FDA Research Activities

Purpose

In response to a FY 2006 appropriations conference report, FDA is providing a budget justification for its research activities that describes the activities funded at the base level and the activities funded by proposed increases.

A funding table will display FDA's total research funding followed by a descriptive justification by each FDA Center, ORA, and OC.

FDA Research Activities Funding

(Dollars in $000)

FDA Program	**FY 2007**	**FY 2008**	**FY 2009**
Foods	$25,922	$30,178	$33,039
Field (non-add)	$1,100	$1,100	$1,100
Research Increase (non-add)			*$2,862*
Human Drugs**	$24,853	$25,288	$25,288
Biologics	$16,870	$16,735	$16,735
Animal Drugs and Feeds	$7,994	$8,253	$8,253
Devices and Radiological Health	$10,075	$10,576	$10,891
NCTR	$42,056	$44,006	$45,816
Research Increase (non-add)			*$1,683*
Headquarters and the OC	$5,605	$5,821	$5,799
TOTAL	**$133,375**	**$140,857**	**$145,821**

** Includes Orphan Product Development Grants (FY 2007 - $14.1 M; FY 2008 - $14.0M, and FY 2009 - $14.0M)

Foods Program Research Activities

The FDA Foods Program (Center and Field) FY 2009 funding for research activities are estimated to be $33,039,000. Of this amount, 30,178,000 represents base funding to support the research activities described below. $2,862,000 represents the funding increase supporting new or expanded existing research described below.

Base Funding Supporting Research - Center Activities

The Center for Food Safety and Applied Nutrition (CFSAN) conducts food, cosmetic, and color additive safety research to protect the public's food and cosmetic supply from harmful illnesses, environmental contaminants, or other threats caused by natural or man-made events.

CFSAN conducts research that identifies and then seeks to understand the risks caused by--microbiological contaminants in foods (*e.g.*, *Listeria monocytogenes* in ready-to-eat foods, *Vibrio vulnificus* and *V. parahaemolyticus* in seafood, *Enterobacter sakazaki* in infant formula), chemical contaminants in foods (*e.g.,* perchlorate, acylamide, furans, melamine), inherent food substances that may cause adverse events in humans (*e.g.,* allergens and glutens), and nanoparticles and permanent tattoo inks in cosmetics -- so that appropriate risk assessment models and response mechanisms may be developed to deal with these threats.

CFSAN also conducts research in order to understand the emergence or re-emergence of foodborne microbial pathogens, by studying evolutionary or adaptive changes in virulence, antibiotic resistance, the resistance to traditional food preservation technologies (*e.g.,* acid tolerance), and the resistance to traditional interventions such as pasteurization.

CFSAN partners with industry, academia, and the Federal sector to develop new tools that employ the latest developments in science and technology (*e.g., ,* mass spectrometry, micro-array-based screening, optical arrays, phenotypic arrays, nanotechnology *etc.*) to evaluate and test for their appropriateness in the rapid identification of contaminated product, the source of product contamination, the effectiveness of process interventions. With these developments CFSAN can effectively communicate to the public the extent and nature of the risk. CFSAN studies consumer and producer behavior in response to FDA regulations and policies, risk assessment and economic analysis, and consumer awareness on diet, nutrition, and health issues, especially nutrition information labeling in pursuing healthier lifestyles.

Base Funding Supporting Research – Food Field Activities

The Office of Regulatory Affairs (ORA) funding of research activities for FY 2009 are estimated to be $1,100,000. This $1,100,000 represents the base funding that supports ORA's research activities described below. ORA's research, development, and evaluation activities are conducted in order to provide convincing and prevailing scientific and analytical base for regulatory decisions that protect and promote public health. It is this research that informs policy and regulation to improve the safety, efficacy, and quality of FDA-regulated products.

ORA participates in food defense research activities including methods development and validation for the detection of potential bioterrorism agents such as *Bacillus anthracis* and *Clostridium botulinum* neurotoxin, and potential chemical contaminants such as cynadie, ricin, T2 toxin, and radionuclides. Engaging in these and other food defense research activities improves FDA's ability to respond to threats to the American food supply and supports activities of the Food Emergency Response Network (FERN).

Food Protection Program Increases Supporting Research – Center Activities

Funds will be used to provide research and research support in the seven critical areas. These include rapid test kit development, confirmatory methods, allergens, biotechnology, virology, in-vitro testing, and laboratory enhancement. Each of the seven areas is described briefly as follows:

- Rapid test kit development – develop kits that can be used in the field with little or no expertise.

- Confirmatory methods – develop methods to support results from rapid, field deployable test kit.

- Allergens – develop and evaluate reference standards, rapid test kits, methods of confirmation and new methods for evaluating allergencity of processed foods.

- Biotechnology – develop techniques and methods for evaluating/detecting foods modified by approved or accidental manipulation of genes to support risk assessment development and the establishment of a surveillance program.

- Virology – develop methods such as culturing techniques for viruses which can not currently be cultured.

- In vitro testing – develop new methods for assessing significant and unreasonable risk in dietary supplements, toxicology, new food additives, cosmetics and nanotechnology.

- Laboratory enhancement— enhance capital equipment; standard equipment; capacity for handling of select agents; improvements and expansion of safety; maintenance and oversight of research tracking and reporting database; laboratory build-outs and renovations; and quality assurance program.

Human Drugs Program Research Activities

The Human Drug Program Research Activities for FY 2009 are estimated to be $25,288,000. This amount represents the base funding that support research activities in the Human Drugs Program as part of its mission to ensuring the American public has adequate access to safe, effective, and high quality drug and therapeutic biologic products.

A significant portion of the funding accounted for as research activities within the Human Drugs Program covers the Orphan Drug Program. The Office of Orphan Products Development (OOPD) promotes development of products that demonstrate promise for diagnosis and/or treatment of rare diseases or conditions by administering a grant program that provides funding for clinical research in rare diseases.

As part of its efforts to develop medical counter measures in the case of terrorist attacks, CDER studies broadly acting stimulators of the immune system in animal models to assess protective effects against various infectious agents potentially used in bioterrorist attacks. CDER models studies in animals to ensure that products are safe to study in humans. This research analyzes specific immune deficiencies in animal models of bioterrorism-related radiation injury to clarify clinical problems potentially treatable with therapeutic proteins. CDER develops new assays for anthrax toxin that more closely model toxin activity in humans than current mouse cell assays, and provide biomarkers for assessing anthrax toxin effects in vivo.

CDER also performs research to develop regulatory standards and risk assessment criteria to reach sound, science-based public health decisions when evaluating the safety and effectiveness of drug products. This research allows CDER to clarify mechanisms of cell death induced by cancer drugs in order to enable better bioassays to serve as markers for safety and efficacy of novel cancer drugs. This research also allows CDER to identify biomarkers of cancer development and progression to facilitate diagnosis and monitoring of treatment efficacy.

Biologics Program Research Activities

The Biologics program research activities for FY 2009 are estimated to be $16,735,000. This $16,735,000 represents the base funding that support research activities described below.

In order to advance scientific and biomedical research and development related to the public's health, FDA maintains a scientific staff with a unique regulatory, product development, cross-product category perspective, with complex biological product manufacturing expertise and the ability to problem solve throughout the manufacturing process:

- maintain experts in multidisciplinary, disease-oriented science required for biological product evaluation, and include physician scientists

- convene cooperative groups of sponsors, academia, and other government agencies to resolve specific product scientific challenges

- recognize early the significant challenges in product development, permitting problem avoidance and early resolution

- provide a science base for regulatory decisions (including the development of new tools) and for the regulatory requirements (regulations and guidances), FDA is able to approve successful applications of novel technologies and products made from, or manufactured using novel technologies.

Animal Drugs and Feeds Program Research Activities

The Animal Drugs and Feeds Research Activities for FY 2009 are estimated to be $8,253,000. This $8,253,000 represents the base funding that support research activities described below.

The Animal Drugs and Feeds (ADF) research program conducts applied and basic research in support of current and evolving FDA regulatory issues. The research answers regulatory questions and provides data for policy formulation related to the ADF's core functions.

Studies in animal drug safety and efficacy, antimicrobial resistance mechanisms, metabolism, standardization of test methods, and pharmacokinetics/pharmacodynamics support the drug review function, providing a science base for guideline development. Regulatory research supporting premarket and medical product safety validates the safety and efficacy of animal derived food and animal health products to ensure approved products are safe to eat for humans and animals.

Development of analytical methods and evaluation of screening tests for detection of drug residues in imported and domestic food products supports the ADF compliance program. ADF research also involves development of methods to detect material prohibited by the BSE feed regulation that could compromise animal feed safety.

The ADF program monitors antimicrobial drugs used in food-producing animals to determine the development of resistance. The ADF program serves as leader for the National Antimicrobial Resistance Monitoring System (NARMS) program, which monitors trends in the antimicrobial drug susceptibilities of selected enteric bacterial organisms in humans, animals, and retail meats to a panel of antimicrobial drugs important in human and animal medicine.

The ADF research program also conducts regulatory research in support of Pandemic Influenza Preparedness (enforcement against extra label use of antiviral drugs in poultry) and bioterrorism (screening methods to detect the presence of pesticides and industrial contaminants that could be introduced into the United States animal feed supplies by bioterrorists).

Devices and Radiological Health Program Research Activities

The Medical Devices and Radiological Health Program Research Activities for FY 2009 are estimated to be $10,891,000. This $10,891,000 represents the base funding that supports the research activities described below. The research activities focus activities in four crucial areas: critical path, premarket research, patient safety, and Ionizing Radiation Measurements

Critical Path research addresses the urgent need for innovative medical therapies and promotes more predictable, efficient and less costly product development by developing data and expertise on future technologies that CDRH must address:

- Methods development in biomarkers, image quality, modeling, electromagnetic compatibility, in vitro diagnostic assays, and materials performance improves the

development process for medical products and increases the number of premarket applications.

- Assessment of critical properties and biological effects of nanoparticles in cells and evaluations of the compatibility of nanomaterials in the body provide answers to help demonstrate with more certainty the safety of new products.

Premarket research activities advance the premarket and inspection programs and the scientific understanding, standards and guidance development, and experimental capabilities CDRH needs to assess new technologies and speed reviews:

- Biological risk assessment, infection control, toxicity, and radiation bioeffects to promote improvement of medical devices
- Chemistry and materials science to develop analytical procedures, mathematical models and data related to the safety and performance of implanted devices
- Imaging and applied mathematics to provide scientific expertise in radiation-emitting products, medical imaging systems, and devices using computer-assisted diagnostics
- Optical physics, sensors, fiber optics, electrophysics, electromagnetics, electrical stimulation, and electrophysiology for improved safety and performance
- Ultrasound and blood flow research to develop measurement methods and instrument calibration procedures to characterize devices and device materials.

Patient Safety research significantly advances understanding of the root causes of medical device failures and user errors to assess risk throughout the product life cycle:

- Application of electronics, software engineering, and systems engineering to assess medical device safety and performance
- Human factors studies to improve product designs that minimize or eliminate user errors.

Mammography Quality Standards Act (MQSA)'s Ionizing Radiation Measurements Laboratory provides support to the Center's safety mission. The laboratory provides traceability in support of both the MQSA and the Radiation Control for Health and Safety Act.

National Center for Toxicological Research (NCTR) Activities

NCTR's mission is to conduct research that enables FDA product centers to make sound science-based regulatory decisions. Therefore, its estimated FY 2009 funding of $45,816,000 will be used entirely for research. Of this amount, $44,006,000 represents base funding support for research activities and the remaining $1,683,000 represents an increase targeted for food protection research conducted at the NCTR. NCTR's base funding supports new research or the expansion of existing research at the NCTR which is described below.

Base Funding Supporting Research Activities

Using base funding, NCTR executes its research responsibilities in three program areas: Personalized Nutrition and Medicine, Food Protection, and Enhancing Product Safety. Under Personalized Nutrition and Medicine, NCTR aims to define and characterize individual responses to regulated products and to assess innovative products for possible uses–that is, identify persons most likely to benefit from, or experience adverse reactions to, particular drugs, devices, biologics, cosmetics, and nutrients. In support of Food Protection, NCTR will provide techniques to *prevent* food contamination of the food supply or the environment and to ensure timely *intervention* strategies by developing rapid, field-ready standards for the early detection of microbial or chemical threats to the food supply. Under Enhancing Product Safety, NCTR scientists conduct customized bioassessments of regulated products that enable scientists to translate toxicity data into a comprehensive risk-based evaluation and develop reliable and reproducible techniques for conducting safety assessments of FDA-regulated products. A sampling of research conducted at NCTR includes projects to:

- define and characterize individual responses to regulated products
- explore new approaches to better understand how individual attributes affect responses to drugs, foods, nutrients, dietary supplements and their interactions with toxins and drugs
- develop methods to rapidly distinguish bioterror hoax material in samples containing pathogenic and nonpathogenic bacteria
- develop methods and recommend industry guidelines to evaluate the safety of antimicrobial agents on human health
- develop methods to assess and manage risks associated with food products that have been adulterated, intentionally contaminated, or otherwise found to be detrimental to human health
- establish safe exposure times for ketamine, a commonly used pediatric anesthetic to enable clinicians to avoid overdosing children
- advance the use of panomics (genomics, proteomics, metabolomics, and bioinformatics technologies) in medical product development and personalized medicine
- participate, as essential partners, in the ongoing Voluntary Genomic Data Submission, a process vital to developing personalized medicine and enhancing product development

- direct the continued partnership with other FDA Centers and microarray industry providers in the Microarray Quality Control Phase II project to address the quality standards and data analysis challenges of using microarray technology in the clinical setting
- provide software systems and analysis capability to manage and integrate data from panomics technologies with traditional toxicological data
- investigate sex differences in biomarkers for the diagnosis or treatment of disease and responses to regulated products
- continue research to increase the understanding of the uptake and toxicity of nanomaterials to the neurological system to enable FDA to identify biomarkers of toxicity and provide early recognition of potential safety issues before they become adverse events in the patient population

Food Protection Increase Supporting Research Activities

The FY 2009 program increase of $1,683,000 targeted for Food Protection enables NCTR to expand its ongoing Food Protection research activities. The additional funds will support scientists' development of microarray techniques to detect genes in bacteria that are resistant to multiple antibiotics; thus allowing FDA to more quickly identify disease outbreaks that pose especially high risks for the American public because they involve antibiotic-resistant strains. Understanding the mechanisms of drug resistance is critical, not only for the development of effective new drugs, but also to provide a tool to find out if the new drugs overcome these mechanisms.

Headquarters and Office of the Commissioner Activities

The Office of the Commissioner has two subordinate organizations that support research activities. There are the Office of Orphan Products Development and the Office of Women's Health.

The Office of Orphan Products Development (OOPD) Program supports new and continuing extramural research projects that test the safety and efficacy of promising new drugs, devices, and medical foods for rare diseases and conditions through human clinical trials. Orphan product grants are a proven method of successfully fostering and encouraging the development of new safe and effective medical products for rare diseases/conditions. Grants ensure that product development occurs in a timely manner with a very modest investment.

In general, OOPD grant funding is for up to three years. The list below of RD&E activities is representational and not comprehensive:

- reviewing of solicited grant applications by OOPD staff to ensure program requirements are met
- coordinating and convening peer review panels to provide technical review of grant proposals to ensure the best scientific proposals are funded
- selecting grant applications for funding

- conducting site visits to grantees to ensure extramural funded studies, which involve human subjects, are consistent with grant agreement terms and minimize FDA's exposure to risk of violations in human subjects protection requirements
- monitoring the grant-funded products to satisfy regulatory and program requirements
- modernizing the transmission of applications and other review information through full electronic submissions
- improving the OOPD database system to allow for more efficient and effective retrieval of information and other internal management practices.
- seeking out opportunities to present the OOPD scientific programs and facilitate discussion in scientific and regulatory issues and research needs.

The Office of Women's Health (OWH) Research and Development Program addresses gaps in current knowledge, uses novel approaches for conducting and funding research, and sets new standards of excellence for women's health research. The program funds research projects at FDA and occasionally at academic facilities. The program is also responsible for meeting Congressional mandates to track the participation of women in clinical studies. The list below of RD&E activities is representational and not comprehensive:

- aligning OWH research priorities with FDA's Critical Path Initiative and identifying key opportunities especially in information technology and data management to advance our understanding of sex/gender based science
- using a peer review process to select the highest quality research projects of regulatory significance to FDA
- implementing a process to identify the highest priority women's health research needs in FDA in order to advance a science program that integrates these priorities with FDA's Critical Path Initiative
- partnering with other HHS organizations to identify gaps in women's health and sex/gender differences research and leveraging current funding to address those gaps
- seeking internal and external opportunities to present OWH's scientific portfolio and facilitate discussion in cross cutting women's health scientific issues including identifying research needs.