelerated Approval allows approval of a drug that demonstrates an effect on a "surrogate endpoint" that is reasonably likely to predict clinical benefit, or on the basis of an effect on a clinical endpoint that can be measured earlier than effect on survival or irreversible morbidity, that is reasonably likely to predict an effect on irreversible

morbidity or mortality or other clinical benefit. One of the major goals of FDA's regulatory science efforts and collaborations is to help develop better clinical or biologic markers that can predict benefit, which can help both in drug and vaccine development and speed product approval.

FDA has long had in place a review system to ensure that the most critical medical products are reviewed on a priority basis. The goal for Priority Review applications for products that offer major advances in treatment, or provide a treatment when no adequate therapy exists, is to complete them within a six-month period, compared to the 10-month goal for standard review of other products.

The Food and Drug Administration Amendments Act of 2007 (FDAAA) granted FDA the authority, beginning in 2009, to award Priority Review vouchers to a company that submits and, after review, receives marketing approval for certain products for one of 16 neglected "tropical" diseases listed in the legislation. If transferred to apply to a blockbuster drug, the four months of earlier market access available when a Priority Review voucher is redeemed could, in some circumstances, be very valuable. Two such vouchers have been granted for two rare diseases: Sirturo for the treatment of multi-drug resistant tuberculosis and Coartem for the treatment of acute, uncomplicated malaria infections. These approvals are discussed below.

More recently, to further encourage the development of drugs and biologics for the prevention and treatment of rare pediatric diseases, FDASIA authorized FDA to award Priority Review vouchers to sponsors upon approval of certain rare pediatric disease product applications that meet specific criteria that the law enumerates.

FDASIA also established another program, intended to expedite the development and review of drugs for serious or life-threatening conditions, known as Breakthrough Therapy designation. To obtain a Breakthrough Therapy designation, a drug must be intended to treat a serious or life-threatening condition, and preliminary clinical evidence must demonstrate that the drug may provide substantial improvement on at least one clinically significant endpoint over available therapy. A Breakthrough Therapy designation conveys all of the Fast Track program features, as well as more intensive FDA guidance for an efficient drug development program, including an organizational commitment to involve senior managers and experienced review staff.

The Humanitarian Use Device Designation (HUD) and Humanitarian Device Exemption (HDE) Programs

The HDE pathway refers to a premarket approval application submitted seeking an exemption from the otherwise applicable effectiveness requirements for devices. In order to be eligible for marketing approval under the HDE pathway, devices must first be designated as a HUD. This first step, performed by OOPD, evaluates whether the device benefits patients in the treatment or diagnosis of a disease or condition that affects fewer than 4,000 individuals in the United States per year. To receive approval from FDA under the HDE marketing pathway, the device must meet certain criteria, including a determination by FDA that the probable benefits outweigh the risks of injury or illness from use of the device and that there is no comparable device. Recent examples of devices granted an HDE include the Berlin Heart EXCOR Pediatric Ventricular Assist Device and the Argus II Retinal Prosthesis System. The Berlin Heart is designed to assist pediatric patients with heart failure while they await a heart transplant. The Argus II Retinal Prosthesis System is a device implanted in the eye to improve the visual function of patients with advanced retinitis pigmentosa, a rare genetic eye disease that often leads to total blindness.

Diagnostic Tests for Tropical Diseases

FDA's Center for Devices and Radiological Health (CDRH) has worked with manufacturers, other government agencies, and WHO to successfully foster the development of diagnostics for tropical diseases, including those considered neglected. CDRH is an active consultant to WHO for its pre-qualification program to help assess and make available effective new diagnostics for developing countries. CDRH also provides recommendations to many sponsors through the pre-submission consulting and an interactive review process.

Close cooperation with CDC has resulted in recently cleared diagnostic tests for dengue and Emergency Use Authorization for Middle East Respiratory Syndrome. Similar cooperation with the Department of Defense and manufacturers has resulted in breakthrough rapid diagnostics for malaria. Ongoing efforts to reclassify TB diagnostics will substantially reduce barriers to the development of rapid diagnostics for TB and multi-drug-resistant TB. FDA's Center for Biologics Evaluation and Research (CBER) has also been very active in performing research and helping provide needed standards, often as part of international collaborations, to improve diagnosis of tropical and neglected diseases; for example, TB, malaria, dengue, and Chagas disease, particularly in terms of ensuring safety of our blood supply. Ongoing cooperation with CDC, WHO, and others in developing diagnostic and blood-screening tests for emerging infectious diseases will help ensure their availability when needed.

Other FDA Efforts to Enhance Development and Review of Products to Treat Rare Diseases

In February 2010, FDA created a position of Associate Director for Rare Diseases in the Center for Drug Evaluation and Research (CDER), which has since expanded to become the Rare Diseases Program (RDP). The RDP's mission is to facilitate, support, and accelerate the development and approval of products to treat rare diseases. RDP responsibilities include,

among others, the development of rare-disease-specific guidance, policy, and procedures, education and training programs for the review and approval of treatments for rare diseases, and enhanced collaborations with external and internal rare disease stakeholders. FDASIA included provisions for the expansion of RDP and the establishment of a rare disease liaison in CBER. FDASIA also included additional provisions promoting rare disease efforts, including, but not limited to: enhanced opportunities for interaction between FDA and rare disease patient representatives, and the aforementioned Pediatric Rare Diseases Priority Review Voucher program and expanded profit provisions for HUDs approved under an HDE.

FDA Rare and Neglected Disease Review Groups

In March 2010, FDA established two expert working groups, the Rare Disease Review Group and the Neglected Disease Review Group, to make recommendations on appropriate preclinical, trial design, and regulatory paradigms as well as optimal solutions to prevent, diagnose, and treat: (1) rare diseases; and (2) neglected diseases of the developing world.[2] FDA held public meetings in 2010 and in 2011 to discuss these issues and submitted its recommendations to Congress. These recommendations included increasing the foundation of biomedical and regulatory science to support development of products for rare diseases, increasing collaboration within and outside FDA, analyzing the history of orphan drug approvals to identify effective development approaches, and issuing guidance documents on neglected-disease-related topics.

Collaboration with Stakeholders

FDA has participated in a number of stakeholder conferences, workshops, and meetings to foster education and to promote the development of products for rare and neglected diseases. FDA is enhancing collaborations to increase transparency, advance science, share advice, and establish

[2] Section 740 of the 2010 Appropriations Act, Public Law 111-80, directed FDA to establish these review groups.

new programs with several pertinent organizations, such as the National Organization for Rare Disorders (NORD); the National Institutes of Health's (NIH) Office of Rare Diseases Research, Therapeutics for Rare and Neglected Diseases Program, and other NIH Institutes and Centers; the Critical Path to TB Drug Regimens Initiative, patient advocacy groups; academia; and the Institute of Medicine (IOM).

The following are a few examples:

1. On March 1, 2012, FDA hosted the first ever FDA Rare Disease Patient Advocacy Day to enhance the rare disease patient advocacy community's awareness of FDA's roles and responsibilities in the development of products for rare diseases.
2. FDA partnered with NIH to conduct two important scientific workshops: The first to discuss the role of natural history studies in the development of therapies for rare diseases and the second to focus on small clinical trial design and statistical issues.
3. In collaboration with NORD, NIH, the Drug Information Association, and Duke University Medical Center, FDA presents an annual regulatory education and training program for external stakeholders, the "United States Conference on Rare Diseases and Orphan Products."
4. FDA has hosted multiple orphan product designation workshops in the United States, Europe, and India to educate and collaborate with national and international stakeholders in furthering the development of medical products for rare diseases.

In addition, FDASIA includes a requirement for a public meeting to discuss ways to encourage and accelerate development of new therapies for pediatric rare diseases.

Global Collaboration

FDA recognizes the tremendous needs and opportunities to engage globally to solve the problems of rare and neglected diseases. FDA has traditionally worked closely and interactively with manufacturers to evaluate and approve vaccines intended for the U.S. population. However, new paradigms of vaccine development supported by the Gates Foundation and other initiatives to prevent or treat diseases, often endemic outside the United States, have provided FDA an impetus for the development of new regulatory strategies and support for resolving key regulatory science issues. In 2008, FDA issued guidance on the development of vaccines to protect against global infectious diseases. The guidance helps facilitate the development and review of such vaccines and has been extremely well-received by the global health community. FDA scientists also played an important role, along with our colleagues at CDC and NIH, in developing the Global Vaccine Action Plan, which was recently adopted by the World Health Assembly and was particularly involved in its recommendations in support of vaccine research and development.

We are also actively involved in efforts to collaborate with and, where requested, assist foreign regulators, in assessing vaccines and in helping to ensure their quality and safety. A core component of FDA's efforts in this regard is its commitment to support and complement the efforts of WHO. FDA's contribution to the WHO vaccine quality and safety goals is long-standing and was formalized in 1998, with its designation as a Pan American Health Organization (PAHO)/WHO Collaborating Center for Biological Standardization. In recent years, FDA's support has grown beyond the routine collaboration of providing expert input to WHO consultations and laboratory collaborations for international reference standards. FDA now is an active key partner with WHO in its vaccine pre-qualification program and its efforts to build regulatory capacity in developing countries.

The vaccine pre-qualification program is a service provided by WHO to United Nations agencies that purchase vaccines, providing independent guidance and advice to the United Nations on the quality, safety, and efficacy of vaccines being considered for purchase. This assistance helps to ensure that each vaccine under consideration is suitable for target populations and complies with established standards of quality. In 2007, WHO designated FDA as a "reference" national regulatory authority (NRA) for WHO pre-qualified vaccines. In 2008, FDA and WHO signed confidentiality agreements specific to communications that would be undertaken in the context of the WHO vaccine pre-qualification process. Currently, FDA's CBER is the reference NRA for a total of eight U.S.-licensed vaccines, attesting to their safety, efficacy, and quality and facilitating their worldwide use.[3]

CBER provides support to multiple WHO scientific working groups and to several WHO regional vaccine networks to enhance scientific and regulatory capacity needed to ensure the development of high-quality vaccines. Specifically, CBER actively engages with WHO's Developing Country Vaccine Regulator Network (DCVRN), a WHO-funded network of NRAs from Brazil, China, Cuba, South Korea, India, Indonesia, the Russian Federation, South Africa, and Thailand. The DCVRN builds regulatory capacity among vaccine-producing developing countries through information sharing, training, and mentoring activities. Representatives from member DCVRN countries meet on a biannual basis to gain timely information from independent experts and developers on specific issues relating to vaccine trials occurring in

[3] Rotavirus Vaccine, Live, Oral, Pentavalent (Tradename: RotaTeq®); Prequalified Oct 7, 2008; Influenza Virus Vaccine (Tradename: Fluvirin®); Prequalified Dec 4, 2009; Influenza A (H1N1) 2009 Monovalent (No tradename; Manufacturer: Novartis Vaccines and Diagnostics Limited), Prequalified by WHO Dec 9, 2009; Pneumococcal 7-valent Conjugate Vaccine (Diphtheria CRM197 Protein)(Tradename: Prevnar®), Prequalified by WHO Dec 28, 2009; Influenza Virus Vaccine (Tradename: Fluzone®), Prequalified Jan 21, 2010; Influenza A (H1N1) 2009 Monovalent (No tradename; Manufacturer: Sanofi Pasteur, Inc.), Prequalified Jan 27, 2010; Influenza A (H1N1) 2009 monovalent (No tradename; Manufacturer: MedImmune LLC), Prequalified Feb 25, 2010; ; Meningococcal ACYW-135 Polysaccharide, ten dose vial (Tradename: Menomune; Manufacturer: Sanofi Pasteur), Prequalified by WHO, May 22, 2013.

developing countries and to develop institutional plans and other activities that aim to strengthen regulatory capacity.

CBER provides expert input to the WHO African Vaccine Regulatory Forum (AVAREF). WHO coordinates this forum, in conjunction with the WHO African Regional Office, to assist in defining the role of NRAs of African nations in regulating clinical trials of vaccines, in interactions with national and local Institutional Review Boards (IRB) and ethical committees, and in strengthening the capacity of the NRAs to regulate new products. In this capacity, FDA participates as expert advisors, providing guidance on how to evaluate the safety and efficacy of investigative products.

In addition to rich global collaborations in the vaccine area, FDA is actively collaborating on global drug and diagnostic efforts and has joined the Executive Committee of the International Rare Diseases Research Consortium (IRDiRC), launched by the European Commission and NIH in 2011. IRDiRC's goals are to develop 200 new therapies for rare diseases, and to develop diagnostic tests for most rare diseases, by 2020.

It is not only critical to develop new drugs, vaccines and diagnostics, but also to make sure people in need have access to safe and effective currently approved products. Counterfeit and substandard medicines are serious problems that occur commonly in Asia and Africa and have been well-documented to lead to treatment failures and deaths and, potentially, to the exposure of already-sick people to contaminants and toxins often found in such medicines. Subpotent anti-infective drugs can also foster the development of antibiotic resistance, when infections are inadequately treated. For example, malaria kills more than 660,000 people globally each year, mostly children. Compromised anti-malarial medicines, often ranging in surveys from 10-50 percent or more of the available drug supply in some countries, typically have too little or none

of the labeled active ingredients, preventing adequate and timely treatment. Anti-malarial medicines made with subpotent dosages of active ingredients will not cure patients, and they can lead to resistant strains of the parasite, making it tougher to treat malaria, even with authentic medicines.

In a recent report[4] commissioned by FDA, IOM concluded that making counterfeit detection technology more accessible to low- and middle-income countries would be invaluable in controlling the trade in counterfeit, falsified, or substandard medicines. In April 2013, FDA announced a unique public-private partnership to help identify counterfeit or substandard anti-malarial medicines, including falsified products, with the deployment of the FDA-developed Counterfeit Detection Device, called CD-3. The partnership includes the Skoll Global Threats Fund, the U.S. Pharmacopeia (USP), NIH, CDC, and the multi-agency President's Malaria Initiative (PMI), which is led by the U.S. Agency for International Development (USAID). The partnership will focus on evaluating and optimizing the use of the handheld CD-3 to identify counterfeit or substandard anti-malarial medicines, including falsified products, in Africa and parts of Southeast Asia, where the rates of malaria infection are high and where counterfeit anti-malarial medicines are prevalent.

The effectiveness of the tool in detecting counterfeit or substandard versions of two common anti-malarial therapies will be tested in Ghana in 2013 and 2014. The USP's Promoting the Quality of Medicines Program (PQM), with funds from USAID and PMI, collaborates with the Ghanaian Food and Drug Authority to conduct drug surveillance programs at test sites in Ghana, and the new partnership will leverage this existing infrastructure. CDC and NIH will provide

[4] *http://www.iom.edu/Reports/2013/Countering-the-Problem-of-Falsified-and-Substandard-Drugs.aspx*

technical support, and The Skoll Global Threats Fund will provide additional funding for the initial testing program in Ghana.

The Role of Regulatory Science

Researchers have now defined the genetic basis of more than 2,000 rare diseases and identified potential drug targets for many rare and neglected diseases. However, a large gap exists between advances in basic scientific research and needed applied product development and evaluation research, a gap that contributes to the lack of real products getting to patients for many such diseases. This gap can be filled in part through enhanced regulatory science, which is the development of tools, methods, assays, standards, and models that help speed and improve the development, review, and approval of innovative products. In particular, there is a need for better approaches to assess the effectiveness of candidate drugs and vaccines for neglected diseases, and to perform more efficient and simpler clinical trials, often under challenging field circumstances. Better models of disease and diagnostics are especially needed for rare diseases. In addition, better predictive biomarkers, that is, measurements that can help predict whether a treatment or vaccine will be safe and effective and potentially do so faster than waiting for what are often long-term clinical outcomes, can be extremely powerful and helpful in developing products for both rare and neglected diseases. Examples of applied regulatory science research at FDA in these areas include development of a new model to help develop drugs and vaccines against leishmaniasis (a disease that also can affect U.S. citizens who have lived or worked in the Middle East) and research to identify correlates of protection that could predict vaccine efficacy against TB. With respect to TB, FDA has also supported several researchers to develop better tools that can predict long-term cure of TB (or, conversely, identify hidden or latent TB) and the efficacy of drug combinations.

Also with respect to TB, which generally requires treatments with combinations of drugs and where drug resistance is an urgent problem, FDA issued science-based guidance that addresses the study in a more timely and less-costly manner of several new drugs in combination, rather than studying each one separately. FDA is partnering with the Critical Path to TB Regimens Initiative (CPTR), launched by the Gates Foundation, a collaboration of industry, civil society, government, and global regulatory officials. The collaboration is working to develop needed data standards that can allow researchers to combine and evaluate data from multiple studies.
A remarkable example of how regulatory science can contribute to global health is in the recent development of a new vaccine to protect people against the Serogroup A meningitis, which causes devastating epidemics in parts of Africa. Working through a unique public-private partnership, the Meningitis Vaccine Project, FDA scientists developed and made available an innovation that allowed a safe and effective vaccine to be produced efficiently and at greatly reduced cost. To date, over 100 million people have been vaccinated, and this dreaded disease dramatically reduced in incidence across what had been called the "meningitis belt."

Strong science, whether lab-based, clinical, or involving population and statistical sciences, is also critical in supporting the kind of interactive review processes that we know can improve the odds of success in product development. This is particularly true for diseases where experience is limited or to support product developers with more limited experience. FDA scientists can meet with sponsors early in product development, even before human studies are planned, to help identify and resolve critical issues and provide input on proposed development plans. Such meetings, and continued high-quality scientific interactions, while labor intensive, are particularly critical in identifying and resolving scientific issues with respect to products for rare and neglected diseases.

Selected Recently Approved Products to Treat Rare and Neglected Diseases

The approved products now on the market that qualified for orphan product designation are a testament to the important accomplishments and successes of FDA's programs and collaborations to facilitate the development and approval of products for rare diseases. Such success stories include:

- IXIARO (Japanese encephalitis vaccine, inactivated, adsorbed) was approved on May 17, 2013, for treatment of infants, children, and adolescents two months to less than 17 years of age for active immunization, for the prevention of disease caused by Japanese encephalitis virus. Japanese encephalitis is a viral infection of the brain that is endemic in several tropical and subtropical regions in Asia and affects over 50,000 people annually.

- Sirturo (bedaquiline) was approved in December 2012, and is indicated as part of combination therapy in adults with pulmonary multi-drug resistant TB (MDR-TB); Sirturo should be reserved for use when an effective treatment regimen cannot otherwise be provided. According to CDC, there were about 100 cases of MDR-TB in the United States in 2010, and WHO estimates there were more than 310,000 MDR-TB cases worldwide in 2011.

- Coartem (artemether and lumefantirne) was approved in 2009 for the treatment of acute, uncomplicated malaria infections due to *Plasmodium falciparum*. CDC states that in 2009, there were about 1,500 cases of malaria diagnosed in the United States, almost all occurring in persons who traveled to areas with ongoing malaria transmission. Worldwide, there are an estimated 300-500 million cases each year, and most deaths from malaria occur in children.

- Anascorp (Centruroides immune $F(ab)_2$) was approved on August 4, 2011, for the treatment of clinical signs of scorpion envenomation. Poisonous scorpion stings present a problem worldwide, and the number of stings reported yearly in the United States averages around 12,000.

- Kalydeco (ivacaftor) was approved on January 31, 2012, for the treatment of cystic fibrosis (CF) in patients age six years and older who have a G551D mutation in the CF transmembrane conductance regulator (CFTR) gene. CF is a genetic disease that affects approximately 30,000 people in the United States, and Kalydeco was approved to treat a subset of CF patients with a specific genetic mutation (approximately 5 percent of the CF population). Kalydeco is the first FDA-approved treatment for CF that addressed the underlying genetic defect in CF, and not just the symptoms and clinical manifestations.

CONCLUSION

FDA's multifaceted and collaborative approach to product development and evaluation for rare and neglected diseases, including regulatory science to address gaps in knowledge and speed product development, has resulted in many successes and real progress. Congressional engagement, innovation, and support of FDA programs, from ODA to FDASIA to GAIN, have made a real impact. We look forward to continuing to work with you and our colleagues in both the public health arena and private sector to address the challenges that we face. Thank you again for this opportunity to discuss rare and neglected diseases. We are proud that our nation and our Agency can make a difference, and we also know that these activities directly benefit and help ensure the health and security of the United States. I welcome your comments and questions.