C·D·R·H
Center for Devices and Radiological Health

FY 03 CDRH Annual Report

U.S. Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Devices and Radiological Health

United States Department of Health & Human Services

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Opening Remarks from the Center Director

I'm pleased to issue the annual report for FDA's Center for Devices and Radiological Health covering Fiscal Year 2003. In a sense, I'm doing this "by proxy," since I hadn't yet been appointed Center director in FY 03. I'm also issuing the report a bit belatedly—as I'm sure you've noted, FY 03 came to a close eight months ago! Nonetheless, I'm very proud of what the staff was able to accomplish during that year in fulfilling the Center's major goals, and I thought it was important to share their successes with you.
Let me mention just a few highlights. You'll find the rest of the information in the remainder of this document.

We had two major objectives in FY 03: to implement the provisions of the Medical Device User Fee and Modernization Act (MDUFMA), and to carry out the goals we set for ourselves under the Center's strategic plan.

Under MDUFMA, I'm pleased to say that we managed to meet all the statutory start-up dates for FY 03. The provisions of this law are complex and far-ranging, and so we made every effort to give stakeholders the opportunity to provide their views on implementation, including establishing Internet sites to gather feedback and conducting a nationwide interactive video teleconference.

A key element in our ability to successfully implement MDUFMA is strengthening the expertise of our staff. We made significant headway in that area during FY 03 by filling 75 new positions, including scientists, engineers, project managers, statisticians and medical officers. And to help existing staff, we launched a joint project with Georgetown University and Virginia Tech, in which our people received graduate-level training in such areas as biostatistics and product development.

In response to the MDUFMA requirement that pediatric expertise be represented on our advisory panels when appropriate, we developed guidance on the circumstances under which pediatric input should be used, as well as guidance on the premarket evaluation of pediatric medical devices.

A major accomplishment in fulfilling the goals of our Strategic Plan was the establishment of the Office of In Vitro Diagnostic Device Evaluation and Safety, a multidisciplinary group organized to regulate these products in both their premarket and postmarket phases.

A Message from the Center Director

We continued to strengthen our MedSun system, a pilot program through which medical facilities across the country are recruited and trained to report device-related adverse events; at the close of FY 03, 180 facilities were participating. And we continued to work towards the accreditation of third parties to perform inspections; at the close of FY 03, seventeen applications were under full review.

I should also mention that we made significant progress in improving the expertise and efficiency of our own staff. For example, we implemented a Scorecard system to better manage, measure and track our own performance, and we're using "shared hires," a flexible system that enables staff members to apply their skills across the entire Center. We also established a Medical Device Fellowship Program, in which outside experts bring their special skills to the Center for varying periods of time, and in which our staff members expand their knowledge by working with universities and hospitals.

Aside from personnel improvements, we're also concerned about improving the way we operate across the board, and so we established a Continuous Process Improvement program, in which we analyze and attempt to improve the processes that we routinely use in regulating devices. Among the processes subjected to this analysis during FY 03 were PMA filing and closeout, Turbo-510(k) inspections, BIMO procedures and risk-based inspections. During FY 03 we also prepared for our eventual move to FDA's new White Oak, with the expectation that about 50 lab employees would move in FY 04. Finally, we contributed to FDA's ongoing effort to enhance emergency preparedness by identifying medical devices most likely to be needed in the event of a terrorist attack, establishing a manufacturer database for these products, and setting up 24-hour emergency contacts with major U.S, medical supply firms. In addition, we finished revising the emergency response plan for radiological or nuclear emergencies. Again, there's much more in the full report. I hope you find it useful and informative.

Daniel G. Schultz. M.D.
Director, Center for Devices and Radiological Health

The Center for Devices and Radiological Health

The Center for Devices and Radiological Health (CDRH) is part of the U.S. Food and Drug Administration (FDA). CDRH helps ensure that medical devices are safe and effective as authorized by the 1976 Medical Device Amendments to the Federal Food, Drug, and Cosmetic Act and helps reduce unnecessary exposure to radiation from medical, occupational, and consumer products as authorized by the Radiation Control for Health and Safety Act of 1968.

Office of the Center Director (OCD)

OCD provides leadership and direction for all Center activities and is responsible for their evaluation and coordination. It provides advice and consultation on policy matters about medical device and radiological health activities to the Commissioner and other FDA officials, Congress, the Department of Health and Human Services, the Public Health Service, other government agencies, the scientific and academic community, and representatives of the regulated industry. It supports the Equal Employment Opportunity (EEO) program and management within the Center. OCD also manages the CDRH Medical Device Fellowship Program.

The CDRH Ombudsman is located in OCD. In 2003 it received a total of 120 complaints and disputes mostly from medical device firms. The three most common reasons for these contacts were: miscommunication, lack of timeliness, and premarket data and testing requirements. The Ombudsman's 2003 Annual Report is available at http://www.fda.gov/cdrh/ombudsman/annual/ombudar2003.html.

Office of Compliance (OC)

OC is the enforcement hub of CDRH with responsibility for directing and evaluating field inspections of manufacturers of medical devices and radiological health products nationally and abroad. OC advises the Center Director and other FDA officials on legal, administrative, and regulatory programs and policies. It oversees the compliance and surveillance programs of the regulated industry and conducts field tests and inspections needed for regulatory purposes. OC also evaluates industry quality control and testing programs and advises the FDA field offices and CDRH regarding legal actions, case development, and contested case assistance. OC is responsible for the Establishment Registration, Medical Device Listing, Government-wide Quality Assurance, and Bioresearch Monitoring Programs. It trains federal and state compliance personnel and advises manufacturers about the requirements of the Federal Food, Drug, and Cosmetic Act and its implementing regulations.

Office of Device Evaluation (ODE)

ODE is the office responsible for review of marketing applications from the medical device industry. It plans, conducts, and coordinates Center actions regarding the approval, denial, and withdrawal of approval to market a medical device. ODE also reviews applications to conduct investigational clinical studies of unapproved medical devices under the Investigational Devices Exemptions. The data gathered in these clinical studies supports marketing applications. ODE reviews four types of marketing applications: Premarket Notification (or a 510(k) application), Premarket Approval (PMA), Product Development

Protocol (PDP), and Humanitarian Device Exemption (HDE). Most devices are cleared for marketing through the 510(k) process; PMA applies only to the highest risk and newly developed (class III) devices. ODE coordinates Center classification activities; reviews and initiates petitions for reclassification of devices; interacts with and provides support to the advisory panels which make recommendations on FDA actions regarding selected devices; and conducts continuing review, surveillance, and medical evaluation of device labeling and clinical experience.

Office of Health and Industry Programs (OHIP)

OHIP specializes in the areas of program-based communication, education, radiological health, mammography quality, and resolution of device user problems. Audiences include the radiological health and device industry, health professionals, consumers, CDRH staff, and foreign governments. In support of Center programs, OHIP provides expertise in communications technology and produces national and international teleconferences and educational videos; applies human factors theory to the design and labeling of devices to reduce use errors; conducts qualitative research studies for use in Center information programs for health professionals, consumers, and industry; operates a program to implement the Mammography Quality Standards Act of 1992 and provides technical expertise in applying health physics procedures and radiation protection principles; provides technical assistance to medical device manufacturers, coordinates international activities, and provides information to consumers; develops regulations for medical devices and radiological health activities; and provides educational programs for Center employees.

Office of In Vitro Diagnostic Devices Evaluation and Safety (OIVD)

OIVD combines the functions of all the offices within CDRH into one organizational unit for cradle-to-grave regulation of in vitro diagnostic devices (IVDs). It carries out this mission by combining the premarket review responsibilities of ODE, the enforcement responsibilities of OC, and the postmarket surveillance responsibilities of OSB. To support these regulatory responsibilities, OIVD maintains strong ties to OST for technical assistance, OHIP for communication and outreach assistance, and OSM for program management assistance. OIVD consists of a multidisciplinary group of scientists and other professionals who are collectively dedicated to promoting and protecting public health through clear and consistent regulation of IVDs by applying good scientific principles throughout the Total Product Life Cycle of the device. OIVD has a dual charge to foster the rapid transfer of good new IVDs into the medical market while preventing marketing of unsafe or ineffective devices. The Office strives to ensure the work is transparent in order to allow all stakeholders to obtain the knowledge required to make informed decisions about the development, production, and use of IVDs. In addition, OIVD administers the Clinical Laboratory Improvement Amendments (CLIA) '88 complexity program for the Center for Medicare and Medicaid Services (CMS) by categorizing commercially marketed in vitro diagnostic tests by level of complexity.

Office of Science and Engineering Laboratories (OSEL) (formerly the Office of Science and Technology [OST])

OSEL, the laboratory research hub of CDRH, supports FDA's regulatory decisions with laboratory research in the areas of standards, test methods development, technical consultation, forensic analysis, and applied research. It leads the development and

evaluation of standards used for regulatory assessments. OSEL supports other Center offices when specific expertise is required for solving problems or reviewing 510(k) or PMA applications. It identifies and analyzes failures of marketed devices. OSEL conducts research in the areas of life, physical, and engineering sciences as they relate to the health effects of radiation and medical device technologies. One such example is the study of the effects of electrical fields around consumer products on cell development. OSEL's research assists the regulatory programs of CDRH and FDA in anticipating the impact of technology on the use, safety, and effectiveness of regulated products.

Office of Surveillance and Biometrics (OSB)

OSB develops and implements surveillance programs to assure that marketed products are safe and effective. It is the Center's source of expertise in the biometrics sciences and provides expert statistical consultation in the evaluation of premarket device applications in ODE and OIVD. OSB administers a nationwide surveillance system to monitor and evaluate the safety and effectiveness of marketed devices by analyzing adverse-event reports and other data from device users. In collaboration with the other Center offices, OSB directs and monitors the analysis, resolution, and development of implementation strategies for postmarket issues through the Center's ad hoc process and postmarket safety notifications.

Office of Systems and Management (OSM)

OSM advises the Center Director on all management issues. It plans, develops, and implements cost effective Center management policies and programs concerning financial and human resource management, contract and grants management, ethics and program integrity, committee and conference management, occupational health and safety, and facilities. OSM develops and implements the Center's long-range, strategic, and operational plans; evaluates the effectiveness of Center programs; and designs administrative, scientific, and technical information systems to support Center programs. As the Center's electronic communications hub, OSM provides computer support services to the Center and Web-based information to the public. The library provides scientific information for Center staff, and the Freedom of Information (FOI) staff responds to public requests for information.

For additional information about CDRH, call: 1-888-INFO-FDA or visit the CDRH website at: http://www.fda.gov/cdrh.

Bringing New Products to the Market

New Leadership

Office of In Vitro Diagnostic Device Evaluation and Safety

The Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD) (www.fda.gov/cdrh/oivd/index.html) was established on November 17, 2002. OIVD combines the functions of all the offices within the Center for Devices and Radiological Health (CDRH) into one organizational unit for cradle-to-grave regulation of in vitro diagnostic devices (IVDs). Lead by Dr. Steven Gutman, OIVD Director, the Office consists of a multidisciplinary group of scientists and other professionals who are collectively dedicated to promoting and protecting public health through clear and consistent regulation of IVDs by applying good scientific principles throughout the Total Product Life Cycle of the device. OIVD has a dual charge to foster the rapid transfer of good new IVDs into the medical market while preventing marketing of unsafe or ineffective devices.

Medical Device Fellowship Program

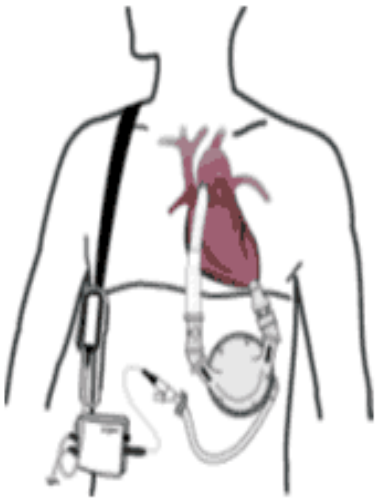
To keep pace with the rapid development of new technology, and to make decisions based on the best scientific information and knowledge available, CDRH routinely consults with experts in the academic community, other government entities, clinical practice, and the military. CDRH established the Medical Device Fellowship Program (MDFP) (www.fda.gov/cdrh/mdfp) in 2002 to increase the range and depth of collaborations between CDRH and the outside scientific community. The MDFP offers short- and long-term fellowship opportunities for individuals interested in learning about the regulatory process and sharing their knowledge and experience with medical devices from the relatively simple to the highly complex. The MDFP is also developing professional development opportunities for CDRH staff at universities and hospitals, to help staff stay current with new technology and clinical practice. CDRH's Medical Device Fellowship Program helps the Center achieve the goal of becoming a "magnet for excellence" by attracting, developing and retaining a highly skilled and diverse workforce to advance public health mission. The MDFP, in turn, supports the agency's goal of having a strong FDA and objective of ensuring a high quality, diverse and motivated workforce. Under the leadership of Dr. Susan Homire, the program has established Biomedical Engineering Co-op and Engineering Internship Programs with Carnegie Mellon University, Marquette University, University of Iowa, Texas A&M, University of Maryland, Catholic University of America, University of Kansas, Drexel University and George Washington University. Additional academic partners include Medical College of Wisconsin, University of Illinois at Champagne-Urbana, Stanford University, Case Western Reserve University, Uniformed Services University of the Health Sciences, University of Houston, University of Puerto Rico, Howard University and Virginia Tech. Some MDFP participants come to the Center through the National Research Council Associateship Program and the Brigham and Women's Hospital Resident Exchange Program. The MDFP had 42 participants in FY 03.

Advances in Patient Care

Last year the CDRH approved and cleared thousands of devices used to diagnose and treat a wide variety of medical conditions. Below are highlighted several new medical devices and devices with new indications approved or cleared during this past fiscal year that have a particular impact on patient care.

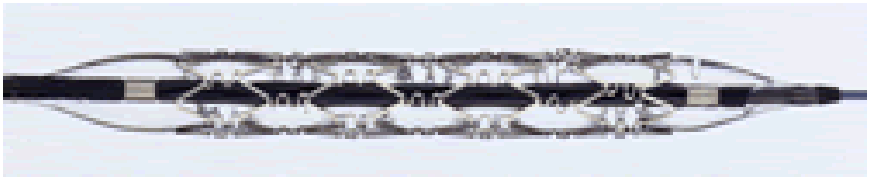
The Premarket Approval Application (PMA) Approval website describing recently approved devices with patient information is available at www.fda.gov/cdrh/consumer/mda/index.html.

Left Ventricular Assist Device (LVAD)



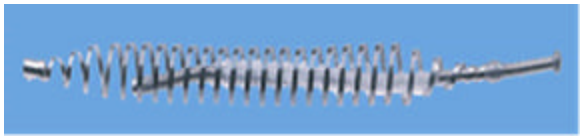
HeartMate® SNAP-VE LVAS (Sutures Not Applied-Vented Electric Left Ventricular Assist System) by Thoratec Corporation is the first LVAD approved for long-term implant. It was originally approved for use as a bridge to cardiac transplantation in cardiac transplant candidates at risk of imminent death from nonreversible left ventricular failure. It is now also approved for use in patients who are not eligible for cardiac transplantation with New York Heart Association Class IV end stage left ventricular failure who have received optimal medical therapy for at least 60 of the last 90 days, and who have a life expectancy of less than two years. The device system is approved for use both inside and outside of the hospital.

Drug-Eluting Stent



CYPHER™ Sirolimus-eluting Coronary Stent by Cordis Corporation is the first drug-eluting stent for angioplasty procedures to open clogged coronary arteries. The device is an expandable, slotted, stainless steel tube, with a drug (sirolimus) contained within a thin polymer coating on its surfaces. The Stent is mounted over a balloon on the end of a long thin flexible tube called a "delivery catheter" (RAPTOR™ Over-the-Wire Delivery System or RAPTORRAIL® Rapid Exchange Delivery System). This new stent slowly releases a drug, and has been shown in clinical studies to significantly reduce the rate of re-blockage that occurs with existing stents. The device should not be used in patients: who cannot take aspirin or blood-thinning medicine, who have an allergy to the drug sirolimus, its derivatives or the polymers used to coat the stent, or who have a blockage in the coronary artery that will not allow complete inflation of the balloon.

Sterilization Procedure for Women

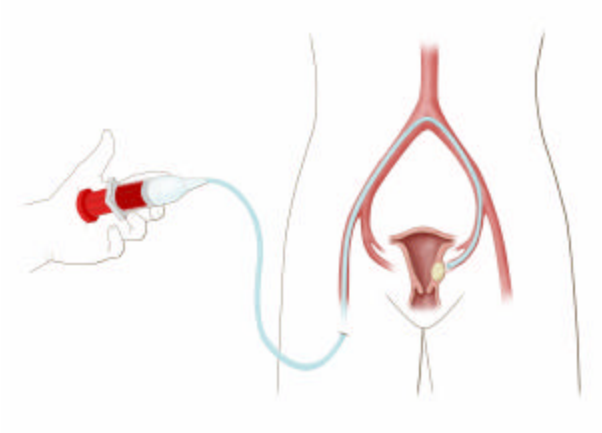


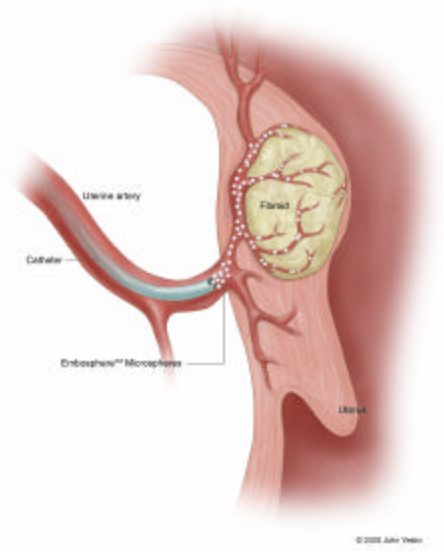
The Essure™ System by Conceptus, Inc. is a new method of permanent birth control (sterilization) for women. Unlike other sterilization procedures for women, this system does not require incisions or general anesthesia. Instead, a doctor

implants small metal coils in a woman's fallopian tubes by threading them through the vagina and uterus using a specialized delivery catheter. After the catheter is removed, the coils remain in place permanently. Over time, scar tissue forms around the implanted coils and blocks the fallopian tubes, preventing sperm from fertilizing a woman's eggs. Initial one and two-year data from clinical studies showed no pregnancies at the time of approval. Longer term data will be available over time with postmarket follow-up of these patients.

Fibroid Embolization

Uterine Fibroid Embolization by Biophere Medical, Inc. is the first 510(k) cleared for Uterine Fibroid Embolization (UFE). It is indicated to treat noncancerous tumors (symptomatic fibroids). A radiologist makes a small nick in the skin (less than one-quarter inch) and inserts a thin tube (catheter) into the main artery of the thigh (femoral artery).





Using X-ray imaging, the radiologist guides the catheter through the femoral artery into the uterine artery. Tiny spheres or particles made of plastic or sponge material the size of grains of sand are pumped through the catheter into the uterine artery on one side of the body, where they block the blood supply to the fibroids. The procedure is then repeated on the other side of the body so the blood supply is blocked in both the right and left uterine arteries. With decreased blood supply, part of the fibroid tissue dies. The overall effect is the shrinking of the fibroid.

Limb Salvage System

Children who require replacement of their knee joints often lose the ability for growth in the affected limb. This necessitates several surgeries throughout childhood and adolescence to expand the child's prosthesis as the child grows to maintain limb length equality.

The REPIPHYSIS™ Limb Salvage System, manufactured by Wright Medical Technology, Inc., is an artificial knee joint with a unique femoral component that can be expanded without surgical intervention. The device utilizes a coil that fits around the patient's leg that produces an electromagnetic field (EMF). The EMF induces an electrical current and subsequent heating of an internal wire. The generated heat softens a polymer-locking ring, allowing a slow expansion of an internal compressed spring. The spring expansion pushes the spring housing and femoral housing apart, thus increasing the overall length of the implant.

Deep Brain Stimulator

Medtronic Activa® Dystonia Therapy is a totally implanted brain stimulator to treat long-term primary dystonia (abnormal contraction of muscles at rest) that is not responsive to drug therapy. An implanted pulse generator (IPG) is connected with an insulated wire (a lead) extension, to another lead with four electrodes. The electrodes are in contact with a specific structural area within the brain. The IPG is implanted under the skin of either the abdomen or under the collarbone, and sends programmable electrical stimulation pulses to the electrodes that were implanted in the brain. Two IPG device systems may be implanted, so that both sides of the brain can be stimulated to relieve symptoms on both sides of the body. It may improve some symptoms associated with primary dystonia. However, individual results vary and the specific benefit for an individual cannot be predicted.

Stair-Climbing Wheelchair

The INDEPENDENCE™ iBOT™ 3000 Mobility System by Independence Technology, L.L.C. is a new indoor/outdoor power mobility device for use by people with mobility impairments and the use of at least one upper extremity. It provides mobility on smooth surfaces and inclines at home and in the community; movement over obstacles, uneven terrain, curbs, grass, gravel, and other soft surfaces; mobility in a seated position at an elevated height; ascent or descent of stairs with or without assistance; and transport of the unoccupied wheelchair. Because of its unique balancing mechanism, the device remains stable and the seat stays level under most conditions. The iBOT™ is available by prescription only, from specially trained health professionals.

External Insulin Pump

The Medtronic MiniMed Paradigm Model 512 Insulin Pump and BD Paradigm Link Blood Glucose Monitor by MiniMed, Inc. is an ambulatory, battery operated, rate-programmable microinfusion pump. The Model 512 Insulin Pump is indicated for the continuous delivery of insulin at set and variable rates for the management of diabetes mellitus in persons requiring insulin. The BD Paradigm Link Blood Glucose Monitor is an in vitro diagnostic device intended to be used for the quantitative measurement of glucose in whole blood samples obtained from the fingertip, by people with diabetes mellitus in the home, as an aid to monitor the effectiveness of diabetes control. When used together, the glucose monitor can automatically telemeter glucose values to the insulin pump using radio frequency communication. The glucose monitor can also serve as a radiofrequency interface to allow communication between the insulin pump and a personal computer running the appropriate Medtronic MiniMed communications software.

A1cNow® for Home Use

On December 13, 2002, FDA cleared the A1cNow® for Home Use device. This device provides a quantitative measurement of the percent of glycated hemoglobin levels in capillary blood samples. This test is used at home by patients who have diabetes to monitor long-term glycemic control.

Bayer ADVIA Centaur Serum HER-2/Neu Assay

On January 30, 2003, FDA cleared the Bayer ADVIA Centaur Serum ERr-2/Neu Assay used in the follow-up and monitoring of patients with metastatic breast cancer whose initial serum Her-2/neu level is greater than15 ng/ml. Her-2/neu values should be used in conjunction with information available from clinical and other diagnostic procedures in the management of breast cancer. The clinical utility of the measurement of Her-2/neu in serum as a prognostic indicator for early recurrence and in the management of patients on immunotherapy has not been fully established.

Invasive Fungal Infection

On May 16, 2003, FDA cleared The Platelia® Aspergillus EIA test, manufactured by Bio-Rad Laboratories. This is the first rapid laboratory test to detect *Aspergillus* galactomannan antigen in blood, as an indicator of invasive infection. The test will help doctors diagnose invasive *Aspergillus* infection, a life-threatening invasive fungal infection that often occurs in leukemia patients, organ and bone marrow transplant patients, and patients whose immune systems are compromised by illness or chemotherapy, much sooner than current laboratory methods. Results are available in about three hours. By comparison, the standard culture method of testing for *Aspergillus* takes a minimum of four weeks before results are available. Earlier detection means earlier intervention with life-saving treatment for these critically ill patients.

West Nile Virus Infection

On July 3, 2003, FDA cleared the West Nile Virus IgM Capture ELISA test, manufactured by PanBio, Limited. This is the first test for use as an aid in the clinical laboratory diagnosis of West Nile Virus infection. The test is intended for use in patients with clinical symptoms consistent with encephalitis. West Nile virus is a mosquito-borne flavivirus that until 1999 was found only in the Middle East, Eastern Europe and Africa. The disease first appeared in the United States in 1999. In 2002 over 3300 cases were identified. Transmission to humans is primarily by mosquito. While the virus often presents as a mild infection that clears without further treatment, some patients develop severe infection resulting in severe neurological disease and even death. Antibodies for IgM can be seen within the first 1 to 8 days after onset of disease and can assist in the diagnosis of these patients. The disease is most prevalent during the mosquito season which is expected to begin in July and end in October. Over the past several years, the geographic range of the virus as well as the

number of new infections has expanded and now covers most of the continental United States. This test will be of use in helping to diagnose this growing public health problem.

Diagnosis of Congestive Heart Failure

On November 19, 2002, FDA cleared the Elecsys proBNP Immunoassay test. This test is a first-of-a-kind fully automated test for diagnosing congestive heart failure. The automation allows the laboratory to run a higher volume of samples, making the test more readily available to patients who need it. The Elecsys proBNP Immunoassay test is made by Roche Diagnostics, Inc. and is run on the Roche Diagnostics Elecsys Analyzers. The test detects the level of a peptide, NT-proBNP, which is secreted almost exclusively by the heart. An elevated level can indicate the presence of congestive heart failure. The higher the blood levels of proBNP, the more serious the condition. FDA cleared the first laboratory test for use as an aid in diagnosing congestive heart failure, the Biosite Diagnostics Triage BNP test in November 2000. The test can help doctors differentiate between congestive heart failure and other problems, such as lung disease. Early detection of congestive heart failure is important because, if detected early, it can often be managed with medication.

Ruling Out Heart Attack

On February 14, 2003, FDA cleared the Albumin Cobalt Binding Test (ACB Test). This test is a new first-of-a-kind blood test that measures Ischemia Modified Albumin (IMA). IMA helps in determining that a patient has NOT had a heart attack when he or she presents to an emergency room with severe chest pain. The ACB Test is manufactured by Ischemia Technologies Inc. It uses human serum and detects IMA by measuring how much cobalt is bound to the blood protein albumin. The ACB Test works by detecting albumin levels. A cobalt solution is added to serum and the unbound cobalt is detected by a color indicator. In the serum of normal patients more cobalt is bound to albumin leaving less cobalt to be detected by the color indicator, and forms less color. In patients with non-normal albumin levels, less cobalt is bound to albumin, which leaves more free cobalt to react with the color indicator, forming more color. The ACB Test is used as an additional test with both electrocardiogram (ECG) and another chemical marker—Troponin. ACB is not intended for use as a stand alone heart attack test. A normal ACB Test with a normal ECG, and a normal Troponin, gives doctors more confidence that patients can go home because they did not have a heart attack.

Monitoring Asthma Better

On April 30, 2003, FDA cleared the Nitric Oxide (NIOX) Test System. This test is a first-of-a-kind, non-invasive test system to measure the concentration of nitric oxide in exhaled human breath. The test system helps make it easier for doctors to monitor a patient's asthma. The NIOX Test is manufactured by Aerocrine AB of Sweden. It combines equipment that detects nitric oxide and equipment that analyzes exhaled breath with a special computer system. To use the device, a patient places the mouthpiece over his or her mouth. The mouthpiece is connected to the equipment and the computer. A patient inhales nitric oxide-

free air to total lung capacity, and then slowly exhales into the mouthpiece. The nitric oxide concentration is then displayed immediately on the computer screen. Doctors can use the device in their offices to evaluate their patient's response to anti-inflammatory treatment.

Predicting Coronary Heart Disease

On July 18, 2003, FDA cleared the PLAC Test. This test is a first-of-a-kind, laboratory blood test that will increase the ability of doctors to predict the risk of coronary heart disease (CHD). The PLAC test is manufactured by diaDexus, Inc. The test works by measuring an enzyme called lipoprotein-associated phospholipase A2. This enzyme is made by a type of white blood cell called a macrophage. Macrophages make more of this enzyme and release it into the blood when a person has CHD. The test provides supportive information when used with clinical evaluation and other tools for patient risk assessment. An elevated PLAC test result with an LDL-cholesterol less than 130 mg/dL gives doctors increased confidence that patients have 2 to 3 times the risk of CHD when compared with patients having lower PLAC test results.

Medical Device Review Programs

CDRH's ODE and OIVD are responsible for the program areas through which medical devices are evaluated or cleared for clinical trials and marketing. This section provides summary information about the major programs and includes a brief description of the premarket approval, product development protocol, humanitarian device exemption, investigational device exemption, and premarket notification programs.

Premarket Approval Applications (PMAs)

Under the Federal Food, Drug, and Cosmetic Act (the Act) and the FDA regulations, *Code of Federal Regulations, Title 21* (the Regulations), a manufacturer or others must submit a PMA for FDA review and approval before marketing certain new Class III devices. The PMA submitter must provide reasonable assurance that the device is safe and effective for its intended use and that it will be manufactured in accordance with current good manufacturing practices. As part of the review process, FDA may present the PMA to an expert advisory panel for recommendations. After obtaining the panel recommendations, the agency makes a determination to approve the PMA, deny it, or request additional information. When the FDA either approves or denies the PMA, it must publish a notice in the *Federal Register* to inform the public of the decision and make available a summary of the safety and effectiveness data upon which the decision is based. This publicly available summary does not include proprietary data or confidential information submitted by the applicant.

Product Development Protocols (PDPs)

The 1976 Medical Device Amendments to the Food, Drug, and Cosmetic Act allowed for two product pathways for a class III device: the PMA or, with prior FDA permission, the notice of completion of a PDP. The PDP process is based upon early consultation between the sponsor and the FDA leading to a device development and testing plan acceptable to

both parties. It minimizes the risk that the sponsor will unknowingly pursue — with the associated waste of capital and other resources — the development of a device that FDA will not approve. The PDP plan incorporates four discrete stages of FDA review during the device design process: a PDP Summary Outline; FDA/Advisory Panel review of the full PDP; consideration and, where appropriate, pre-approval of design modifications and protocol revisions made during execution of the PDP; and action on the sponsors Notice of Completion. FDA review of the PDP summary may take up to 30 days; the review of the full PDP may take up to 120 days; and FDA must declare the PDP "completed" or "not completed" within ninety days of receiving the Notice. If the FDA finds that the Notice — together with other information previously submitted — shows that the requirements of the PDP, including Quality System Regulation Inspection (or GMP inspection in the case of sponsors without an established satisfactory inspection history) has been met, the agency will declare the PDP complete.

Humanitarian Device Exemptions (HDEs)

An HDE application is essentially the same as a PMA in both form and content but is exempt from the effectiveness requirement of a PMA. Even though the HDE is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose, the application must contain sufficient information for FDA to determine, as required by statute, that the device does not pose an unreasonable or significant risk of illness or injury to patients and that the probable benefit to health outweighs the risk of injury or illness from its use. An HDE application must also contain information that will allow FDA to make the other determinations required by the Act. An approved HDE authorizes marketing of the humanitarian use device (HUD).

PMA Supplements

After a PMA is approved, the PMA holder may request FDA approval of changes to be made. For example, it may request changes to the device, its labeling or packaging, or the manufacturing processes used in its production. Unless prior approval is expressly not required by the PMA regulation, changes that affect the safety or effectiveness of the device require FDA premarket approval. FDA's review of a PMA supplement may be easy or difficult depending on the type of device, the significance of the change, and the complexity of the technology. Some PMA supplements can be as complex as the original application. Although the statutory time frame is 180 days for PMA Supplements, FDA is committed to reviewing these in shorter time frames and has reduced review time frames through the use of the real-time supplement process, 30-day notices, and expedited reviews.

Investigational Device Exemptions (IDEs)

Under the Act and Regulations, an individual, institution or company may sponsor the clinical investigation of a medical device to establish its safety and effectiveness. Before conducting a clinical trial, however, the sponsor must obtain the approval of an institutional review board (IRB) as well as informed consent from the study subjects at the time of their enrollment in the study. If the investigational device study presents a significant risk to the subjects, the sponsor must obtain FDA's approval of an "investigational device exemption" application (IDE) under 21 *CFR* 812. The IDE must contain information concerning the study's investigational plan, report of prior investigations, device manufacture, IRB actions, investigator agreements, subject informed consent form, device labeling, cost of the device, and other matters related to

the study. FDA has 30 calendar days from the date of receipt of the application to approve or disapprove an IDE submission.

IDE Amendments

Although not provided for in the IDE regulations, all submissions related to an original IDE that has been submitted, but not approved, are referred to as "IDE amendments". After an IDE is approved, related submissions are called "supplemental applications" under the regulations. Identification of IDE amendments enables FDA to track each IDE from the time it is originally submitted until the time it is approved.

IDE Supplements

The IDE regulation requires the sponsor of an investigation of a significant risk device to submit a supplemental application for a number of reasons. For example, a sponsor must submit a supplement if there is a change in the investigational plan when such a change may affect the scientific soundness of the study or the rights, safety, or welfare of the subjects. Supplemental applications also are required for the addition of investigational sites. This regulation also requires the submission of various reports, which are logged in as supplements to IDE applications. These include reports on unanticipated adverse effects of the device; recall and device disposition; failure to obtain informed consent; and annual progress reports, final reports, investigator lists, and other reports requested by FDA.

Premarket Notifications (510(k))

At least 90 days before placing a medical device into commercial distribution, a person required to register must submit to FDA, a premarket notification, commonly known as a "510(k)." The exception to this is if the device is exempt from the 510(k) requirements of the Act by statute or regulation. In addition to other information concerning the device, e.g., a description of the device, a 510(k) summary or a 510(k) statement, the 510(k) submitter must include information to substantiate that the device is "substantially equivalent" to a legally marketed device that is not subject to premarket approval. A substantially equivalent device is marketed subject to the same regulatory controls as the device to which it is found to be substantially equivalent. A device may not be marketed pursuant to a 510(k) until the submitter receives written clearance from FDA.

Medical Device Evaluations and Clearances

CDRH reviews five major types of submissions: Premarket Notification (i.e., a 510(k) submission), Premarket Approval Application (PMA), Product Development Protocol (PDP), Humanitarian Device Exemption (HDE) and Investigational Device Exception (IDE). Devices cleared for marketing through the 510(k) process are too numerous to list here but can be found at http://www.fda.gov/cdrh/consumer/mda.
During Fiscal Year 2003, no PDPs were completed, but CDRH approved the following 31 PMAs and 2 HDEs. These are listed on the next page. The PMA Approval website, available at http://www.fda.gov/cdrh/consumer/mda, contains easy-to-understand one-pagers for each PMA approved.

Original PMA/HDE Approvals for Fiscal Year 2003

		COMPANY	DEVICE
04-Nov-02	P020014	Conceptus, Inc.	Essure System (Contraceptive Tubal Occlusion Device)
06-Nov-02	P020004	W. L. Gore & Associates, Inc.	EXCLUDER™ Bifurcated Endoprosthesis
07-Nov-02	P020011	Gen-Probe, Inc.	Versant™ HCV RNA Qualitative Assay
27-Nov-02	P990069	EPMedSystems, Inc.	ALERT® System
12-Dec-02	P020008	Karl Storz Endoscopy-America, Inc.	Karl Storz Autofluorescence System
18-Dec-02	P020007	Medtronic, Inc.	Medtronic AVE Bridge™ Extra Support Over-the-Wire (OTW) Renal Stent System
23-Dec-02	P010055	Prostalund Operations AB	ProstaLund CoreTherm System Microwave Thermotherapy for BPH (Benign Prostatic Hyperplasia)
03-Jan-03	P020028	Phillips Medical Systems, Inc	Series 50 XMO Fetal/Maternal Monitor (Model M1350C) with Integrated Fetal Oxygen Monitoring (Fetal Oximeter)
24-Jan-03	P020027	Dade Behring, Inc.	Dimension FPSA Flex Reagent Cartridge and Dimension T/F PSA
03-Feb-03	P010001	Ceramtec AG	Ceramic Transcend Hip Articulation System
03-Feb-03	P000013	Howmedica Osteonics Corp.	Osteonics ABC System and Trident Ceramic System
14-Mar-03	P010065	E MED Future	Needle Zap™
28-Mar-03	P020022	Bayer Corp.	Bayer Versant™ HCV RNA 3.0 Assay
28-Mar-03	P020041	FemCap Incorporated	FemCap™ Barrier Contraceptive
15-Apr-03	H020007	Medtronic, Inc.	Medtronic Activa® Dystonia Therapy
17-Apr-03	P020045	CryoCath Technologies Inc.	7F Freezor® Cardiac Cryoablation Catheter and CCT.2 CryoConsole System
22-Apr-03	P020006	Enteric Medical Technologies, Inc.	Enteryx™ Procedure Kit
24-Apr-03	P020026	Cordis Corporation	CYPHER™ Sirolimus-eluting Coronary Stent on RAPTOR™ Over- the-Wire Delivery System or RAPTORRAIL® Rapid Exchange Delivery System
07-May-03	P020052	St. Jude Medical	Response™ CV Catheter System
14-May-03	P020024	AGA Medical Corporation	AMPLATZER® Duct Occluder and 180° Delivery System
23-May-03	P020018	Cook Incorporated	Zenith® AAA Endovascular Graft and H&L-B One-Shot Introduction System
06-Jun-03	P020002	Cytyc Corp.	ThinPrep™ Imaging System
11-Jun-03	P020037	Guidant Corp.	FX miniRAIL™ RX Percutaneous Transluminal Coronary Angioplasty (PTCA)

			Catheter
07-Jul-03	P030027	Wright Medical Technology, Inc.	Ceramic Transcend Hip Articulation
07-Jul-03	H020004	Smith and Nephew Wound Management	Dermagraft®
16-Jul-03	P020047	Guidant Corporation	MULTI-LINK RX and OTW VISION™ Coronary Stent Systems
29-Jul-03	P020049	Hancock Jaffe Laboratories, Inc.	ProCol® Vascular Bioprosthesis
01-Aug-03	P020021	AXCAN Scandipharm, Inc.	Wizard X-Cell Photodynamic Therapy Balloon with Fiber Optic Diffuser
12-Aug-03	P020036	Cordis Corporation	S.M.A.R.T.™ and S.M.A.R.T.™ Control™ Nitinol Stent System
13-Aug-03	P020033	Independence Technology, L.L.C.	INDEPENDENCE™ iBOT™ 3000 Mobility System
25-Aug-03	P020025	Boston Scientific	EP Technologies EPT-1000 XP™ RF Ablation System
23-Sep-03	P020031	Microsulis Medical, Ltd.	Microwave Endometrial Ablation System (Thermal Endometrial Ablation Device)
30-Sep-03	P020035	X-Site Medical, L.L.C.	X-PRESS™ 6 French Vascular Closure System

The following devices were approved via PMAs, PMA Supplements, and HDEs or cleared via 510(k)s or classified via the Automatic Evaluation of Class III Designation process during FY 03. They represent significant medical breakthroughs because they are first-of-a-kind, e.g., they use a new technology or energy source, or they provide a major diagnostic or therapeutic advancement, such as reducing hospital stays, replacing the need for surgical intervention, reducing the time needed for a diagnostic determination, etc. The information for each device includes the trade name and/or classification name, firm, and date of approval or clearance.

PMA/HDE Approved Devices

- NeedleZap™ by E MED Future (March 14, 2003)
- Thoratec HeartMate® SNAP-VE LVAS (Sutures Not Applied-Vented Electric Left Ventricular Assist System) by Thoratec Corporation (November 6, 2002)
- CYPHER™ Sirolimus-eluting Coronary Stent on RAPTOR™ Over-the-Wire Delivery System; CYPHER™ Sirolimus-eluting Coronary Stent on RAPTORRAIL® Rapid Exchange Delivery System by Cordis Corporation (April 24, 2003)\
- Ceramic Transcend Hip Articulation System by Ceramtec AG (February 3, 2003)
- Osteonics ABC System and Trident Ceramic System by Howmedica Osteonics Corp. (February 3, 2003)
- Medtronic Activa® Deep Brain Stimulation (DBS) System by Medtronic, Inc. (April 15, 2003)
- INDEPENDENCE™ iBOT™ 3000 Mobility System by Independence Technology, L.L.C. (August 13, 2003)

- LADARVision® 4000 Excimer Laser System by Alcon Laboratories, Inc. (October 18, 2002)
- STAR S4 ActiveTrak™ Excimer Laser System and WaveScan WaveFront® System by VISX, Inc. (May 23, 2003)
- The Essure™ System by Conceptus, Inc. (November 4, 2002)
- ThinPrep™ Imaging System by Cytye Corporation (June 6, 2003)

510(k) Clearances or Automatic Evaluations of Class III Designation Devices

- Reactive Skin Decontamination Lotion (RSDL) by O'Dell Engineering Ltd./E-Z-EM Canada Inc. (March 25, 2003)
- Repiphysis Limb Salvage System by Wright Medical Technology, Inc. (December 4, 2002)
- TenoFix Tendon Repair System by Ortheon Medical Llc. (January 22, 2003)
- TGDc-01 "PRA" Tonometer by Truvision Instruments (October 11, 2002)
- MP-1 Micro Perimeter by Nidek Technologies (December 23, 2002)
- Embosphere Microspheres and Embogold Micropheres by Biosphere Medical, Inc. (November 22, 2002)
- Contour Emboli Pva and Fastracker-325 Infusion Catheter by Boston Scientific Corp. (September 23, 2003)
- Group B Streptococcus Detection Assay by Infectio Diagnostic, Inc. (November 18, 2002)
- QCS Her/2 Immunocontrols by OC Sciences (June 18, 2003)

Electronic Submissions

In FY 03, CDRH received 97 complete electronic copies of submissions for PMAs, IDEs, and 510(k)s from 25 different sponsors in addition to the paper submission. These numbers show an increase from FY 02 when 73 complete submissions were received from 14 different sponsors. Prior contact with CDRH's ODE or OIVD divisions is still requested before developing and sending an electronic copy. Electronic copies enhance the efficiency of the review process, especially when several CDRH offices are involved in the review of the submission. Instructions for submitting submissions in electronic form can be found on the CDRH home page at the address http://www.fda.gov/cdrh/elecsub.html.

Patient Labeling

Improved patient labeling on medical devices allows the patient or caregiver to better understand both instructions for use and risk-benefit information. OHIP reviews patient labeling for all new Premarket Approval (PMA) submissions and also for 510(k) and HDE submissions when CDRH's Office of Device Evaluation (ODE) thinks that the patient labeling for a device is particularly important.

Medical Device Review Performance Statistics

CDRH is responsible for protecting the rights, safety and welfare of patients participating in clinical studies of significant risk medical device research and for evaluating the safety and effectiveness of medical devices before these devices enter the U.S. marketplace. Following are the details of the review activities and performance for FY 03. Next, the Premarket Approval Applications (PMAs) are reviewed in terms of review time as well as

volume. This same analysis is done for PMA supplements. The remainder of this section deals with Humanitarian Device Exemptions (HDEs), Investigational Device Exemptions (IDEs), and Premarket Notifications (510(k)s).

Workload

During FY 03, CDRH received 9,872 major submissions compared to 10,323 major submissions in FY 02. [See Table 1 for a breakdown of major submissions received.]

Table 1. Major Submissions Received FY 02 – FY 03

TYPE OF SUBMISSION	2002	2003
Original PMAs	49	54
PMA Supplements	645	669
Original IDEs	312	242
IDE Amendments	252	216
IDE Supplements	4,724	4,415
510(k)s	4,320	4,247
Original HDE	5	10
HDE Supplements	16	29
Total	**10,323**	**9,872**

On the decision side, CDRH completed the processing of 9,570 major submissions, compared to 10,238 major submissions in FY 02. [See Table 2 for major submissions completed.]

Table 2. Major Submissions Completed FY 02 - FY 03

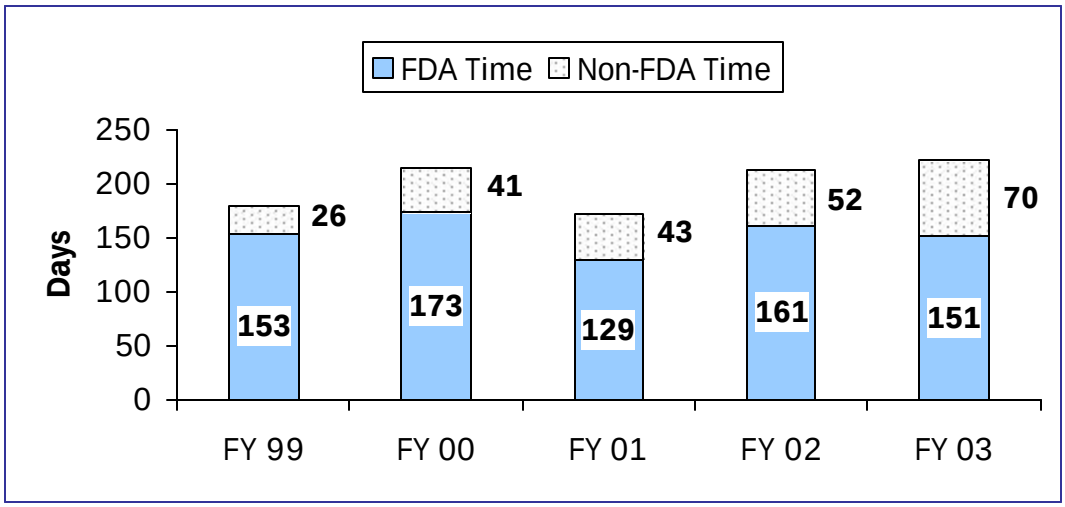
TYPE OF SUBMISSION	2002	2003
Original PMAs	41	31
PMA Supplements	533	494
Original IDEs	307	246
IDE Amendments	251	217
IDE Supplements	4,711	4,424
510(k)s	4,376	4,132
Original HDE	6	2
HDE Supplements	13	24
Total	**10,238**	**9,570**

Premarket Approval Applications (PMAs)

CDRH received 54 original PMAs (5 more than the number received in FY 02). The total number of PMAs in inventory (active and on hold) at the end of this fiscal year increased from 73 in FY 02 to 83. The number of active PMAs under review decreased at the end of

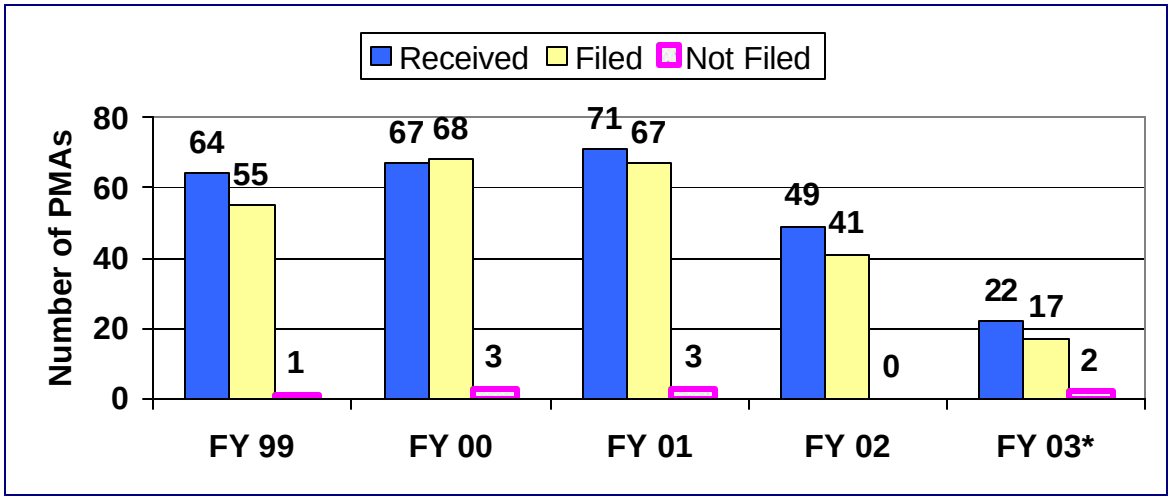
FY 03 to 35 compared to 42 last year, and those on hold increased from 31 in FY 02 to 48 in FY 03. The total number of PMA actions decreased from 237 to 198 actions. These actions included 54 filing decisions, 87 scientific review decisions, and 57 approval/approvable/not approvable decisions. The 57 original PMA decisions comprised 31 approved PMAs, 16 approvable PMAs, and 10 not approvable PMAs. Of the 31 approvals, 5 were expedited PMAs. See Part 2 (INDUSTRY INFORMATION) for a complete list of PMA approvals. Average FDA review time for original PMAs reaching approval decreased from 161 days in FY 02 to 151 days in FY 03. The non-FDA component of review time increased from 52 days in FY 02 to 70 days this fiscal year. Thus, the total average review time increased to 221 days from 213 days.

Figure 1. Average Review Time for PMA Decision Cohort Approvals



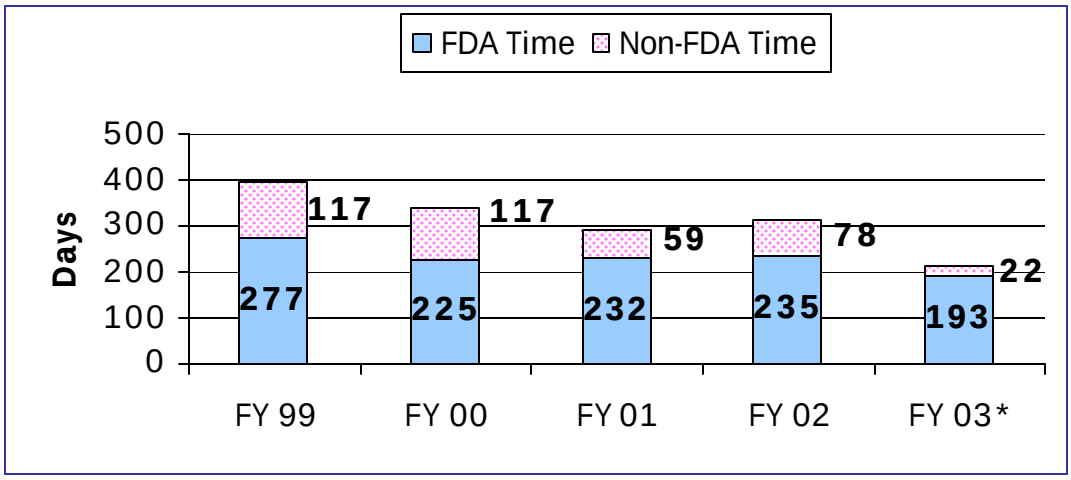
Of greater significance to industry is the total elapsed time from submission to decision. In FY 03, the total average elapsed time for PMA decision cohort performance decreased to 359 days from 364 days in FY 02.

Figure 2. Original Receipt Cohort PMAs Received and Filed



*First six months

Figure 3. Receipt Cohort PMA Average Elapsed Time from Filing to Final Action

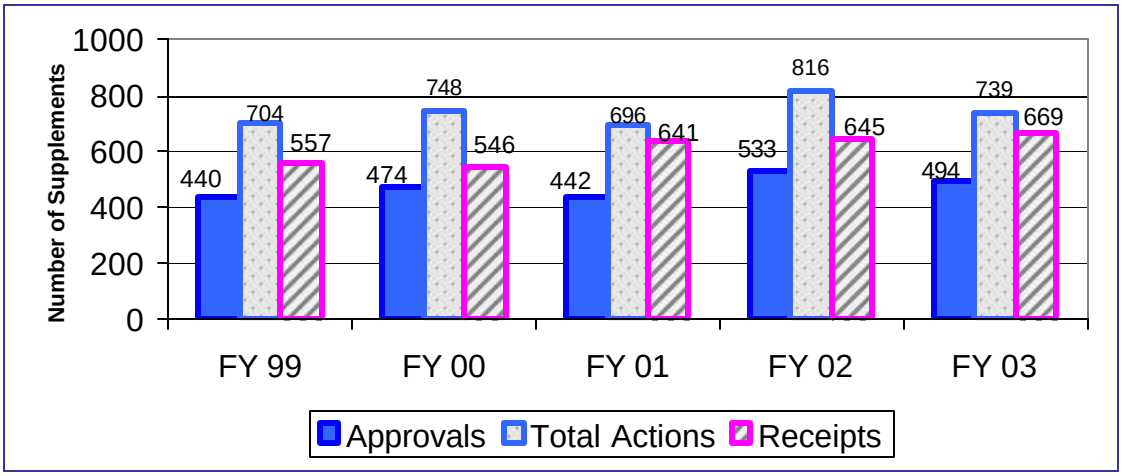


***First six months**

For the first 6 months of FY 03 for PMA receipt cohort performance, the average FDA days from filing to first action increased from 136 in FY 02 to 144 days. The average FDA (total) elapsed time to an approval or to a denial decreased from 235(313) in FY 02 to 193(215) days in FY 03 (see Figure 3). The median FDA (total) elapsed time to an approval or denial decision decreased from 198(300) in FY 02 to 174(218) days in FY 03. All of the statistics of the PMA receipt cohort for FY 03 indicated that CDRH is making decisions faster.

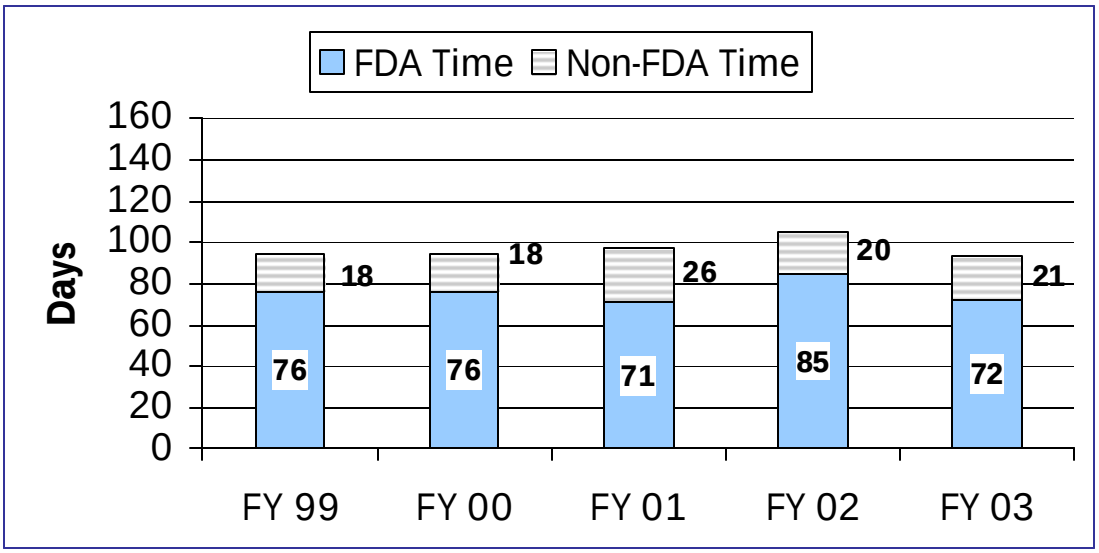
The number of PMA supplements received increased from FY 02's 645 to 669 in FY 03. There were 739 PMA supplement actions which are down from last year's 816 total actions. These actions included 6 panel track PMA supplement filing decisions, 98 scientific review decisions, and 635 approval decisions (see Figure 4).

Figure 4. Annual Receipts and Actions for PMA Supplement Decision Cohort



For PMA supplements reaching final action, the average total review time decreased from 105 days in FY 02 to 93 days in FY 03 (see Figure 5), and the average total elapsed time decreased from 124 days to 111 days.

Figure 5. Average Review Time for PMA Supplement Decision Cohort Final Actions



There were 4 PMA supplements active and overdue at the end of this fiscal year. The number of active supplements decreased to 123 in FY 03 from 127 in FY 02, and the number of supplements on hold increased from 97 to 111. CDRH received 24 more PMA supplements and are reaching final decisions on fewer, but CDRH is taking an average of 13 less days for the decisions. For the first 6 months of FY 03 for PMA supplements receipt cohort performance, the first action and final action are as follows. The average FDA days from filing to first action decreased from 71 in FY 02 to 61 days in FY 03. The average FDA (total) elapsed time to an approval or denial decreased from 74(89) in FY 02 to 57(67) in FY 03. The median FDA (total) elapsed time to an approval or denial decreased from 35(43) in FY 02 to 30(36) days in FY 03.

Real-Time Review of PMA Supplements

A total of 193 requests were received and processed for real-time PMA supplements in FY 03 which represents 29% of all supplements received. Of those submissions, 164 were approved. Most applicants chose telephone conferencing versus a face-to-face meeting or a videoconference. Overall, average review time from receipt to final approval was 44 days.

Product Development Protocols (PDPs)

No original PDPs were approved in FY 03. Three routine PDP supplements and four "Real-Time" PDP Supplements were "approved." Note that a PDP that has been "declared complete" is considered to have an approved PMA. CDRH continues to encourage the use of the PDP process and will work with interested applicants to fully evaluate their PMA options.

Modular PMA Review

For FY 03 CDRH received a total of 30 PMA shells and 73 modules. A total of 17 modules were found to be acceptable while 5 received deficiency letters. Seventeen modules were

rolled into PMA review during FY 03 because they were under review or on hold at the time the PMA was received. Applicants with modular submissions that were under review or deficient when the PMA was received continued to receive feedback under the PMA for those modules. However, this is based on a small number of submissions achieving PMA approval since modular review was implemented. A tracking system with modular PMA query capability became available during FY 99.

Humanitarian Device Exemption (HDE) Applications

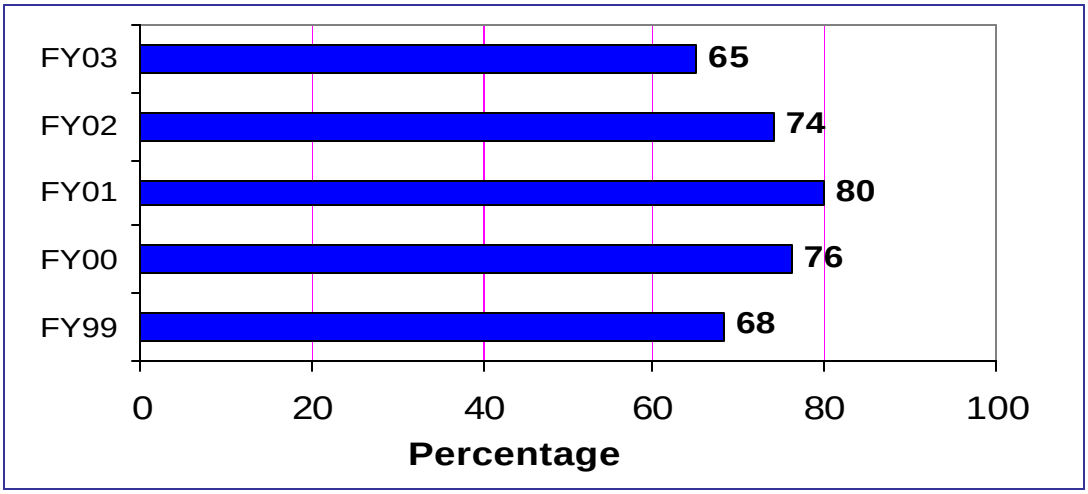
CDRH received 10 original HDEs, an increase from 5 received in FY 02. The total number of original HDE actions increased from 23 in FY 02 to 26 in FY 03. These actions included 13 filing decisions, 9 review determinations, 2 approval decisions and 2 other final decisions. A total of 3 first actions were made this fiscal year, a decrease from 6 made last year. The average time from filing to first action decreased from 53 days in FY 02 to 48 days in FY 03. Sixty-seven percent of the first actions made in FY 03 occurred within 75 days. In FY 03, the average elapsed time (from filing to final approval) for original HDEs was 248 days, a decrease from 302 days in FY 02. The average FDA time was 152 days, a decrease from 175 days in FY 02. The average non-FDA time was 96 days, a decrease from 127 days last year. The total number of original HDEs in inventory (active and on hold) at the end of this fiscal year was 10. Of these, 4 were under review and 6 were on hold. There were no active HDEs that were overdue at the end of the fiscal year.

The number of HDE supplements received increased to 29 in FY 03 from 16 in FY 02. There were 37 HDE supplement actions in FY 03, up from 27 in FY 02. These actions included 24 approval, 5 approvable, and 6 not approvable decisions. A total of 29 first actions for HDE supplements were made this fiscal year, an increase from 17 last year. The average time from filing to first action decreased from 53 days in FY 02 to 37 days in FY 03. Ninety percent of the first actions were made within 75 days. The average elapsed time (from filing to final approval) for HDE supplements increased from 74 days in FY 02 to 95 days in FY 03. The average FDA time decreased from 60 days in FY 02 to 43 days in FY 03. Non-FDA time increased from 14 days in FY 02 to 52 days in FY 03. The number of HDE supplements in inventory (active and on hold) at the end of this fiscal year was 11. Of these, 5 were under review and 6 were on hold. There were no active HDE supplements that were overdue at the end of the fiscal year.

Investigational Device Exemptions (IDE)

During FY 03, CDRH reviewed 309 pre-IDEs. Based on these reviews, guidance for the pre-original IDE submissions were provided through meetings with the sponsors, letters, fax, or by phone. CDRH received 242 original IDEs, a decrease from 312 received in FY 02. There were 246 decisions made on original IDEs, a decrease from 307 last year. One hundred percent of all original IDE decisions were issued within 30 days in FY 03. The average review time was 27 days.

Figure 6. Percentage of IDEs Approved on First Review Cycle*



*Based on those IDEs complete enough to permit substantial

Of the original IDEs which were complete enough to support substantive review, the percentage of IDEs approved on the first review cycle decreased from 74% in FY 02 to 65% in FY 03 (see Figure 6).

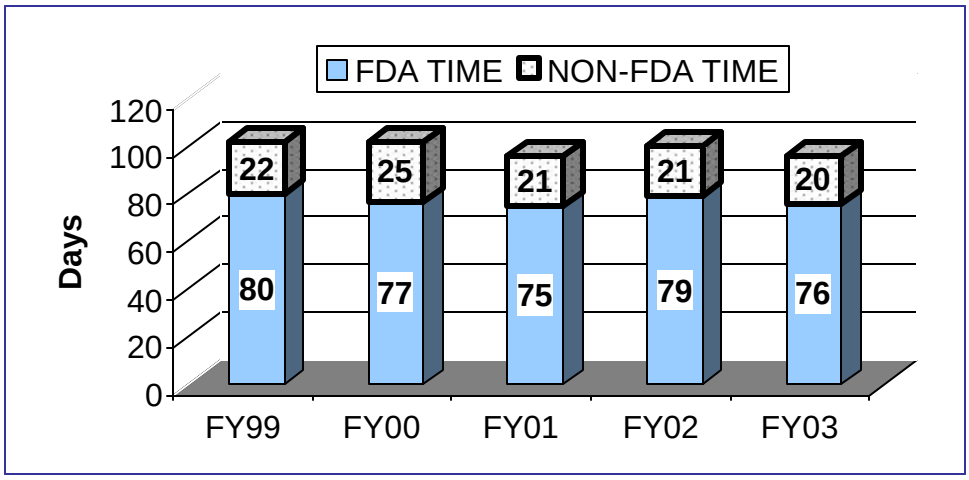
During this fiscal year, 216 IDE amendments were received. Decisions were made on 217 amendments: 73 approvals (34%); 40 disapprovals (18%); and 104 other administrative actions (48%). One hundred percent of these decisions were made within 30 days. It took an average total time of 180 days to approve IDEs that were initially disapproved, up from 135 days in FY 02. This average approval time consisted of 68 days for FDA time, the same as last year, and 112 days for non-FDA time, up from 67 days in FY 02.

CDRH received 4,415 IDE supplements during FY 03. There were no overdue supplements at the end of the year, and the percentage of supplements reviewed within the 30-day statutory timeframe was 100% in FY 03. The average review time for IDE supplements was 19 days, down from 20 days in FY 02.

Premarket Notification (510(k)s)

CDRH received 4,247 original 510(k)s, as well as 1,856 510(k) supplements (responses to hold letters, the receipt of which restart the 90-day review clock), and 1,690 510(k) amendments (additional information received while the 510(k) is under review, the receipt of which does not affect the review clock). Four 510(k)s were granted expedited status. The total average review time decreased to 96 days in FY 03 from 100 in FY 02, and the average FDA review time was 76 days, down from 79 days in FY 02. The median review time, i.e., the time it took to review 50% of the 510(k)s, has been falling from a high of 164 days in FY 93 to 72 days in FY 03.

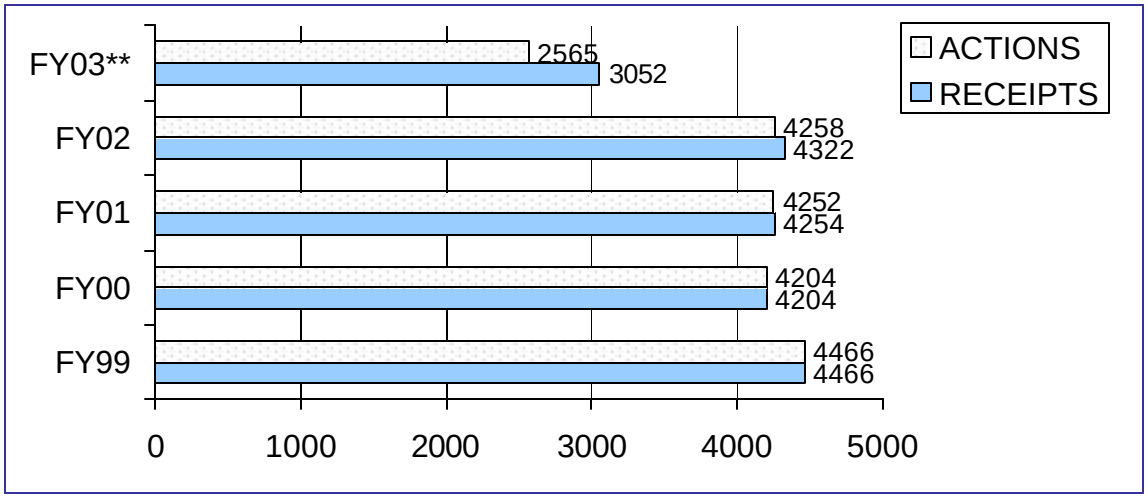
Figure 7. Average 510(k) Review Time for Decision Cohort



There were 1,391 510(k)s in inventory (those under active review or on hold) at the end of this fiscal year. The number on hold at the end of FY 03 was 376. Most important, for the eighth consecutive fiscal year there were no 510(k)s active and overdue at the end of the reporting period.

For the first 9 months of FY 03 for receipt cohort performance, the FDA time from receipt to final decision was 68 days.

Figure 8. Receipts and Actions for 510(k) Receipt Cohorts*

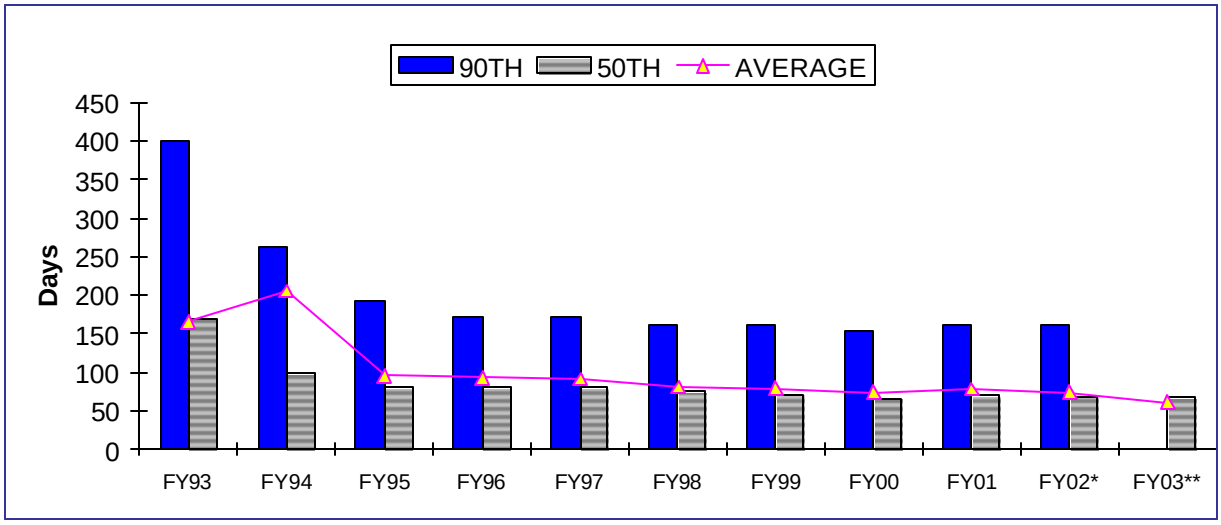


*Cut Off Date of 9/30/03 for all receipt cohorts.

**12 month projection based on first 9 months of receipts.

For the first 9 months of FY 03 for receipt cohort performance, the total time from receipt to final decision decreased to 73 days.

Figure 9. FDA Days from Receipt to Final Action for 510(k) Receipt Cohorts*



*Cut Off Date as of 9/30/03 for all receipt cohorts.
**For the first 9 months of FY 03. 90th percentile data not available for FY 03.

Third-Party Review of 510(k)s

During FY 03, CDRH received 190 510(k)s reviewed by third-party organizations under the Accredited Persons provisions (section 523) of the Federal Food, Drug, and Cosmetic Act. This was a 50 percent increase over the 127 submissions received last fiscal year. The increase may be attributable, at least in part, to FDA's implementation of MDUFMA's user fee provisions during FY 03 that require applicants to pay a fee when submitting 510(k)s without a third-party review.

CDRH made final decisions on 169 "third-party" 510(k)s in FY 03, an increase from the 132 final decisions in FY 02. The average total elapsed time from a third-party's receipt of a 510(k) to CDRH's issuance of a substantial equivalence decision was 74 days, as compared to the average total elapsed time of 112 days for the substantial equivalence decisions on comparable 510(k)s that did not have a third-party review. (This comparison is based on "traditional" and "abbreviated" 510(k)s; "special" 510(k)s are excluded because they typically are not submitted to third parties.) Thus, 510(k)s with a third-party review received marketing clearance 34 percent faster, on average, than comparable 510(k)s reviewed entirely by FDA.

Information on the 510(k) Accredited Persons Program is available on the Center's Third-party webpage at http://www.fda.gov/cdrh/thirdparty .

Special 510(k)s

From October 1, 2002 to September 30, 2003 CDRH received 864 Special 510(k)s out of the 4,247 total number of 510(k)s received. Of these 831 have received final decisions (792 were found substantially equivalent, 7 were found not substantially equivalent, and the remaining 32 had other decisions such as withdrawn or deleted) with the average FDA review time of 28 days and the average total time of 34 days.

Abbreviated 510(k)s

During this fiscal year, CDRH received 206 Abbreviated 510(k)s out of the 4,247 total number of 510(k)s received. Two hundred twelve received final decisions (165 substantially equivalent, 3 not substantially equivalent, and 44 other decisions) with a FDA average review time of 96 days and total time of 119 days.

Greater Efficiency and Effectiveness

CDRH continued efforts to increase efficiency of premarket reviews and to focus review resources on devices that present the most risk. Examples of actions taken during FY 03 are listed in this section.

Proposed Classification Actions

- Published a proposed rule in the *Federal Register* on October 22, 2002 to classify the Human Dura Mater into class II.
- Published a proposed rule in the *Federal Register* on March 20, 2003 to classify the Silicone Sheeting into class I exempt from premarket notification.

Final Classification Actions

- Published a final rule classifying the medical washer and medical washer-disinfector intended for general medical purposes to clean and dry surgical instructions, decontaminate or disinfect anesthesia equipment, hollowware, and other medical devices into class II (special controls). [Effective December 16, 2002]
- Published a final rule classifying resorbable calcium salt bone void filler device intended to fill bony voids or gaps of the extremities, spine, and pelvis that are caused by trauma or surgery and are not intrinsic to the stability of the bony structure into class II (special controls). [Effective July 2, 2003]

Device Reclassification

Any interested person may submit a petition to the agency for reclassification of a device, e.g., from class III to class II, or class II to class I. Additionally, the agency on its own initiative may follow procedures to reclassify a generic type of device. There are five sections under the Federal Food, Drug, and Cosmetic Act by which CDRH may reclassify a device, section 513(e), 513(f) 514(b), 515(b) and 520(l) depending on the status of the device type, such as new device types found to be not substantially equivalent or transitional devices formerly regulated as drugs. The reclassification petition needs to contain sufficient information to allow FDA to determine that the proposed classification can provide reasonable assurance of safety and effectiveness. Reclassification petitions and their final decisions are put on public display at the Dockets Management Branch.

Proposed Reclassification Actions

- Published a proposed rule in the *Federal Register* on December 13, 2002 to reclassify the arrhythmia detector and alarm from class III (premarket approval) to class II (special controls) based on new information regarding the device. FDA is also proposing to revise the identification of the arrhythmia detector and alarm

to separate the automated external defibrillator (AED) from the identification of the arrhythmia detector and alarm.

Final Reclassification Actions

- Published a final rule in the *Federal Register* on December 19, 2002 to reclassify the Absorbable Polydioxanone Surgical Suture from class III to class II. [Effective July 17, 2002]
- Published a final rule in the *Federal Register* on December 31, 2002 reclassifying the cutaneous carbon dioxide (PcCO2) monitor from class II (performance standards) into class II (special controls). FDA also reclassified the cutaneous oxygen (PcO2) monitor for an infant patient who is not under gas anesthesia from class II (performance standards) into class II (special controls) and is reclassifying the cutaneous oxygen (PcO2) monitor for all other uses from class III (premarket approval) into class II (special controls).
- Published a final rule in the *Federal Register* on March 24, 2003 to reclassify the Knee Joint Patellofemoral Metal/Polymer Porous-coated Uncemented Prosthesis and the Knee Joint Femoraltibial (Unicompartmental) Metal/Polymer Uncemented Prosthesis from class III to class II. [Effective February 3, 2003]

Automatic Evaluation of Class III Designation

- Issued an order on April 30, 2003 classifying NIOX Breath Nitric Test System into class II CFR 862.3080
- Issued an order on June 16, 2003 classifying Endotoxin Activity Assay into class II CFR 866.3210
- Issued an order on July 8, 2003 classifying West Nile Virus IgM Capture ELISA Assay into class II CFR 866.3940

513(g) Submissions

Under Section 513(g) of the Federal Food, Drug, and Cosmetic Act, a person can request information about the classification of a device and the regulatory requirements applicable to the device. Within sixty days of the receipt of such a request, the Office of Device Evaluation (ODE) or the Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD) will provide a written response to such request.

During this fiscal year, CDRH received 156 513(g) requests for information. CDRH has responded to 135 of these requests, while reviews of the remaining 21 requests are ongoing.

New Challenges

Significant Jurisdictional Issues

Title 21 of the Code of Federal Regulations Part 3 - PRODUCT JURISDICTION describes the procedure the agency uses to assign Center jurisdiction over medical products whose jurisdiction is not clear or is in dispute. Requests for Designations (RFDs) over such products are made in writing to the Office of Combination Products which took this role over from the Office of the Chief Mediator and Ombudsman in mid-FY 03. These formal

submissions contain the material describing the requester's product and/or products; a proposal regarding which Center should be given lead designation over their product, and whose authorities (biological, device or drug) should apply.

In FY 03 CDRH participated in the review of 26 out of 34 RFDs received by the FDA's Ombudsman's Office, in addition to completing the reviews of 5 RFDs received in FY 02. Of the 31 RFDs [26 assigned in 2003 and the 5 carry over from 2002] which CDRH completed reviews of in FY 03 by both CDRH:

- CDRH was assigned the lead center in 14 of those requests
- CDER was assigned lead center in 8
- CBER was designated lead in 6 RFDs
- One was ruled by the Office of Combination Products as not an FDA-regulated product and
- 2 were not due for completion until FY2004.

Least Burdensome

The two sections of the Food, Drug, and Cosmetic Act commonly referred to as the "least burdensome provisions" were enacted by Congress in 1997 to ensure the timely availability of safe and effective new products that will benefit the public and ensure that the United States continues to lead the world in new product innovation and development. During the last few years, CDRH has been working with stakeholders to develop an interpretation of the least burdensome provisions. In the May 3, 2001 *Federal Register*, the draft guidance document entitled, "The Least Burdensome Provision of the FDA Modernization Act of 1997: Concept and Principles" was released for comment. While the agency received very few comments on the draft, almost all of them strongly supported the guidance and encouraged full implementation of it as soon as possible. Several comments recommended that FDA develop a training program for its staff as well as ways to assess both the agency's success in implementing the principles and the stakeholders' satisfaction with FDA's incorporation of them into daily activities. The agency agreed with these recommendations and has incorporated them into the final guidance. The final document was released on the Internet on September 30, 2002 and in the October 4, 2002 *Federal Register* (67 FR62252). The guidance may be found on the Center's website at www.fda.gov/cdrh/ode/guidance/1332.html.

Study Determination Inquiries

Every year, CDRH receives numerous inquiries regarding the need to submit an IDE application for research involving medical devices. These inquiries are received through a variety of means - in meetings, by telephone, e-mail, fax or letter. Such inquiries are initiated by a wide variety of entities, including device manufacturers, clinical investigators, and IRB members. In order to respond to these inquiries, CDRH may refer to the IDE regulation (21 CFR 812), particularly sections 812.1 (Scope), 812.2 (Applicability), and 812.3 (Definitions), and the FDA Information Sheet entitled, "Significant Risk and Nonsignificant Risk Medical Device Studies" (hereafter referred to as SR/NSR guidance).

Often, inquiries received can be easily answered by referring to the sources identified above. Occasionally, inquiries will present new situations not clearly identified in the regulation or the SR/NSR guidance. A few inquiries involve the scope of the IDE

regulation and/or jurisdictional issues that may require consultation with the other FDA centers. An IDE Memorandum (#D01-1) dated October 26, 2001 was issued to establish written procedures for handling inquiries regarding the need for an IDE application for research involving medical device.

When responding to these inquiries, there are three possible responses: the research is exempt from the IDE regulation; the abbreviated IDE requirements must be met (nonsignificant risk [NSR] study); or the full requirements of the IDE regulation must be met, that is, an IDE application must be submitted to FDA (significant risk [SR] study). In FY 03 ODE received 49 inquires. Of the 49 inquires, there were 13 SR determinations, 13 NSR determinations, 22 exempt determinations, and 6 inquires still under review.

Access to Information

CDRH Website

CDRH's website (http://www.fda.gov.cdrh) provides information on topics important to consumers, health care professionals and the industry. For example:

- **The Patient Safety Portal** (http://www.fda.gov/cdrh/patientsafety/) informs and educates health care professionals on patient safety issues related to medical devices, by providing a convenient mechanism in which to access current and emerging issues within the Federal domain.
- **CDRH Consumer Information** (http://www.fda.gov/cdrh/consumer/product.html The Consumer Information website provides consumers information about medical devices. This website appears in a searchable format for the public.

CDRH also maintains dedicated websites on key public health issues ("Hot Topics"). Examples include:

- Diabetes - http://www.fda.gov/diabetes/
- LASIK - http://www.fda.gov/cdrh/lasik/
- CT scanning - http://www.fda.gov/cdrh/ct/
- Breast implants - http://www.fda.gov/cdrh/breastimplants/
- Cell phones - http://www.fda.gov/cellphones/

Patient Safety News (PSN)

FDA Patient Safety News is a monthly video news show for health care personnel, carried on satellite broadcast networks aimed at hospitals and other medical facilities across the country. It features information on new drugs, biologics and medical devices, on FDA safety notifications and product recalls, and on ways to protect patients when using medical products. The show is distributed to 4 health TV networks – with a combined reach of nearly 4,500 hospitals. More importantly, the program has a website – http://www.fda.gov/psn - where viewers can view either the entire show or just a select story, find more information on each story, search for previous stories, e-mail stories to colleagues, report adverse events (through a link to MedWatch) and sign-up for the PSN listserve. They also can e-mail a story to a colleague. The PSN website is currently receiving over 4,000 "hits" each month. The webcast center, where viewers can watch the whole show or just a select story, currently receives over 2,500 requests per month.

FDA Patient Safety News has made significant progress in the past year. Starting with the November 2002 show (#10), PSN realized its goal of incorporating all medical product centers into the program. CBER and CDER have been active partners and have made significant contributions to the program. PSN also has been able to occasionally include stories from other FDA centers. For example, it recently completed a story from CFSAN on the new trans-fatty acid labeling. In December PSN will reach the two year mark with episode # 24.

Starting with the November show, viewers will be able to download a video story to their own computer, network, or even a DVD – for viewing then or at a later time. PSN has received numerous requests for video copies of stories for use during staff meetings and in-services.

This capability will allow users to download high-resolution mpeg files that can be played back either on a computer or TV.

Laboratory Safety Tips

The Laboratory Safety Tips webpage maintained by the Office of In Vitro Diagnostic Device Evaluation and Safety (http://www.fda.gov/cdrh/oivd/laboratory.html), gives information about maintaining a safe clinical laboratory environment, including laboratory safety tips, a discussion of quality control and quality assurance, details about reporting IVD problems, and resources for additional information. Examples of safety tips published this year include:

- Follow good laboratory practices with waived laboratory tests
- Performance and cautions in using rapid influenza virus diagnostic tests
- Built in controls for single use disposable tests
- Common problems with the use of glucose meters
- Make sure glucose meters used in testing neonates are FDA-cleared for testing in neonates
- Useful tips to increase accuracy and reduce errors in test results from glucose meters

Notifications

Notifications, in the form of Safety Alerts, Public Health Advisories and Public Health Notifications, are the primary means for CDRH to communicate to medical device users important information regarding postmarket safety issues. Web Notifications are updated as additional information becomes available so the public is encouraged to check back at this site. Alerts can be found at http://www.fda.gov/cdrh/safety.html.

- **Web Notifications**

10/31/2002 and Updated 4/1/2003	Complications Related to the Use of Bone Cement in Treating Compression Fractures of the Spine
10/23/2002	Non-Corrective Decorative Contact Lenses Dispensed Without a Prescription
7/24/2002and Updated: 9/25/2003	Risk of Bacterial Meningitis in Children with Cochlear Implants

- **Public Health Notifications**

12/19/2002	Diathermy Interactions with Implanted Leads and Implanted Systems with Leads

Targeted Outreach Efforts

In FY03 CDRH placed six articles in periodicals, one North American Precis Syndicate (NAPS) article on consumer websites and posted a contacts listing database (http://www.fda.gov/cdrh/contactslisting) in 188 newspapers, reaching 7.4 million potential readers.

- **Tampons and Toxic Shock Syndrome (TSS)** - The new recommendations on tampons and TSS were disseminated though outreach efforts using women's

magazines and through the *FDA & YOU* newsletter available at http://www.fda.gov/cdrh/fdaandyou/.

- **Hospital Bed Safety** - Patient/Clinical video aimed to inform the public on how to prevent hospital bedrail entrapments by the elderly, frail, and long-term care patients was developed and distributed. The video entitled, "Do No Harm" was produced by American Association of Retired People (AARP). This 22 minute video for caregivers and health care facilities provides real-life situations on the use of bed rails in both acute and long-term care environments and offers insights by patients and their families, nurses and other caregivers.
- **Secondary School Project** - The objective of this project is to effectively deliver device messages to secondary school students. During FY 03 CDRH talked with 50 secondary school experts to determine the best mechanism to use in reaching this audience and obtained contact points in 96% of states. CDRH developed a Web-based newsletter *FDA & YOU*, http://www.fda.gov/cdrh/fdaandyou/. A packet containing a letter from CDRH officials, a one-time printed version of *FDA & YOU* and the Contacts Listing brochure was sent to 16,038 Health Educators, 19 FDA Public Affairs Liaisons (PALS) and 43 Public Affairs Specialists (PASers).
- ***FDA & YOU*** is an educational newsletter intended for use by health educators, secondary school students and their parents. *FDA & YOU* is a cooperative effort, combining the skills and support of FDA's five centers and was initiated to inform and encourage health educators and students to learn about the latest FDA medical product and health news. To coincide with the typical school year *FDA & YOU* is published three times per year, in the fall, winter and spring. The newsletter is now available online at: www.fda.gov/cdrh/fdaandyou.

The FDA Industry Website

At the end of FY 02, FDA (http://www.fda.gov) launched a new portal page - http://www.fda.gov/oc/industry - to make it easier for FDA-regulated companies to find information they need to comply with regulations. Featured links on the page include:

- Guidance documents
- Inspection references
- Information on imports
- Warning letters and other FDA enforcement activities

The portal also provides easy access to regulatory information from FDA's centers. CRDH is a regular contributor to this website. Companies can use the portal to contact FDA with questions, submit comments online about proposed FDA regulations, or sign up to attend meetings for which registration is required.

Additional Consumer Information Resources

The Division of Small Manufacturers, International and Consumer Assistance (DSMICA) also provides information to consumers regarding medical devices and radiation-emitting products to enhance users ability to avoid risk, achieve maximum benefit, and make informed decisions about the use of such products.

Website: http://www.fda.gov/cdrh/consumer/index.html
E-Mail: dsmica@cdrh.fda.gov

Phone: Toll Free 1-888-463-6332 or 301-827-3990 directly between the hours of 8:00 a.m. – 4:30 p.m. EST
Fax: 301-443-9535

Regulatory Science and Standards

Science and Technology

Science and Technology Activities and Accomplishments

The CDRH Office of Science and Engineering Laboratories (OSEL) supports the scientific basis for the agency's regulatory decision-making by developing independent laboratory information for regulatory and other public health activities of the CDRH. The Office is responsible for developing and supplying expertise on key FDA-specific scientific and technical concerns; for providing CDRH with independent data for premarket analysis and regulatory enforcement, allowing the Center to be free of overdependence on regulated industry as the sole source of performance data; and to identify the right scientific questions and develop reliable testing methods. The Office also is forging increased internal collaborations with other Center offices, such as the Office of Surveillance and Biometrics and the Office of Device Evaluation, and extramural collaborations, such as with the National Institute of Biomedical Imaging and Bioengineering (NIBIB) and AdvaMed.

One segment of the Office, the Division of Biology, relocates to the brand new FDA Life Science facility at the White Oak campus in November 2003. Approximately 50 employees, contractors, and students will begin to set up the biology laboratories for CDRH. CDRH staff is working in a coordinated effort to ensure that working conditions, furniture and equipment installations and necessary information technology, health and safety and security procedures are in place for the upcoming move to White Oak.
Program areas active in FY 03 include:

- **Genomic and Genetic Devices** - The Genomic and Genetic Devices program area focuses its expertise on the newly developing areas of human genetics and genomics. This new area includes the integration of genetic information into routine medical practice, e.g., for use in optimizing individual therapies; and using the new technologies to address the issues of safety and efficacy of products undergoing premarket review and postmarketing issues such as adverse responses.
- **Host Response: Tissue-Materials Interactions, Tissue-Device Interactions** - This program encompasses an interconnected program of laboratory research, risk assessment, and standards development activities designed to provide a scientific basis for regulatory decision making in CDRH. It encompasses three major areas:
  - Biological Effects of Chemicals and Medical Device Materials
  - Research to Support Risk Assessment
  - Infection Control
- **Biological Risk Assessment** - Risk assessment is the process of determining the extent of human health hazard relative to exposure conditions. Staff in this program area conduct research to address CDRH's regulatory need for improved methods of detecting and quantifying specific risks:
  - Chemical compounds released from medical device materials
  - Microorganisms associated with medical devices
  - Exposure to radiation
- **Biotechnology and Biomolecular Studies -** Research in this program is designed and conducted to address safety concerns about current and impending submissions

of combination products, including the importance of possible immunotoxic reactions to incorporated biomaterials. The goal of these studies is to develop critical issues in the emerging field of combination products (i.e., biological matrices used in wound healing); issues in cardiovascular surgery; and issues addressing cell encapsulation. These studies will also address the potential of combination products to cause chronic inflammation.

- **Materials Characterization and Polymer Degradation** - Under this program research and testing is conducted in support of the Center's mission-related activities in the areas of materials characterization, degradation, and materials-tissue interactions. The primary focus of the program is to characterize materials' composition, degradation, and stability to ensure safety in use. Several models of materials degradation have been developed to predict the effect of the human body on materials in terms of degradation routes and ultimate outcome of degradation products, including unidentified particles in PVC blood bags, defective IV set fabrication, Intergel Adhesion Barrier and counterfeit polypropylene hernia repair mesh.
- **Fluid Dynamics and Ultrasonics** - Much of the research in this program area focuses on test method development that examines specific device attributes. The medical products in this area are among the most complex that the Center evaluates, and their public health significance is often profound. Similarly, the rapid growth of diagnostic techniques and minimally invasive therapies drives current work in ultrasonics. Projects in this program include collaborative work with standards groups for test method development. An ongoing example is the performance assessment of heart valve hydrodynamics task in the heart valve project. In the area of ultrasonics, OSEL personnel have helped draft measurement standards for all forms of medical ultrasound except for high intensity focused ultrasound (HIFU), which is a primary focus of current research.
- **Electrophysiology and Electrical Stimulation** – Investigations of the electrophysiology and electrical stimulation program area focus on clarifying the interaction mechanisms of this technology with the body, e.g., drug interactions with cardiac stimulation devices and high-frequency stimulation. Specific areas of research, which will serve as a basis for establishing industry safety standards for electrical stimulation devices, include the cellular basis of electrical stimulation safety in nerve and heart, cardiac electrophysiology and defibrillation, and retinal electrophysiology and stimulation.
- **Radiation Bioeffects** -The goal of the radiation bioeffects program is to develop scientifically-based criteria for evaluating radiation-emitting medical devices and consumer products and for developing relevant CDRH/FDA guidelines and standards. Program scientists are closely involved with the national and international standards committees that promulgate standards for exposure to ionizing and non-ionizing radiation. In addition to CDRH programs, the bioeffects effort is currently providing support to CFSAN, NCI, the Federal Communications Commission, and the Department of Defense. OSEL maintains the FDA Human Photosciences Facility fully equipped for clinical research in dermatology and photomedicine. It is currently used by researchers from CDRH, CFSAN, and NCI, with NCTR involvement, to generate scientific data for modernization of the FDA policies in the area. It is available for other human studies.

- **Medical Imaging and Diagnostics** - A wide variety of new digital imaging and display devices with a broad range of performance characteristics is under development by academia and industry. OSEL scientists are developing evaluation methodologies for diagnostic medical imaging systems such as mammography and fluoroscopy, computed tomography, nuclear medicine, diagnostic ultrasound, and magnetic resonance imaging, as well as novel soft-copy display devices for viewing medical images. Expertise developed through this program is being applied to the following:

    - Review of PMAs for ultrasound bone sonometers and new digital radiographic imaging systems
    - Development of amendments to the diagnostic x-ray performance standard
    - Development of an advisory pertaining to pediatric CT exposures, and
    - Joint planning of a consensus development conference on CT with NIH

  The x-ray spectral measurements program provides a source of otherwise unavailable data to the entire mammography research community, and the investigation of computer-assisted diagnosis devices is providing the Center with the scientific foundation to effectively regulate this fast-growing field. The program has made fundamental contributions to the field of statistical analysis of diagnostic imaging and systems for computer-aided diagnosis.
- **Electrical, Electronics and Software Engineering** - This program provides highly specialized technical support to Center and agency regulatory activities in the areas of electrical/electronics engineering, software engineering, and systems engineering. The program focuses on product realization, a term used by engineers to describe the process of converting a design concept into a viable product.
    - Regulatory support - In FY 03 staff performed substantive analysis and/or participated in on-site investigations in 17 compliance cases and provided informal guidance to investigators in numerous other situations.
    - Staff reviewed several CBER premarket applications last year and participated in an inspection of a blood bank. These activities uncovered a number of deficiencies requiring correction by the manufacturers.
    - Standards development - Staff participates directly in the development and/or maintenance of several of the high-profile “horizontal” standards —notably as members of the committees responsible for the IEC 60601 series and ISO 14971—as well as several “vertical” standards (e.g., apnea monitors, pulse oximeters).[1] CDRH has played a leadership role in developing a new AAMI standard covering software life cycle processes and has continued to encourage AAMI, IEEE, and ISO/IEC to work jointly to develop additional guidance for the medical device software community.
    - Engineering support services - Staff has earned a number of patents for their innovative designs and also has developed and deployed a data acquisition system for use in a clinical study at NIH.

[1] IEC 60601 is a mature and widely cited family of standards addressing requirements for safety and performance of all medical electrical devices. ISO 14971 is a seminal new standard that delineates a risk management process for medical devices. In CDRH jargon, these are examples of horizontal standards that apply to a wide range of medical devices across clinical boundaries, while vertical standards apply to one or a limited number of categories of devices within a single clinical specialty.

- **Optical Physics – Diagnostics and Therapeutic -** The rapid development of medical devices employing minimally-invasive optical technologies is revolutionizing modern health care. The Optical Physics laboratory program is directed at early identification of the following:
  - Key scientific questions
  - Safety and effectiveness issues
  - Mechanisms of interaction for new optical diagnostic and therapeutic technologies

  This information should facilitate the development of relevant evaluation criteria early in the review process. During the 5-year period ending in December 2002, 10% of PMAs and 7% of IDEs received by CDRH were in the area of minimally invasive optical technologies. Scientists are developing analytic techniques to identify optical tissue properties by using diffuse reflectance data, evaluating fiber optic probes used in optical diagnosis, and developing mathematical models to assist in quantifying the distribution of optical energy within tissues. CDRH's OSEL also is studying laser therapy devices in order to elucidate the mechanisms of interaction in order to maximize treatment effectiveness.
- **Electromagnetics and Wireless Technologies -** This program focuses on the several needs associated with medical devices that utilize or are affected by electromagnetic (EM) fields. The wireless technology revolution together with a flood of new medical devices incorporating sensitive microelectronics is leading to a highly unstable and potentially incompatible situation. The objective of the program is to develop independent data, measurement and computational techniques, and test methods that will serve as solid scientific foundations for regulatory guidance and proposals for national and international standards. OSEL has an active program of testing high-risk medical devices for susceptibility to electromagnetic interference (EMI) emitted by a wide variety of common sources of electromagnetic fields,. Specifically:
  - OSEL was a principal contributor in developing the recent ANSI/AAMI consensus standard on electromagnetic compatibility for pacemakers and defibrillators, developing the primary testing procedure and providing independent laboratory data.
  - OSEL tested and began coordinating an international intercomparison of measurements of the absorption of wireless phone radiation in a simplified human head model. The international standard for dosimetry is being drafted under the auspices of the Institute of Electrical and Electronics Engineers (IEEE) and is chaired by an OSEL engineer.
- **Radiological Health and Safety -** The scope of this program is to provide laboratory and technical support to the Center's Radiological Health mission. It maintains measurement and calibration facilities for x-ray, laser, noncoherent optical sources, and microwave measurements. These calibration labs perform the following functions:
  - Provide traceability for standards enforcement measurements
  - Facilitate uniformity of measurements
  - Provide metrology expertise for premarket and postmarket issues

  Laboratory staff have been instrumental in establishing the national standard for mammography x-ray calibrations and continue to work closely with NIST.

Additionally, staff have been closely involved in the effort to align the FDA standards for Lasers and Sunlamps with their international equivalents. The laboratory's services are used for leveraging state agencies to test newly installed radiological equipment against FDA requirements, resulting in hundreds of additional inspections per year.

- **Mechanics of Materials and Structures -** The Mechanics of Materials and Structures program is structured to help CDRH understand materials issues of concern in both premarket evaluations and postmarket reported adverse events. Medical device performance and safety require reliable and safe use of materials. Performance failure can result from improper material selection, inadequate stress analysis during device design, manufacturing errors, or misuse/abuse of devices. Materials of interest include synthetics like metals and polymers, materials of biological origin, and those used in tissue engineered medical products (TEMPs).

Interagency Agreements (IAG) and CRADAs

CDRH continued efforts to increase external collaborations. Examples include:

- **Models of Renal Failure and Biomarkers or Renal Injury** – IAG with GovWorks for the Department of Interior
- **Development of an Assay to Detect Endocrine Disruptor of Medical Agency**- IAG with the Minerals Management Service at the Department of Interior
- **Device Material and Drugs using Bisphenol A (BPA) as a Model Estrogenic Compound** - IAG with U.S. Army Medical Research and Material Command (USAMRMC),
- **Electromagnetic Compatibility (EMC) of Wireless Personal Digital Assistants (PDAs) with Active Medical Devices** – IAG with Telemedicine and Advanced Technology Research Center (TATRC)
- **Health Effects of RF Emissions from Wireless Phones (Mobile Units for Commercial Mobile Radio Services)** – The Cellular Telecommunications Industry Association
- **Collaborative Research and Testing of Medical Implants** – IAG with Armed Forces Institute of Pathology and the American Registry of Pathology
- **Investigation of Medical Device Electromagnetic Interference (EMI) from Wireless Data Devices and Interlaboratory Comparison of Radiofrequency (RF) Dosimetry Data from Hand-held Transmitters** – CRADA with Mobile Manufacture Forum (Brussels, Belgium)

Regulatory Science Activities

CLIA Activities

Congress passed the Clinical Laboratory Improvement Amendments in 1988, establishing quality standards for all laboratory testing to ensure the accuracy, reliability and timeliness of patient test results regardless of where the test is performed. The categorization of commercially marketed *in vitro* diagnostic tests under CLIA has been the responsibility of the FDA since January 31, 2000. OIVD performs the CLIA complexity categorization that includes the assignment of these test systems to one of three CLIA regulatory categories

(high, moderate and waived) based on their potential risk to public health. During FY 03 CDRH performed categorizations on a total of 2170 tests including 215 High, 1661 Moderate, and 194 Waived tests. FDA, CMS, and CDC are working together to publish a final rule on CLIA waiver. More information on the CLIA program can be found at http://www.fda.gov/cdrh/clia/index.html.

Site Visit Program

In FY 03, ODE continued the Site Visit Program that was developed in 1993 to enhance reviewer knowledge of how specific medical devices are designed, manufactured, and tested. The program includes not only visits to medical device manufacturing firms but also to hospitals for the observation of certain devices in use. Twenty-one firms and/or hospitals were visited by 194 scientific reviewers to learn about such things as laser refractive surgery, diVinci robotic system, left ventricular assist device, catheters, anesthesiology, breast implants, vascular stents, MR-guided focused ultrasound ablation of uterine fibroids, antimicrobial testing for new surface modification, cardiac electrophysiology devices, spinal implants, fecal incontinence devices, ophthalmic contrast sensitivity, and other devices.

Transmissible Spongiform Encephalopathy (TSE)

CDRH has been an active participant in agency TSE activities. During FY 03, the CDRH Transmissible Spongiform Encephalopathy (TSE) Working Group developed a TSE risk document to address medical device TSE risk issues. CDRH joined CDER, CBER, and CFSAN in the Center for Biologics July 17-18, 2003 FDA CBER TSE Advisory Committee (TSEAC) meeting. It was responsible for planning the medical device portion of the meeting, including recruiting speakers, developing the agenda and making presentations regarding decontamination of medical devices that have been exposed to TSE. The TSEAC meeting was evidence of the CDRH TSE WG FDA-wide collaboration. CDRH participated along with other centers in FDA - CBER, CDER and CFSAN, developed sessions and shared information.

At the TSEAC meeting, CDRH initiated a 2 hour session with the panel experts where medical device questions related to decontamination of medical devices and equipment used in manufacturing were presented to the expert CBER panel that included a CDRH ODE panel expert on infection control. CDRH participation along with the comments from the panel provided the opportunity to initiate discussion on TSE decontamination of medical devices at this public meeting with HHS, industry and international attendance. The TSEAC panel recommended a workshop to further assess the current state of knowledge of decontamination/inactivation of TSE for medical devices, facilities, and other medical applications of animal derived products. The CDRH TSE Working Group is investigating the potential benefits of an international workshop on medical device decontamination.

Advisory Panels

The Center's Medical Devices Advisory Committee (MDAC) with its 18 panels provide clinical and scientific advice to FDA in several areas of activity fundamental to the regulation of medical devices. The most significant of these areas of activity are to: (1) classify and reclassify medical devices into one of three classes based on risk, (2) review and make

recommendations on premarket submissions such as Premarket Approval Applications (PMAs), Product Development Protocols (PDPs), and Premarket Notification submissions (510ks), (3) provide advice on guidance documents which convey to industry and the agency staff FDA's expectations for studies and data for premarket review, and (4) provide input on issues or problems concerning the safety and effectiveness of medical devices.

In FY 03, CDRH held thirteen panel meetings. The panels reviewed and made recommendations on: twelve PMAs, one 510(k), two reclassification petitions, and three general issues. In FY 03, there were 12 training sessions for members and consultants. The panels reviewed PMAs for significant medical device breakthrough technologies such as a drug-coated coronary artery stent and a stair climbing wheelchair.

A new draft guidance document, "Pediatric Expertise for Advisory Panels" issued for comment on June 3, 2003. This guidance document describes the process that CDRH intends to follow to ensure that an advisory panel review of a PMA or 510(k) includes pediatric specialists on the panel, when appropriate. The website for this draft guidance document is: http://www.fda.gov/cdrh/ode/guidance/1208.pdf. This year, the Center has recruited more than twenty pediatric specialists to serve as members or consultants on an advisory panel for any premarket submission that may be indicated for use in a pediatric population.

CDRH continuously recruits highly qualified experts to serve as members and consultants on panels. Potential candidates are asked to provide detailed information concerning financial holdings, employment, and research grants and contracts to identify any potential conflict of interest. Interested individuals should send their curriculum vitae to njp@cdrh.fda.gov.

The MDAC advisory panels are key to ensuring that the agency has access to the nation's most esteemed medical experts and to making the FDA medical device review process transparent to stakeholders. CDRH greatly appreciates the significant contributions that the advisory panel members and consultants make to the medical device review program.

Guidance Development

Scientifically sound guidance protects and promotes public health by helping ensure manufacturers conduct the correct device performance testing and clinical trials and by enhancing FDA's ability to review study results, bringing beneficial products to market without undue delay.

Guidance Development Templates

The need for clear science communication in guidance documents and the need for a streamlined procedure for developing certain kinds of guidance documents has led to an exceptionally useful innovation in CDRH guidance development. In collaboration with the Regulations Staff in the Office of Health and Industry Programs and the FDA Office of Chief Counsel (OCC), CDRH developed template formats for Class II special controls guidance documents. It also has developed templates for special controls for devices that are exempt from 510(k) and templates for non-special control guidance documents.

This year, CDRH also created instructions to authors of guidance, a format for concept papers for guidance developed with the use of templates and other plain language materials for science writing in CDRH.

The use of templates and these associated materials in guidance development has contributed to efforts to reclassify, more efficiently, numerous preamendments class III devices helping to reduce regulatory burden while still ensuring that the risks to health associated with the device are appropriately addressed in the premarket review. Efforts in creating templates for special controls guidance documents used in *de novo* classification have helped CDRH meet statutory timeframes for these submissions as well.

Risk Management in Guidance Development Templates

Guidance is an effective risk management tool and a critical element of the Commissioner's Strategic Plan. Moreover, clear, accurate scientific communication in guidance reduces the burden on both industry and FDA. The opportunity to incorporate FDA-recognized standards in guidance provides industry and FDA with testing methods and acceptance criteria vetted by experts who represent the international device community, further ensuring clear communication and reducing the burden of regulation. CDRH guidance development templates focus on addressing the risks to health associated with the use of devices and the measures FDA has identified to mitigate those risks, measures that follow the systems theory approach, by showing how quality systems requirements, premarket review, and postmarket oversight serve together as a system of regulatory controls to assure the safety and effectiveness of devices marketed in the U.S.

Guidance Documents

During the fiscal year, Center management initiated an effort to speed the development of guidance documents in an effort to reduce regulatory burden, foster greater consistency in scientific evidence provided in premarket submissions and optimize evaluation processes to achieve the MDUFMA performance goals. CDRH began efforts to involve scientists from throughout the Center in the guidance development process. Furthermore, specific efforts are underway to insure that FDA-recognized consensus standards are fully integrated into appropriate guidance documents in an attempt to further streamline the FDA review and promote greater international harmonization.

Guidance documents and other previously issued guidance documents are available on the World Wide Web (CDRH homepage: http://www.fda.gov/cdrh) which provides easy access to the latest information and operating policies and procedures. They also may be obtained from the Division of Small Manufacturers International and Consumer Assistance (DSMICA, HFZ-200). To contact DSMICA, call 800-638-2041 or 301-443-6597; fax 301-443-8818; E-mail dsma@cdrh.fda.gov or write to DSMICA (HFZ-200, Food and Drug Administration, 1350 Piccard Drive, Rockville, Maryland 20850-4307). Many guidance documents also are available through the CDRH Facts-On-Demand (faxback service at 800-899-0381 or 301-837-0111).

Final Guidance Documents Adopted

5-Sep-03	Part 11, Electronic Records; Electronic Signatures - Scope and Application
5-Sep-03	Information Disclosure by Manufacturers to Assemblers for Diagnostic X-ray Systems; Guidance for Industry and FDA Staff
19-Aug-03	Guidance for Industry and FDA Staff on the Mammography Quality Standards Act Final Regulations Modifications and Additions to Policy Guidance Help System 6
1-Aug-03	FY 04 MDUFMA Small Business Qualification Worksheet and Certification; Guidance for Industry and FDA
1-Aug-03	Implantable Middle Ear Hearing Device; Guidance for Industry and FDA
28-Jul-03	Class II Special Controls Guidance Document: Breast Lesion Documentation System; Guidance for Industry and FDA Staff
16-Jul-03	Frequently Asked Questions about the Reprocessing and Reuse of Single-Use Devices by Third-Party and Hospital Reprocessors; Three Additional Questions; Guidance for Industry, FDA Staff, Third-Party and Hospital Reprocessors
15-Jul-03	Coronary and Peripheral Arterial Diagnostic Catheters; Guidance for Industry and FDA Staff
14-Jul-03	Criteria for Significant Risk Investigations of Magnetic Resonance Diagnostic Devices; Guidance for Industry and FDA Staff
8-Jul-03	Medical Device User Fee and Modernization Act of 2002, Validation Data in Premarket Notification Submissions (510(k)s) for Reprocessed Single-Use Medical Devices; Guidance for Industry and FDA Staff
7-Jul-03	Breath Nitric Oxide Test System - Class II Special Controls; Guidance Document
26-Jun-03	A Pilot Program to Evaluate a Proposed Globally Harmonized Alternative for Premarket Procedures; Guidance for Industry and FDA Staff
19-Jun-03	510(k) Submissions for Coagulation Instruments; Guidance for Industry and FDA Staff
3-Jun-03	Pediatric Expertise for Advisory Panels; Guidance for Industry and FDA Staff
3-Jun-03	Class II Special Controls Guidance Document: Surgical Sutures; Guidance for Industry and FDA
2-Jun-03	Class II Special Controls Guidance Document: Resorbable Calcium Salt Bone Void Filler Device; Guidance for Industry and FDA
5-May-03	Medical Device Tracking; Guidance for Industry and FDA Staff

1-May-03	Premarket Approval Application Filing Review; Guidance for Industry and FDA Staff
28-Apr-03	Implementation of the Inspection by Accredited Persons Program Under the Medical Device User Fee and Modernization Act of 2002 Accreditation Criteria; Guidance for Industry, FDA Staff, and Third Parties
22-Apr-03	Class II Special Controls Guidance Document: Optical Impression Systems for Computer Assisted Design and Manufacturing (CAD/CAM) of Dental Restorations; Guidance for Industry and FDA
1-Apr-03	User Labeling for Devices that Contain Natural Rubber (21 CFR 801.437); Small Entity Compliance Guide; Guidance for Industry
31-Mar-03	Section 206 of the Medical Device User Fee and Modernization Act (MDUFMA) (New Section 502(f) of the Federal Food, Drug and Cosmetic Act) Electronic Labeling for Prescription Devices Intended for Use in Health Care Facilities; Blue Book Guidance Memorandum #G03-1
27-Mar-03	Guidance for Industry and FDA: FY 03 MDUFMA Small Business Qualification Worksheet and Certification
26-Feb-03	Analyte Specific Reagents; Small Entity Compliance Guidance; Guidance for Industry
25-Feb-03	Assessing User Fees: PMA Supplement Definitions, Modular PMA Fees, BLA and Efficacy Supplement Definitions, Bundling Multiple Devices in a Single Application, and Fees for Combination Products; Guidance for Industry and FDA
11-Feb-03	Guidance for Saline, Silicone Gel, and Alternative Breast Implants; Guidance for Industry and FDA
5-Feb-03	Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA
3-Feb-03	Quality System Information for Certain Premarket Application Reviews; Guidance for Industry and FDA Staff
28-Jan-03	The Mammography Quality Standards Act Final Regulations Modifications and Additions to Policy Guidance Help System #7; Guidance for Industry and FDA
16-Jan-03	Class II Special Controls Guidance Document: Knee Joint Patellofemorotibial and Femorotibial Metal/Polymer Porous-Coated Uncemented Prostheses; Guidance for Industry and FDA Note – the following dates don't line up w/ text.
31-Dec-02	Supplementary Guidance on Premarket Notifications for Medical Devices with Sharps Injury Prevention Features; Guidance for Industry and FDA

13-Dec-02 Class II Special Controls Guidance Document: Cutaneous Carbon Dioxide (PcCo2) and Oxygen (PcO2) Monitors; Guidance for Industry and FDA

3-Dec-02 Determination of Intended Use for 510(k) Devices; Guidance for CDRH Staff

12-Nov-02 Class II Special Controls Guidance Document: Intraoral Devices for Snoring and/or Obstructive Sleep Apnea; Guidance for Industry and FDA

12-Nov-02 Needlesticks - Medical Device Reporting; Guidance for User Facilities, Manufacturers, and Importers

7-Nov-02 Class II Special Controls Guidance Document: Transcutaneous Air Conduction Hearing Aid System (TACHAS); Guidance for Industry and FDA

4-Oct-02 The Least Burdensome Provisions of the FDA Modernization Act of 1997: Concept and Principles; Final Guidance for FDA and Industry

3-Oct-02 Intercenter Consultative/Collaborative Review Process; Blue Book Guidance Memorandum #G02-1

16-Sep-02 Class II Special Controls Guidance Document: Cyclosporine and Tacrolimus Assays; Guidance for Industry and FDA

Draft Guidance Documents for Comment Purposes Only

24-Jul-03 Premarket Assessment of Pediatric Medical Devices; Draft Guidance for Industry and FDA Staff

23-Jun-03 Compliance with Section 301 of the Medical Device User Fee and Modernization Act of 2002 – Identification of Manufacturer of Medical Devices; Draft Guidance for Industry and FDA Staff

15-May-03 Surgical Masks - Premarket Notification 510(k) Submissions; Draft Guidance for Industry and FDA

12-Mar-03 Statistical Guidance on Reporting Results from Studies Evaluating Diagnostic Tests; Draft Guidance for Industry and FDA Reviewers

27-Feb-03 Multiplex Tests for Heritable DNA Markers, Mutations and Expression Patterns; Draft Guidance for Industry and FDA Reviewers

27-Jan-03 Chemical Indicators Premarket Notification 510(k) Submissions; Draft Guidance for Industry and FDA

23-Jan-03 Collection of Race and Ethnicity Data in Clinical Trials; Draft Guidance for Industry

19-Dec-02 Class II Special Controls Guidance Document: Surgical Sutures; Guidance for Industry and FDA

13-Dec-02 Class II Special Controls Guidance Document: Arrhythmia Detector and Alarm; Draft Guidance for Industry and FDA

3-Dec-02	Determination of Intended Use for 510(k) Devices; Guidance for CDRH Staff
12-Nov-02	Draft Guidance for Industry on Electronic Records; Electronic Signatures, Electronic Copies of Electronic Records
22-Oct-02	Class II Special Controls Guidance Document: Processed Human Dura Mater; Draft Guidance for Industry and FDA
6-Sep-02	Drugs, Biologics, and Medical Devices Derived from Bioengineered Plants for Use in Humans and Animals; Draft Guidance for Industry
6-Sep-02	Medical Devices Made With Polyvinylchloride (PVC) Using the Plasticizer di-(2-Ethylhexyl)phthalate (DEHP); Draft Guidance for Industry and FDA

Standards

Some Performance Standards for the Industry

- **FDA Laser Standard** – CDRH is developing a package of amendments to regulatory standards for lasers. These amendments will recast the FDA laser standard as two IEC standards with modifications. The IEC standards will be employed by reference to avoid copyright problems. When completed, this project will result in the FDA laser standard being essentially harmonized with the laser standards used by most other regulatory authorities and could be used as a model for changing other regulatory standards.
- CDRH staff is involved with the development of the 3rd edition of IEC 60601-1, the international standard for all safety and essential performance aspects of electrical medical devices. The topics covered by the standard, and CDRH expertise, range from risk management and electromagnetic compatibility to electrical safety, mechanical hazards, and excessive temperatures. The IEC 60601-1 standard has been recognized by CDRH to be used in regulatory submissions for marketing approval. It covers hundreds of the medical devices regulated by FDA.

Regulatory Compliance

Significant Compliance Actions

Dr. Leon LaHaye/LaHaye Center's Laser System for LASIK

CDRH approved a $1.1 million Civil Money Penalty action against Dr. LaHaye and his center for using an unapproved laser on patients before he initiated a study. In addition, Dr. LaHaye treated more subjects than allowed under the study plan that was ultimately approved by the Center. He ignored the parameters established in the study by treating nearsightedness beyond the permitted range and by treating astigmatism and both eyes of some patients. The violations involved studies of a laser system built by LaHaye for LASIK treatment of nearsightedness.

Counterfeit Ethicon Corporation's Prolene Surgical Mesh

In October 2003, Ethicon discovered two counterfeit lots of their Prolene Surgical Mesh in domestic commerce. This device is a flat nonabsorbable mesh used for hernia repair and other fascial deficiencies. The lots of mesh appeared to have been imported from a foreign country, and the Center issued an Import Alert to prevent additional product from entering the country. Preliminary testing by an FDA laboratory indicated that both lots of counterfeit Prolene surgical mesh were bacterially contaminated. After consultation with the Center, Ethicon recalled all product from their distributors and end users. The Center issued a Web Notification to inform the public of this problem. Additional microbiology and physical testing are in progress.

Decorative Contact Lenses

On April 1, 2003, the Center approved the issuance of an Import Alert (IA #86-10) for Decorative Contact Lenses. This Import Alert, which is entitled, "Detention without Physical Examination of Decorative Contact Lenses", defines decorative contact lenses as cosmetics which are intended to alter the appearance of the eye for decorative fashion. Without consultation with a qualified eye care professional practitioner, these products have a high risk of damaging ocular health by causing corneal infection, as well as cornel scarring and potential blindness. Although, CDRH has taken the lead for decorative contact lenses enforcement, CDRH relies on CFSAN for all consults on decorative contact lenses. CFSAN's consults address the violations (Sections 601(a), 601(e) & 602(a) of the Federal Food, Drug and Cosmetic Act) used for decorative contact lenses.

Adven Medical

Adven Medical, Inc., Lubbock, Texas, entered into a Consent Decree of Permanent Injunction in August 2003, for significant, numerous, and repeated violations to the Quality System regulation. Adven Medical, Inc., was a third-party reprocessor of various single use only devices. The firm's most significant violation was the failure to validate the sterilization and cleaning process. They were also cited for violations regarding design controls, corrective and preventive actions, quality control, cleaning processes, device specifications, training, production and process controls, acceptance activities, control of measurement equipment, purchasing controls, device master records, and documentation controls. Adven Medical, Inc., claimed they corrected all of the above violations, however a subsequent

district inspection revealed that none of the corrections made by the firm were adequate. As a result, Adven Medical Inc., believed it could not meet the requirements of the Quality System regulation, and permanently closed its business on October 15, 2003.

Multidata Systems Intl., Radiation Therapy

FDA entered into a consent decree of injunction with Multidata Systems International Corporation to stop them from manufacturing radiation therapy medical devices. Multidata Systems International manufactures devices for use in the treatment of cancer. The company's radiation treatment planning software reportedly contributed to 28 patients receiving excessive amounts of radiation in a Panama facility. Several patients subsequently died. Multidata failed to conform to the Quality System regulation, and also failed to file prompt reports with the FDA after it became aware that its products may have caused or contributed to death or serious injury. A review of the firm's regulatory history revealed that the firm had a history of failing to comply with the Quality System regulation. The consent decree enjoins Multidata from marketing its radiation therapy medical devices until FDA is satisfied that the firm has corrected its problems.

ADI Corporation

ADI Corporation manufactures computer monitors and televisions. The firm agreed to pay $475,000 for violating the Electronic Product Radiation Control Provisions of the Federal Food, Drug, and Cosmetic Act for continuing to certify and ship products to the United States after FDA disapproved its quality control and testing program. This problem was identified when FDA investigators conducted an inspection of ADI Systems Mexico, S.A. de C.V. and the investigators reported a number of serious deficiencies, including the failure of factory technicians to test computer monitors for compliance with the Federal radiation exposure limit under required testing conditions. FDA issued a Warning Letter, disapproving ADI Systems Mexico's quality control and testing program for computer monitors and television receivers, making it illegal for them to certify these television products. FDA placed ADI Mexico on import detention and detained products automatically at the port of entry until the disapproval of the quality control and testing program had been rescinded. Thereafter, ADI Corporation shipped at least 55,000 computer monitors and television receivers into the United States, despite the agency's warning that such shipments would violate the Act, and this led to the $475,000 fine.

Registration and Listing

The Registration and Listing (R&L) staff initiated a pilot project to replace the distribution of paper copies of monthly establishment registration and device listing information change reports to FDA District Office Device Registration Monitors with an electronic copy sent via e-mail. This pilot project was a success and this paperless process is now permanent. This initiative saves supplies and resources. It also ensures that this critical change information is issued to FDA District Offices in a timely manner.

Application Integrity Policy

The Division of Bioresearch Monitoring placed AGA Medical Corporation on the Application Integrity Policy (AIP). This action stops the substantive review of all new or pending

applications before the agency. The AIP was put into place due to concerns that there was a system-wide failure by AGA to ensure the integrity of data submitted to FDA in support of research and marketing permits. The firm will be required to submit a detailed corrective and preventative action plan, and submit to a follow-up inspection once corrections have been made.

Bioresearch Monitoring (BIMO) Activities

As a result of BIMO inspections, the CDRH's Office of Device Evaluation (ODE) integrity officer placed integrity holds on 5 premarket submissions in FY 03 due to incomplete or fraudulent data. These initial actions will, in some cases, lead to additional enforcement actions including invocation of the AIP, rescission of applications, or disqualification of clinical investigators.

Compliance Activities

Inspection Prioritization

CDRH researched existing inspection prioritization models and developed a flexible modular approach for prioritizing device inspections. In addition, CDRH established a draft "criteria list" for prioritizing inspections and developed a risk-based work planning model which incorporates an annual and quarterly review of adverse event and other risk-based databases and inspection results. As part of the work planning model, CDRH is responsible of providing a listing of foreign manufacturers to be inspected under the risk management strategy to ORA. ORA will conduct inspections of both domestic and foreign medical device manufacturers in accordance with the criteria established under the Center's risk management strategy.

Third-Party Inspectors Under MDUFMA

CDRH has the responsibility of accrediting and training third-party inspectors under MDUFMA. In FY 03 it received 23 applications for third-party accreditation. Seventeen applications are under full review, five are under initial review and one application was denied.

Inspections and Product Testing

CRDH provided input to the FY 03 and FY 04 radiological health work plan for the FDA Office of Regulatory Affairs. CDRH revised definitions and provided updates for radiological health inventory for cabinet x-ray, laser, and sunlamp products in related compliance programs.

Assuring Safe Products in the Market

Postmarket Surveillance: Medical Device Adverse Event Reporting

Adverse Event Reports

During FY 03, FDA received 60,767 individual medical device adverse event reports from manufacturers, user facilities, and importers. Additionally, 3602 voluntary reports were submitted by health care professionals and the public. CDRH staff analyzes the reports to determine if the use of a particular product is resulting in unexpected problems or risks, and to identify trends that can improve risk management and reduce use error. The top problems identified this fiscal year were: aortic connector device failures that led to hemorrhage and death; thrombus and reactions associated with coronary stents; meningitis associated with cochlear implants; aneurysm-related deaths associated with endovascular grafts; hospital bed fires; toxic shock syndrome associated with a particular brand of tampon; off-label use of an adhesion barrier; and saline leakage in the access port of the lap band adjustable gastric band.

Alternative Summary Reporting

CDRH continues to accept more reports into the Alternative Summary Reporting (ASR) program. In this program, manufacturers submit abbreviated reports in a line item aggregated way. This program is for devices with problems that are well-known and well-documented. For example, problems with medical devices that are well-known and well-documented include: shearing of central line catheters, endossoeus implants failing to osseointegrate, and breast implant ruptures. Approximately 40 manufacturers participate in this program for 50 different types of classified devices. Three manufacturers are currently participating in the electronic version of ASR, which is still being piloted. FDA received 61,553 reports in the summary database in FY 03.

International Vigilance Report

Policies and procedures for the exchange of information between regulatory authorities continue to be refined by the Global Harmonization Task Force - Study Group 2 (Medical Device Vigilance and Postmarket Surveillance). During 2003, the FDA and 15 countries participated in the electronic global exchange of more than 140 international vigilance reports between National Competent Authorities (NCAs). Postmarket vigilance reports primarily involve recalled devices with a potential for adverse events in countries where the product is distributed. Member countries participating in the exchange periodically evaluate the usefulness of vigilance reports to their safety programs. Evaluations thus far indicate the program is a very effective tool for the rapid global dissemination of device safety information used to protect public health.

Medical Product Surveillance Network (MedSun)

The FDA Modernization Act of 1997 (FDAMA) directed FDA to change the current MDR regulation pertaining to user facilities from a required universal reporting system to a system comprised of a subset of user facilities. Since February 2002, FDA has been collecting data about problems with the use of medical devices from a sample of hospitals and nursing

homes. This data collection, called the Medical Product Surveillance Network (MedSun) is an interactive Internet-based reporting program. During FY 03, FDA continued recruitment of reporting facilities from the east coast and mid-west region of the United States, for a total of 180 facilities (nationwide representation will be achieved in FY 04). FDA has collaborated with these facilities to determine the effectiveness of various incentives and types of feedback on the quantity and quality of reports sent into the system. Throughout FY 03, FDA targeted the MedSun system to obtain specific medical product information. Additionally, in FY 03 a pilot project was begun to more directly target the sending of reports from laboratories (pathology and in vitro diagnostic tests) in the reporting hospitals.

IVD Patient Safety Team

Early in 2003 the IVD Patient Safety Team (PST) was formed as a part of a larger Total Product Life Cycle (TPLC) program. The team's mission is two-fold: first, to explore new avenues to obtain timely, useful and accurate postmarket information on the devices CDRH regulates in order to feed this information back to the premarket review; and second, to facilitate the merger of premarket and postmarket activities to smooth the transition to the TPLC concept. The team now serves as the "umbrella" team to oversee several project teams summarized below.

- **IVD MedSun/LabSun Pilot Team** - During the last year the LabSun Pilot team has been very active. The team designed two report forms: a short form for minor events in the laboratory where patients were not directly impacted and a longer report form for incidents of more significance. Working with CODA, the contractor for the MedSun Project, the team recruited and trained nine sites in the Maryland, Virginia and DC area for a currently ongoing four month pilot of laboratory reporting. CDRH has already had several reports come in, one resulting in a compliance investigation.
- **IVD Listserv Team** - This team has been participating in passive listening on several listservs and feeding issues back to the PST, the postmarket staff, and the respective divisions. There have been several incidences where discussion topics which were monitored resulted in compliance actions or in OIVD posting Lab Safety Tips on the OIVD website.
- **IVD Adverse Event Reporting Activity and Transition to OIVD Team** - At each PST meeting, the team was updated on newly received adverse event reports that met criteria the PST specified – deaths, hospitalization, and voluntary reports. Two computer-based training sessions on review and analysis of adverse event reports were conducted by CDRH's OSB analysts. Currently, nine OIVD staff are being trained as analysts. On August 22, OIVD staff began to receive IVD adverse event reports directly and to manage their follow-up. The OIVD analysts' group meets regularly to discuss problems and issues. Each analyst reports adverse events regularly to the respective OIVD division in order to integrate information from the reports into premarket reviews.

Postmarket Collaborations

Global Medical Device Nomenclature (GMDN)

Since 2001, the further development and maintenance of the GMDN has been the responsibility of the GMDN Maintenance Agency. CDRH is represented in both the Maintenance Agency Policy Group (MAPG) which administers the nomenclature, and the Expert Team (ET) which is responsible for the technical upkeep of the nomenclature. The terminology now contains over 18,000 terms, 7,000 of which are preferred terms with definitions used for product identification. In addition, the GMDN is now an ISO and CEN (European Standardization Organization) standard, and therefore has been adopted by many nations. CDRH continues to migrate towards the eventual adoption of the GMDN, and to that end is systematically reviewing linked procodes in the GMDN for accuracy, and is working with ECRI to attempt to merge the current version of their Universal Medical Device Naming System (UMDNS) with CDRH procodes and the GMDN into one database.

Hospital Bed Safety

Death and injury adverse events associated with patient entrapment in hospital beds continue to be reported to FDA. The Hospital Bed Safety Workgroup (HBSW), under FDA's leadership and in partnership with hospital bed manufacturers, national health care organizations, patient advocacy groups, and the Department of Veterans Affairs, has developed the following products this year:

- **Clinical Guidance for the Assessment and Implementation of Bed Rails in Hospitals, Long-Term Care Facilities and Home Care Setting**. These guidelines are the first to provide a uniform set of recommendations for caregivers in hospitals, long-term care facilities, and in the home when assessing their patients' need for and possible use of bed rails.
- **A video entitled, "Do No Harm" produced by AARP**. The 22-minute video for caregivers and health care facilities that provide real-life situations on the use of bed rails in both acute and long-term care environments and offers insights by patients and their families, nurses and other caregivers. FDA's website for bed safety provides a link to these new clinical guidelines at www.fda.gov/cdrh/beds/. In addition, FDA is developing dimensional guidelines and educational materials for manufacturers, caregivers and consumers to identify and reduce risk of entrapment in new and existing hospital beds.

Systematic Technical Assessment of Medical Products (STAMP)

- **Surgical Stapler and Clip Applier STAMP** -The CDRH Surgical Stapler and Clip Appliers STAMP Committee convened in September 2001 to address adverse events associated with surgical staplers and clip appliers. The reported events described cutting and device component failures, resulting in pain, bleeding, tissue necrosis, hypovolemic shock, cardiac tamponade, and subsequent deaths and serious injuries. Surgical staplers and clip appliers are used in gastrointestinal, gynecologic, thoracic, and other surgeries to resect or transect tissues and to create anastomoses. These devices have been marketed for years and their use results in shortened surgical procedure times. The STAMP is composed of representatives from CDRH and the American College of Surgeons (ACS). In addition to reviewing

adverse event reports, the committee discussed adequacy of training programs for surgical staplers and clip appliers, reuse of single use staplers, and manufacturing/design issues. The ACS believes that reuse of single use staplers is not an issue in the United States, but a common practice in Mexico, South America, Central Europe, and parts of Asia. Additionally, problems with surgical staplers and clip appliers are rarely discussed in professional meetings and manufacturers do not discuss device failures with surgeons. The STAMP believes that some clinicians may not be aware of problems reported with surgical staplers and clip appliers and proposed to present information about these devices through publications, websites, professional meetings, and FDA Advisory Panel meetings. The STAMP also plans to conduct a Rapid Response Survey (RRS) to determine user awareness of device problems.

- **Laparoscopic Trocar Injuries STAMP** CDRH convened a STAMP Committee to address the increasing numbers of reports of deaths and serious injuries related to the use of laparoscopic trocars—devices used to penetrate the abdomen and pelvis for insertion of laparoscopes and surgical instruments. The committee members included FDA staff and health care practitioners with expertise in health care, engineering, laparoscopic procedures and human factors. The committee completed the following activities:
  - Reviewed and analyzed FDA adverse event surveillance data, trocar labeling, patient brochures on laparoscopic surgery;
  - Reviewed FDA device recall data;
  - Reviewed existing published literature; and
  - Published an article (*ACOG Today*, October 2002) to provide information about laparoscopic trocar injuries and FDA's adverse event reporting program. The committee will publish a summary of findings by the end of 2003.

Postmarket Epidemiology

CDRH epidemiologists conduct applied epidemiological research using a variety of methods and databases and provide consultative services to ODE and others on issues requiring epidemiological expertise, from systematic reviews of the literature to risk assessments, to the design and conduct of observational studies. Major epidemiological research during the past year that resulted in publications in scientific journals and presentations at national professional meetings include: allergic reactions to platinum in breast implants; serious injuries associated with the use of hemostasis devices; the epidemiology of tampon associated toxic shock syndrome; patient safety terminology; an active surveillance system to detect medical device associated adverse events that are generally undetectable through routine surveillance; postmarket evaluation of the Oxyfirst fetal oxygen saturation monitoring system; breast implant rupture; evaluation of the completeness of studies undertaken by industry as a condition of premarket approval of their products; adverse events associated with the adjustable silicone gastric band; use of the National Electronic Injury Surveillance System (NEISS) to assess the frequency of injuries due to medical devices; gender differences in pulmonary artery rupture; and uses and outcomes associated with transmyocardial revascularization.

ODE/DRAD/EB Pilot Project

As part of CDRH's effort to formalize Total Product Life Cycle precepts within the premarket review process, ODE's Division of Reproductive, Abdominal, and Radiological Devices (DRARD) participated in a pilot cooperative project from February 2002 to February 2003 with the Epidemiology Branch (EB) of the Office of Surveillance and Biometrics. The purpose of the project was: to determine when and how the EB could best provide appropriate input/recommendations to DRARD regarding potential postmarket investigations and to initiate, and later evaluate, product-specific postmarket plans. Over the course of the year each epidemiologist participated in the review of a PMA being evaluated by DRARD. Two of the PMAs that were approved during the year had post-approval studies. In both cases the epidemiology reviewer played a large role in the study design. There also were a few "firsts" that took place during the pilot project. This was the first time that the EB was involved with an expedited PMA and the first time well-defined Postmarket Plans were developed prior to device approval. It also was the second time that the EB made a presentation to the panel as part of the FDA presentation of the PMA. Both groups believed that the involvement of the EB in the PMA review enhanced the review process. All participants believed that early involvement was the best approach. Both sides believed that there was not enough experience gained from just one year, but that the collaboration looked very promising. Therefore, the decision was made to continue and refine the pilot project over the next year.

Drug-Eluting Stents

FDA and the American College of Cardiology (ACC) began studying drug-eluting stents within the ACC's National Cardiovascular Data Registry (ACC-NCDR). The ACC-NCDR is a confidential quality measurement program for cardiovascular specialists, hospitals, and cardiac catheterizations labs for collecting information on practice patterns and outcomes. The registry collects 142 core data elements needed for measuring the clinical management and outcomes of patients undergoing diagnostic cardiac catherizations and percutaneous coronary interventions. The ACC-NCDR consists of over 1.4 million patient records. FDA currently has a contract with ACC to access data with specific patient- and procedure-level information to examine the prevalence of use and experience of patients with drug-eluting stents.

Medical Errors

Guidance for Industry on Reducing Medical Errors Associated with Patient/Provider Use of New Products

CDRH developed a model of use errors based on real-world experiences of nurses, biomedical engineers, and home users who use a variety of medical equipment and on known examples of use errors from literature and experience within CDRH and Human Factors (HF) and a few from HF in other industries (but which could apply to medical devices). The current model, called UPCARE, consists of four main components: Unmet User Needs, Perception; Cognition, and Actions. These four broad categories represent all cases of use-error that have been collected and each is broken down further within the model into subcategories. The categorizations are based on actual

experiences of users and known use problems. UPCARE represents the only known descriptive model of use-errors with medical devices and was presented at the 8th Annual International Conference of Industrial Engineering Theory Applications and Practice in Las Vegas this year. Upon completion of this work, it will provide a source of specific and useful information for manufacturers, adverse event reporters and evaluators, reviewers of new device submissions, and device users. As such it will help guide design refinements in medical equipment and support other strategies for error-reduction.

Electronic Labeling

Usability Research in Best Rractices for the Presentation of Electronic Labeling

On November 18, 2003 OHIP hosted the "Medical Device Electronic Labeling Conference." The purpose of the conference was to add to the knowledge base about current best practices for conveying medical device information electronically to health care professionals, patients, and consumers. Five experts from the public and private sector presented information about research-based Web design and usability guidelines, user-centered design issues, and writing style and format for Web-based applications. Attendees included representatives from all the Centers.

Medical Device User Fee and Modernization Act (MDUFMA) Implementation

Medical Device User Fee and Modernization Act

The Medical Device User Fee and Modernization Act of 2002 (MDUFMA), amends the Federal Food, Drug, and Cosmetic Act (the Act) to provide FDA important new responsibilities, resources, and challenges. The Act has three particularly significant provisions:

- **User fees and performance goals for premarket reviews** of PMAs, PDPs, premarket reports (a new category of premarket application for reprocessed single-use devices), certain supplements, and 510(k)s. These fees, together with additional appropriations, will allow FDA to make significant improvements to review evaluation processes, reducing the time required to make new medical technologies available to health care professionals and patients.
- **Establishment inspections may be conducted by accredited persons (third-parties)**, under carefully prescribed conditions.
- **New regulatory requirements for reprocessed single-use devices**, including a new category of premarket submission, the premarket report.

Other important provisions of the new law include:

- The third-party 510(k) review program is continued through FY 06.
- The review of combination products will be coordinated by FDA's new Office of Combination Products.
- Electronic labeling is authorized for prescription devices used in health care facilities. The law now explicitly provides for modular review of PMAs.
- New provisions are added concerning devices intended for pediatric use.
- The manufacturer of a device must be identified on the device itself, with certain exceptions.

FDA met all the MDUFMA statutory start-up dates in FY03.

Additional background on MDUFMA, including the full text of the law, a plain-language summary, links to MDUFMA guidance documents and *Federal Register* notices, and other reference materials is available on CDRH's Internet site (www.fda.gov/cdrh/mdufma).

Implementation of MDUFMA

- **Consultation and communication with stakeholders**. - A key feature of FDA's implementation of MDUFMA has been the degree to which stakeholders have had the opportunity to provide their views on FDA's implementation of the new law's complex provision. CDRH established Internet sites to provide MDUFMA information, sent letters to consumer organizations, trade organizations, and manufacturers about MDUFMA (CDRH's site is at www.fda.gov/cdrh/mdufma), gave briefings and presentations at numerous professional meetings (including a nationwide teleconference), and responded to hundreds of phone calls and letters concerning MDUFMA's new requirements. To help to ensure that the guidance and regulations

CDRH issues to implement MDUFMA achieve their objectives without imposing unnecessary burdens, CDRH established an open public docket to receive comments from the stakeholders, and invited comment on specific proposals and actions in numerous *Federal Register* notices. CDRH will be working to build on and expand these efforts during the coming year.

- **Collaboration with CBER and OCP** - CDRH has been working closely with the Center for Biologics Evaluation and Research and FDA's new Office of Combination Products to ensure a smooth implementation of MDUFMA. CDRH has adopted uniform definitions and uniform performance measures, and has carefully coordinated Internet postings to help ensure stakeholders can find the information they need.

MDUFMA Review Performance Goals in Effect During FY 03

MDUFMA user fees and additional appropriations will allow FDA to add essential resources to device review programs. In conjunction with these new resources, MDUFMA also requires FDA to pursue a comprehensive set of challenging review performance goals. These goals are defined in a letter from DHHS Secretary Thompson to Congress.

- **Measurable Goals** - MDUFMA's review performance goals recognize that FDA will need a two-year implementation period (FY 03 - FY 04) to hire and train new staff and rebuild review program infrastructures before it will be possible to show substantial progress in overall review performance. Consequently, most of MDUFMA's measurable performance goals do not go into effect until FY 05. Two measurable goals were in effect during FY 03:
  - **For original premarket approval (PMA), panel-track PMA supplement, and premarket report submissions**, 90% of amendments containing a complete response to an approvable letter will be acted on within 30 days.
  - **For expedited PMAs**, 90% of amendments containing a complete response to an approvable letter will be acted on within 30 days.

During FY 03, the first year of the MDUFMA program, there was no opportunity to apply either of these performance goals because the conditions required did not occur before FY 03 ended. That is, there was no instance where:

- An applicant submitted an application on or after October 1, 2002 (the effective date of MDUFMA's review performance goals), and
- FDA issued an "approvable" letter for that application, and
- The applicant submitted an amendment containing a complete response to FDA's "approvable" letter, and
- 30 days passed for FDA to take action on the amendment, and
- The 30-day period for FDA action closed before the end of FY 03.

This does not indicate a problem with either the PMA or expedited PMA review processes. CDRH often approves a PMA without first issuing an "approvable" letter; for example, during FY 03, CDRH *approved* seven original PMAs without issuing an "approvable" letter, and found four additional original PMAs *approvable subject to GMP inspection* (this action is defined as an FDA decision by the performance goals agreed to for MDUFMA).

Additional Actions to Meet MDUFMA's Review Performance Goals

- **Use of formal and informal meetings** - CDRH encourages meetings as a particularly effective way to ensure that both FDA and applicants understand the clinical, scientific, and technical issues both parties are seeking to resolve. During FY 03, CDRH tracked four types of meetings: pre-IDE meetings, determination meetings, agreement meetings, and 100-day meetings. The pre-IDE meetings have proven to be the most useful to applicants; during FY 03, FDA participated in 99 pre-IDE meetings. The other types of meetings have proven to be of less interest to applicants.
- **Maintenance of current performance in review areas where specific performance goals have not been identified** - Final results for FY 03 are not yet available for all types of submissions (the FY 03 receipt cohort remains open for many types of submissions), but the available data indicate the timeliness of medical device reviews not covered by a specific performance goal was comparable to, or better than, results for FY 02.
- **Application of user fee revenues to support reviewer training and hiring and use of contract expertise.** During FY 03, CDRH filled 75 new positions for MDUFMA implementation, including scientists, engineers, project managers, statisticians, medical officers, review supervisors, and administrative support. CDRH also expanded use of contractors to provide additional flexibility to meet nonrecurring workloads and to supplement staff expertise in highly-specialized areas. FY 03 hiring efforts were delayed because CDRH could not hire new staff until FDA's appropriation for FY 03 was enacted; this did not occur until February 20, 2003. Prior to that time, FDA did not have funds available to hire new staff and CDRH had to rely on existing staff to implement MDUFMA. CDRH implementation of MDUFMA accelerated during the second half of FY 03, as it was able to begin hiring and training new staff.
- **Modular PMA Reviews** - FDA issued initial guidance on modular PMA reviews in "Assessing User Fees: PMA Supplement Definitions, Modular PMA Fees, BLA and Efficacy Supplement Definitions, Bundling Multiple Devices in a Single Application, and Fees for Combination Products", issued on February 25, 2003. The guidance explains that the fee for a modular PMA submission is due upon submission of the first module (not just the "shell" that describes the overall plan for the modular submission). If an applicant submitted the first module (again, not just the shell) prior to the October 1, 2002 effective date of MDUFMA, no fee will be required. (Note: On November 3, 2003, CDRH issued the final guidance, "Premarket Approval Application Modular Review".) During FY 04, CDRH will consult with stakeholders to develop performance goals for modular PMAs.
- **Bundling Policy**. - After consulting with stakeholders, FDA determined that bundling is appropriate in the right circumstances. CDRH issued initial guidance on bundling of multiple related submissions in the guidance document, "Assessing User Fees: PMA Supplement Definitions, Modular PMA Fees, BLA and Efficacy Supplement Definitions, Bundling Multiple Devices in a Single Application, and Fees for Combination Products", issued on February 25, 2003. This guidance explains that bundling may involve multiple devices or multiple indications for use. After issuing this preliminary guidance, CDRH continued to consult with stakeholders, and as a result it was able to provide more comprehensive guidance on bundling early in FY

04 (on November 26, 2003, FDA issued the final guidance, "Bundling Multiple Devices or Multiple Indications in a Single Submission").

- **Electronic Review of Applications** - CDRH worked with applicants to expand the use of electronic submissions during FY 03; 29 sponsors sent 101 submissions *entirely* in electronic form (compared with 14 sponsors and 73 submissions during FY 02). CDRH will continue to expand use of electronic submissions as resources permit.
- **Preapproval Inspections** - During FY 03, FDA began an examination of the factors affecting the timeliness of preapproval inspections to determine how the process can be improved and what resources would be required to make those improvements. During FY 04, FDA expects to commit to specific performance goals for preapproval inspections, and CDRH will begin making the process improvements necessary to achieve those goals.
- **Third-Party Establishment Inspections** - Pursuant to the new section 704(g) of the FD&C Act, establishment inspections may be conducted by accredited persons (third-parties), under carefully prescribed conditions. CDRH determined and published the criteria it will use to accredit third-parties, and invited interested persons to apply. During FY 04, CDRH will train auditors for the first 15 accredited persons (it accredited these persons on October 24, 2003), and third-party inspections will begin.
- **New Safeguards for Reprocessed Single-Use Devices** – The new section 502(v) of the FD&C Act establishes new regulatory requirements for reprocessed single-use devices, including provisions requiring the submission of additional validation data concerning the safety and effectiveness of devices now being reprocessed. MDUFMA also creates a new category of premarket submission, the premarket report (essentially, a PMA for a reprocessed single-use device). CDRH published a *Federal Register* notice on April 30, 2003 that provides a list of reprocessed single-use devices for which validation data is now required and a list of critical devices whose exemption from premarket notification is revoked and for which validation is now required. It will take similar action concerning semi-critical devices during FY 04.

New MDUFMA Provisions

- **Pediatric expertise on FDA advisory panels** - MDUFMA amended section 515© of the FD&C Act to require, where appropriate, that an FDA advisory panel shall include, or consult with, one or more pediatric experts. On June 3, 2003, CDRH issued the guidance, "Pediatric Expertise for Advisory Panels". This guidance defines pediatric populations, discusses the circumstances that indicate pediatric expertise should be employed by a panel, and explains the responsibilities of review team leaders and panel executive secretaries in identifying the need for pediatric expertise and making such expertise available.
- **Protection of children who participate in clinical trials or who use, or are treated with, medical device.** Section 213 of MDUFMA requires FDA to issue guidance, within 270 days of enactment, on:

    - Information necessary to assure the safety and effectiveness of devices used in the pediatric population.

- Protection of children who participate in clinical trials of devices.

On July 24, 2003, FDA issued a draft guidance, "Premarket Assessment of Pediatric Medical Devices". The draft guidance defines pediatric population subgroups and pediatric use for medical devices and device clinical trials, discusses the types of information needed to provide reasonable assurance of the safety and effectiveness of medical devices intended for use in the pediatric population, and discusses the protections sponsors should consider for pediatric subjects in device clinical trials.

- **Electronic labeling** - New section 502(f) of the FD&C Act authorizes electronic labeling for prescription devices intended to be used in health care facilities. The objective is to provide health care professionals with current labeling more rapidly, and at a lower cost, than would otherwise be possible. If a health care facility wants traditional paper labeling, it must be provided at no additional cost. CDRH will publish guidance on electronic labeling during FY 04.
- **Identification of manufacturer** - New section 502(u) of the FD&C Act requires identification of the manufacturer of a device in the device itself, with certain exceptions. This requirement goes into effect April 26, 2004 (18 months after enactment of MDUFMA). FDA received many comments that this time frame presents insurmountable difficulties to many manufacturers, and after careful consideration FDA issued draft guidance advising that CDRH would exercise enforcement discretion and does not intend to object if a manufacturer has not yet fully implemented the requirements of section 301 for up to 18 months after FDA issues final guidance.
- **Identification of reprocessor** - New section 502(v) of the FD&C Act requires reprocessed single-use device to "prominently and conspicuously" bear the statement:

  Reprocessed device for single use. Reprocessed by [name of manufacturer that reprocessed the device].

  This requirement goes into effect January 26, 2004 (15 months after enactment of MDUFMA).

Technical Corrections to MDUFMA

The Medical Devices Technical Corrections Act (MDTCA), P.L. 108-214 amends and expands upon the Medical Device User Fee and Modernization Act of 2002 (MDUFMA). The President signed MDTCA into law on April 1, 2004.

The purposes of MDTCA essentially parallel those of MDUFMA. MDTCA clarifies some potentially confusing language in MDUFMA, modifies important features of the provisions providing for third-party inspections, expands the provision for electronic labeling, delays the effective date of section 502(o) of the FD&C Act (section 301of MDUFMA, requiring a device to "prominently and conspicuously" bear the name of its manufacturer), and requires FDA to prepare and submit to Congress a report on barriers to the availability of devices intended for children.

- **Key Provisions**. - MDTCA makes important changes to MDUFMA in three areas:
  - Changes to the third-party inspection program.
  - Expansion of the provision for electronic labeling.
  - Delays the effective date of new section 502(o) of the FD&C Act until October 26, 2005 (36 months after enactment of MDUFMA, and 18 months beyond the original effective date set by MDUFMA).

- **Additional Changes** -MDTCA makes many other technical corrections and clarifications, mostly minor. For additional information on MDTCA, see the MDUFMA website, www.fda.gov/cdrh/mdufma.

Radiological Health

The Nationwide Evaluation of X-ray Trends (NEXT)

The CRCPD and FDA conduct the Nationwide Evaluation of X-ray Trends (NEXT) survey program, a federal-state collaboration that is the sole mechanism in the U.S. for capturing significant indicators of the state of practice in diagnostic radiology. Each survey collects data on patient exposure, radiographic equipment, image quality, and population workload from a randomly selected sample of facilities performing selected radiographic procedures. Selected exams for survey include adult chest, abdomen, spine, and pediatric chest radiography, fluoroscopy, computed tomography, and dental radiography. Digital x-ray imaging is becoming a significant player in the x-ray field and recent surveys are capturing baseline data with which to observe trends over time. NEXT also is focusing attention on emerging diagnostic procedures and technologies such as computed tomography which is being used for an increasingly diverse array of examinations, coupled with substantially high patient doses compared with conventional film x-ray procedures. NEXT recently completed a survey of computed tomography in 2000, and plans another for 2005 to document not only trends in patient exposure and technology, but also to assist the sectors of the professional community involved with public health efforts and regulatory activities.

Technical Electronic Product Radiation Safety Standards Committee (TEPRSSC)

During the January 10, 2003 TEPRSSC meeting, Lillian Gill, Senior Associate Director, CDRH, presented an update on a number of issues. This was followed by presentations and discussion on a number of topics, including sunlamps, security systems, and fluoroscopy.

Counter-terrorism/Emergency Response Activities

CDRH continues updating emergency plans (including those related to electronic product emergencies and radioactive material emergencies) and integrating these plans with those of FDA and HHS. Training for CDRH personnel in this area has been conducted and additional training is planned as well as in-house radiation emergency response exercises. The Center has developed a Continuity of Operations Plan (COOP) which identifies radiological health and safety as a key element. CDRH has maintained a role in the federal emergency response program through continued involvement in subcommittees of the Federal Radiological Preparedness Coordinating Committee (FRPCC), membership on the Advisory Team for the Environment, Food and Health and the Federal Radiological Monitoring and Assessment Center (FRMAC) Operations Working Group and participation in exercises. The Center participates in interagency working groups which are developing strategies for responding to acts of radiological terrorism. CDRH also has maintained liaison with the states through the Conference of Radiation Control Program Directors E-6 Committee. CDRH participated in the Top Officials II exercise (TOPOFF II), providing technical input to other groups within the FDA and HHS as part of the overall response to the radiological dispersal device (RDD) attack scenario in Seattle.

Mammography Quality

The goal of the Mammography Quality Standards Act (MQSA) is to enhance the detection of breast disease through high quality mammography services. Under the law, mammography facilities must be certified by the FDA and accredited by a non-profit body by meeting federally established quality standards and undergoing annual inspections. For detailed information on the items below, visit FDA's Mammography Program (see http://www.fda.gov/cdrh/mammography). The site includes a search engine that enables users to search by subject matter.

MQSA Policy Guidance Help System (PGHS)

All MQSA regulatory guidance materials and documents are compiled into one system—the PGHS. Mammography facilities and other interested parties now have access to a comprehensive online resource accessible via MQSA's webpage on the Internet. PGHS users can search for answers to specific questions through an indexed list of topics and key words. For example, by selecting a particular subject, such as "revocation of accreditation" or "accreditation and certification," the user will see the regulatory citation, any relevant guidance documents, and any other appropriate information and references.

The National Mammography Quality Assurance Advisory Committee

The Committee met on April 28, 2003 and reviewed and suggested revisions to two MQSA guidance documents. The Committee also discussed how MQSA reauthorization might impact current regulations and possible ways to streamline the regulations and facility inspection procedures.

MQSA Reauthorization

The MQSA reauthorization of appropriation expired in 2002, but the FDA's authority to inspect and certify facilities does not expire. The MQSA is expected to be reauthorized in 2004.

Additional Mammography Review Process (AMR)

CDRH is also beginning a review of AMR process and procedures. An AMR is a review of clinical images and other relevant information to assure that the facility is in compliance with MQSA. CDRH has had preliminary discussions about AMRs internally and with approved accreditation bodies. It is examining a number of issues specific to AMRs and Patient and Physician Notifications (PPNs) that include:

- Reasons for requesting AMRs
- Procedures for performing AMRs (number of cases and number of reviewers)
- Criteria used to evaluate AMRs
- Methods for evaluating the effectiveness of Corrective Action Plans and/or PPNs
- Role of medical outcomes and other evidence in the AMR/PPN process

Digital Mammography

To date, CDRH's Office of Device Evaluation (ODE) has approved the following Full Field Digital Mammography (FFDM) systems for commercial use since January 2000:

- The GE Senographe 2000D in January 2000

- The Fischer SenoScan in September 2001
- The Lorad Digital Breast Imager in March 2002
- The Lorad Holgic Selenia FFDM System in October 2002

This new technology promises to enhance mammography by reducing the need for some women to have additional exposures, while allowing interpreting physicians to quickly and easily manipulate the images. FDA approved the following two Accreditation Bodies (ABs) to accredit FFDM units:

- American College of Radiology –
  - GE Senographe 2000D (approval date 12/18/02; effective date 02/15/03)
  - Fischer SenoScan (approval date 07/24/03; effective date 08/15/03)
  - Lorad Selenia (approval date 09/05/03; effective date 09/15/03)
- State of Iowa –
  - GE Senographe 2000D (approval date of 08/28/03; effective date 10/01/03)
  - Lorad Selenia (approval date 08/28/03; effective date 10/01/03)

As of September 30, 2003, there are 413 FFDM units accredited in the U.S.

States as Certifiers (SAC)

This project successfully transferred certain key MQSA responsibilities to the states of Illinois and Iowa under a demonstration program during the summer of 1998. The program authorizes qualified states to certify mammography facilities within their jurisdiction, to conduct annual inspections, and to enforce the MQSA quality standards under FDA oversight. In the first half of 2004, FDA expects to transition these SACs from the demonstration program under the interim regulations to the final regulations, which were published by the Department of Health and Human Services on January 18, 2002.

Inspections and Compliance

To assure mammography quality, mammography facilities undergo annual inspections by FDA credentialed inspectors. Nearly 9,000 inspections take place each year. Nearly two-thirds of the facilities (65.5%) had no adverse observations during their inspections this fiscal year. About 9% of facilities had nothing worse than minor (Level 3) observations, while 23% had moderate (Level 2) observations as their most significant result. Finally, about 2% had serious (Level 1) observations during their inspection. The percentage of facilities with significant inspection observations continues to decrease compared with previous years and CDRH is confident that mammography facilities will continue to improve their performance.

Inspection Demonstration Program

Under the Mammography Quality Standards Reauthorization Act, Congress authorized the FDA to undertake an inspection demonstration program (IDP) to assess the results of conducting some mammography inspections less frequently than annually. The purpose of the program has been to evaluate whether selected mammography facilities could maintain the same level of quality without FDA's current scrutiny through annual inspections. In final form, the IDP included approximately 160 study group facilities and an equal number of controls in 14 states or other governmental jurisdictions that had agreed not to inspect these

facilities under their own authority during the study period. The first half of these facilities were selected and notified in November 2001 and the second half were selected and notified in May 2002. Each facility was randomly selected from a set of eligible facilities on a jurisdiction-by-jurisdiction basis. To be eligible, the facilities had to have a clean inspection history for the last two inspections. The facilities in the study group were undergoing biennial inspections during the demonstration program and the inspection process looks at the same areas as the current annual inspections but records are reviewed for the entire period since the last inspection date. Most of these facilities have now received their biennial inspection. All study group facilities should be inspected by the end of May 2004 and results should be available by early in FY 05.

MQSA Compliance Activity

FDA is preparing to implement a new enforcement strategy effective October 1, 2003. Under the new strategy, facilities with the most significant observations will be directed to respond in writing within 15 days of the inspection, rather than almost always being sent a Warning Letter. That response will be reviewed by the FDA prior to taking any further action. If there is no response or if the response is inadequate, then a Warning Letter could be issued. If the response appears adequate but the facility has a history of violations, then a fee-based follow-up inspection could be scheduled. In addition, Warning Letters may be followed by a non-fee-based follow-up inspection within a few months to assure that correction has been made. This new strategy will focus more attention on facilities with a history of violations. CDRH also is looking at whether changes may be needed on how repeated inspection violations are defined.

In parallel with the new enforcement strategy, CDRH will increase the rate of enforcement actions to direct appropriate attention to those facilities that exhibit significant problems that they can not or will not correct. During FY 03, CDRH issued 2 directed plans of correction (DPC), 1 civil money penalty (CMP), and 1 patient notification.

International Programs

Global Harmonization Task Force (GHTF)

The GHTF was formed in 1992. The founding members are the United States, Canada, the European Union, Japan, and Australia. The GHTF's mission is to encourage convergence of medical device regulatory practices worldwide while ensuring the safety, effectiveness, and quality of medical devices; promoting technological innovation and facilitating international trade. The GHTF has a steering committee which directs the work of four study groups. Steering committee and study group participants include representatives of regulatory bodies and industry from the founding members. To achieve GHTF's mission, the study groups develop guidance documents on basic regulatory practices which are available to all countries through the GHTF website at http://www.ghtf.org. Each study group focuses on a different aspect of medical device regulation, as follows:

- Study Group 1: regulatory and premarket requirements;
- Study Group 2: postmarket vigilance;
- Study Group 3: quality systems; and
- Study Group 4: regulatory auditing of quality systems.

The United States, through the FDA/CDRH, is a major partner in GHTF and throughout 2003 actively participated in the work of the four study groups and the steering committee. FDA is committed to continue full participation in the advancement of the GHTF's mission and initiatives.

Summary Technical Documentation for Demonstrating Conformity to the Essential Principles of Safety and Performance of Medical Devices (STED) Initiative

The FDA is participating with the other members of GHTF in the STED Initiative to test the utility of the "Summary Technical Documentation for Demonstrating Conformity to the Essential Principles of Safety and Performance of Medical Devices" (the STED document) developed by GHTF Study Group 1. The FDA's part of this initiative was announced in the *Federal Register* as "A Pilot Program to Evaluate a Proposed Globally Harmonized Alternative for Premarket Procedures; Guidance for Industry and FDA Staff." The guidance can be found on the Internet at the CDRH website http://www.fda.gov/cdrh/ode/guidance/1347.pdf. The FDA's pilot program is limited to PMA applications and 510(k) notifications only for certain devices. The STED Initiative offers the potential for harmonized reviews with member countries of the GHTF eventually.

U.S./EC Mutual Recognition Agreement (MRA)

The Medical Device Annex of the United States (U.S.) / European Community (EC) Mutual Recognition Agreement (MRA) went into effect in December 1998, initiating a three-year transitional period encompassing training and evaluation activities. The transitional period was extended, and training and evaluation activities are continuing until the U.S. and the EC are ready to nominate Conformity Assessment Bodies (CABs) for listing and begin the Operational Period of the MRA. The Medical Device Annex of the U.S./EC MRA provides for three types of regulatory activities: (1) the exchange of quality systems inspection/audit reports; (2) product evaluation reviews and/or testing for select low to medium-risk devices;

and (3) establishing a program for exchanging information on serious health risks posed by medical devices. As of this fifth year of the transitional period, the FDA has:

- confirmed that seven EU CABs meet the FDA criteria;
- provided classroom training in the FDA device regulations and inspection procedures and policies to EU CAB auditors;
- authorized four EU CABs to conduct independent inspections of EU device manufacturers on behalf of FDA;
- evaluated U.S. CAB dossiers and confirmed that seven U.S. CABs meet EU criteria;
- forwarded summaries of the dossier evaluations to the EC; and
- observed and evaluated one U.S. CAB auditing a U.S. manufacturer against EU device requirements.

Future work includes observing and evaluating the other U.S. CABs as they audit manufacturers; conducting on-site audits of U.S. CABs at their business sites; and continuing to train, evaluate and qualify EU CABs to conduct independent audits.

Program Support

CDRH Strategic Plan

- CDRH's Strategic Plan (http://www.fda.gov/cdrh/strategic/) was introduced in FY 00. The Plan consists of four major strategic goals:
- Total Product Life Cycle Model (TPLC)
- Public Health Impact (PHI)
- Magnet for Excellence (ME), and
- Knowledge Management. (KM)

These four strategic goals are fundamentally linked to the Center's mission of promoting and protecting the public health through safe and effective medical devices and safe radiological products.

CDRH Strategic Goals and Accomplishments

The Strategic Plan Accomplishments webpage (http://www.fda.gov/cdrh/strategic/accomplishments.html) describes CDRH's strategic goals. Objectives, implementation actions and a summary of accomplishments are available in the website. A brief summary is included in this section.

Total Product Life Cycle Model (TPLC)

The TPLC model promotes working in an integrated manner through the total life cycle of the products CDRH regulates. TLPC encourages education and partnership between staff and stakeholders and promotes working towards harmonizing CDRH and international regulation.

FY 03 TPLC accomplishments include:

- Creation of the Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD). OIVD consists of a multidisciplinary group of scientists and other professionals who are collectively dedicated to promoting and protecting public health through clear and consistent regulation of IVDs by applying good scientific principles throughout the Total Product Life Cycle of IVDs,
- Establishment of six cross-Center product area review groups to work on MDUFMA implementation.
- Establishment of Center-wide initiatives that focus on the development guidance and standards.
- Launching the ODE/DRAD/EB Pilot Project. This pilot project will help CDRH determine when and how epidemiologists could best provide input and recommendations to premarket reviewers regarding potential postmarket investigations and to initiate, and later evaluate, product-specific postmarket plans based on premarket data.
- Participation at meetings attended by CDRH stakeholders and planning of the first annual MDUFMA Stakeholder Meeting, conducted on December 12, 2003.
- Realignment of OSEL research priorities and program review processes to ensure input from all CDRH Offices.

- Participation and work with GMDN and GHTF on harmonization initiatives.
- Using the Continuous Process Improvement (CPI) methodology to study and enhance CDRH processes. Process Improvement Teams (PITs), which evaluate and make recommendations regarding and CDRH specific process, worked on a number of projects Center covering, among other topics, PMA filing, inspections, science prioritization and use of external expertise Information on CPI can be found at http://www.fda.gov/cdrh/strategic/cpi.html.

Public Health Impact (PHI)

The public health impact goal embodies CDRH's commitment to find ways in which to measure and improve the impact of the products it regulates on the public health. The Center is constantly:

- Working towards improving the time to market of new expedited safe and effective devices;
- Assessing and improving risk management processes; and
- Identifying and resolving public health hazards.

Public Health Impact FY 03 accomplishments include:

- Continue working on Mammography Quality Standards Act-related programs. (For additional information, see the Mammography Quality and Radiation Programs section of this report.)
- Recruiting additional MedSun reporting facilities from the east coast and mid-west region of the United States, for a total of 180 facilities.
- Targeting of the MedSun system to obtain specific medical product information.
- Beginning a MedSun pilot project to more directly target the sending of reports from laboratories (pathology and in vitro diagnostic tests) in the reporting hospitals.
- Working with third-parties towards inspection accreditation. In FY 03 CDRH received twenty three third-party inspection accreditation applications. By the end of FY 03 seventeen applications were under full review, five were under initial review and one application was denied.

Magnet for Excellence (ME)

Magnet for excellence means attracting and retaining a diverse workforce that will help the Center accomplish its public health mission. By working towards becoming a magnet for excellence the Center will be able to:

- Become an employer of first choice,
- Provide employees with opportunities to succeed, and
- Link performance to CDRH's public health mission.

FY 03 magnet for excellence accomplishments include:

- Actively supporting the master reviewer career path.
- Launching the Georgetown/Virginia Tech training program to support staff capabilities.
- Using the newly established Medical Device Fellowship Program to bring in outside experts and provide professional development opportunities for staff.
- Using Gallup Survey to assess and improve the quality of workplace.

- Implementing "shared-hires" to share resources and allow staff to better use their expertise across the Center.

Knowledge Management (KM)

Knowledge Management supports the TPLC model in the information age. KM means:

- Working towards becoming an independent source of information on devices and radiological health;
- Finding ways to leverage to create, share, and use knowledge; and,
- Working towards becoming an e-Center.

FY 03 examples of KM accomplishments include:

- Modification of device review tracking systems to include MDUFMA performance goals
- Organization and participation on workshops on relevant scientific and public health issues like the Novel Drug Delivery Systems (July 8, 2003) and Severe Acute Respiratory Syndrome (SARS, July 14, 2003)
- Implementation of Center scorecards to better manage, measure and track performance
- Work on Turbo-510(k) review templates
- Launching of the e-Room
- Support of electronic system such as IMAGE 2000

Strategic Plan Phase II Initiatives

On October 26, 2002, the President signed the Medical Device User Fee and Modernization Act (MDUFMA). MDUFMA presents a wide range of new challenges and opportunities. By FY 07, CDRH will be required to do quality reviews assessing product safety and efficacy far faster than ever before, especially for expedited products. These and other changes since 2000 required updating the Center's goals for the coming years.

In FY 03 CDRH adopted a number Phase II Strategic Initiatives that CDRH believes will to help face the new challenges in FY 04 and FY 05. These strategic initiatives are:

Management Systems for Measured Performance

Through this initiative CDRH will engage the use of scorecards to measure, manage and track performance. Scorecards clarify expectations and can be used to set targets for change for CDRH organizations and staff.

Project Management

The project management initiative guides and facilitates CDRH's efforts to achieve the integration of project managers and project management concepts into CDRH regulatory processes. Project management will help achieve MDUFMA goals, improve overall review and timeline goals; and, enhance CDRH ability to follow through on key milestones in complex work processes.

Consumer Information

The consumer information initiative leads CDRH's efforts to develop systematic, cost-effective ways to provide consumers plain language and up-to-date information about CDRH-regulated products.

E-Center

Coordinated e-Center efforts will bring CDRH numerous opportunities for improved services to stakeholders. As a business practice being an e-Center is cost savings, reduces waste, could improve cycle times and could be used to leverage existing technologies for business benefit. Projects under this initiative include:

- Development of an electronic template, known as Turbo 510(k) that will clarify what is needed to complete OIVD 510(k) reviews; and,
- Use e-consults to improve a achieve consistency regarding how CDRH staff request and provide consults and, to allow recording the results of the consults in a manner accessible to others working on that products.

Scientific Expertise

The scientific expertise initiative deals with enhancing the scientific capabilities of the Center to support and sustain a flexible workforce. CDRH's commitments within this initiative include the implementation of training opportunities for current staff (like the Virginia Georgetown/Virginia Tech training program) and increasing partnerships and exchange programs with outside scientific organizations through programs like the Medical Device Fellowship Program.

Organizational Focus

The organizational focus initiative targets the focus and business practices of CDRH Offices. As part of the initiative CDRH Offices will evaluate their mission, functions, management systems and processes, and will develop strategies for implementing TPLC, MDUFMA, and Executive Branch initiatives.

Emergency Preparedness

Medical Countermeasures Shortages

CDRH's plan for identifying and addressing potential medical countermeasures shortages of medical and radiological health products outlines the procedures that will be taken in 3 categories: identification of products needed; location of sources and capacity; and development of a system to communicate with all stakeholders involved in securing products.

In consultation with internal and external medical professionals, and with emergency response professionals, CDRH identified devices most likely to be needed in the event of a terrorist attack. These devices range from protective clothing, to diagnostic products to life support equipment. Amongst these products, 17 devices were identified as most likely to be in short supply in an emergency. To determine the availability of these products, CDRH established a manufacturer database for potential shortage devices that includes: 24 hour emergency contact information, current and potential production capacities, inventory availability and

locations, and market share. In addition to the manufacturers of these products, CDRH identified 24-hour emergency contacts for the three major U.S. medical supply firms, and established contact information with emergency counterparts in the various medical device industry associations. CDRH continues to work with industry associations to identify ways in which CDRH and industry can collaborate in the event of an emergency shortage. CDRH initiated contact with representatives from the National Pharmaceutical Stockpile program to determine whether CDRH can provide assistance and to ensure that CDRH's current efforts enhance overall emergency preparedness without unnecessarily duplicating efforts. CDRH has met with emergency response representatives from CDC and HHS to better develop a communication process when requests for devices are forwarded from any component.

Response Plans for Radiological Emergencies

CDRH completed the revision of the emergency response plans for radiological or nuclear emergencies which involve FDA-regulated products or require the use of medical products as countermeasures for radiological emergencies. CDRH specialists in health physics, medical physics, physics, medicine, and engineering respond to emergencies through two organized structures: the Radiation Emergency Response Team (RERT) and the Radiation Emergency Response Cadre (Cadre). The RERT is the primary response team for radiological emergencies and is composed of four trained radiation safety experts let by CDR Michael Noska, US PHS. The radiological emergency response plan, which is incorporated into the Center's emergency plans, has been distributed to all Center staff and was shared with other components in FDA who have responsibilities in the radiological health area such as CFSAN and CDER. This plan was successfully implemented during the May TOPOFF II exercise with positive reviews from the FDA EOC and other Centers.

CDRH has been a member of the Environmental Clearance Committee for the Joseph Curseen, Jr., Thomas Morris, Jr. (formerly the Brentwood) Processing and Distributing Center. OSEL's Division of Life Sciences (DLS) has just finished reviewing the Remedial Action Plan for the Trenton, NJ Postal Facility. In addition, DLS is on the Interagency Expert Panel on Efficacy Test Methods and Surrogates for Anthrax Spores (head is from EPA).

CDRH serves as chair for the consensus standard of the American National Standards Institute N43.17, radiation safety for personnel security screening systems using X-rays. CDRH has continued work on updating this standard. In addition CDRH staff serves as consultants to the Department of Homeland Security with regard to screening systems, ionizing radiation monitoring instrumentation and instrument calibration.

CDRH updated both CDRH and FDA levels of the Emergency Counterterrorism Preparedness and Response Plan for radiation during FY 03.

Continuity of Operations Plan (COOP)

CDRH completed COOP plans for all buildings housing essential Center functions. As one of the first Centers to complete COOP plans, CDRH's initial drafts were referenced and used by the agency's consultants as models for others in FDA. CDRH provided training or staff on the plans and successfully exercised them during an observed practice event. The "hot wash" feedback from the consultant group and the Center's internal "after action review" showed that

minimal changes were needed to the draft plans that were developed according to the templates provided by the agency. OHIP led the development of a COOP Plan for one of its buildings. The Plan is complete.

HHS, FDA and CDRH Program Initiatives

Public Health Response

Examples of actions taken that demonstrate CDRH commitment to this goal include:

- **OraQuick® Rapid HIV-1 Antibody Test:** In November 2002, the FDA/CBER Approved OraQuick® Rapid HIV-1 Antibody Test manufactured by OraSure Technologies, Inc., of Bethlehem, Pa. The test is the first rapid HIV point-of-care (i.e., testing and results are available in one visit) test approved by the FDA. It also is the first test for HIV that OIVD has waived under the Clinical Laboratory Improvement Amendments (CLIA). Following the CLIA waiver by OIVD the HHS Secretary Tommy G. Thompson announced that HHS has extended the availability of the OraQuick Rapid HIV-1 Antibody Test from 38,000 laboratories to more than 100,000 sites, including physician offices and HIV counseling centers. The Secretary added "Ensuring the widespread availability of a rapid HIV test to outreach services in communities where people are at high risk of HIV is vital to the public health, without today's action (CLIA Waiver), this test would be limited to use in laboratory settings where many high-risk people do not go for testing." Widespread availability of the rapid HIV test is likely to increase overall HIV testing and decrease the number of people—an estimated 225,000 Americans—who are unaware they are infected with the HIV virus. Early testing enables infected individuals to obtain medical care earlier in the course of their infection, potentially saving lives and limiting the spread of this deadly virus.
- **Severe Acute Respiratory Syndrome (SARS):** An IDE for a SARS Coronavirus, submitted by HHS, Centers for Disease Control and Prevention (CDC), was approved. This allowed CDC to make available to about 100 public health laboratories nationwide, a new experimental laboratory test for patients suspected of being infected with the SARS virus. The experimental diagnostic test was rapidly developed by CDC in an urgent effort to address this pressing public health need. FDA worked closely with CDC to develop appropriate information for patients and health professionals in order to make the test available on an investigational basis. Because information about the test's performance is still being collected, patients will be asked for written consent before the test is used.

Communicating with Consumers, Health Care Professionals and the Industry

CDRH has been developing new, and updating existing webpages dealing with MDUFMA, new product approvals, recalls, patient safety news, advisory committees/panel meetings, CLIA, in vitro devices, and device safety alerts. During FY 03 CDRH worked with many partners throughout HHS to publicize Department public health outcomes on key public health issues. For example, it worked with many partners to provide diagnostic information for the Diabetes website. CDRH worked to publicize information on hospital bedrails, and on oxygen regulators. For example:

- **Diabetes website** - Since OHIP posted the Diabetes website in the Spring of 2002, it has continued to learn about designing and developing usable websites. In the spring of 2003, OHIP decided to perform a heuristic evaluation and a usability evaluation of the Diabetes website. The results of the two evaluations provided valuable feedback about the structure and content of the website. OHIP learned how to improve writing style to make it more appropriate to Web communication, how to increase search engine visibility, and how to structure the website to optimize user satisfaction. In addition, OHIP learned new techniques for conducting usability evaluations throughout the website development.

Implement Results-Oriented Management

During FY 03, CDRH worked with the Commissioner's staff and CDER on the long-term goal of reducing the overall amount of time it will take the FDA to approve original PMAs and expedited PMAs in the next 5 years. This "approval cohort" was announced by the Commissioner in a press release, and is a part of the FDA's Program Assessment Rating Tool (PART) goals developed with OMB. CDRH met with stakeholders to explain this goal and how it will be calculated.

In addition, during FY 03 CDRH modified performance tracking systems so it can track performance on MDUFMA's long-term cycle and decision goals outlined in the MDUFMA commitment letter.

During FY 03, CDRH continued to work with Dr. Richard Chang, an expert in organizational scorecards. Dr. Chang facilitated efforts to develop CDRH organizational scorecards and improve performance metrics:

- **Organizational Scorecards -** CDRH management teams received formal training and actively participated in the Center's initiative to develop office and division-level performance scorecards. These Performance Scorecards contain a series of performance measures that are linked to the Offices' performance goals and CDRH's strategic plan. In FY 04, CDRH will establish baseline data for the performance measures and report initial performance results from these Performance Scorecards.
- **Continuous Process Improvement (CPI) -** CPI involves identifying a process that needs to be improved, analyzing the current process, researching potential improvements, and developing and implementing an improved process. The improved process ultimately will assist the Offices in meeting performance measures identified in the Offices' Performance Scorecards. Processes that were subject to formal Continuous Process Improvement efforts in FY 03 were PMA Filing, PMA Close-Out, Turbo 510(k), Inspections, Subject Matter Expert, External Experts, Science Priorities, After Action Review, BIMO/ODE PMA Review, and Risk-based Inspection.
- CDRH employees were formally certified as Performance Improvement Coaches for performance scorecards and Continuous Process Improvement.

Implement Strategic Human Capital Management

CDRH fully participated in the FDA's evaluation, implementation and migration to a shared services organization for administrative operations, known as the Office of Shared

Services (OSS). CDRH's Executive Officer served on the OSS Steering Committee; meeting routinely to set policy and direction and ensure stand-up of OSS on October 1. CDRH completed the de-layering process. CDRH's organizational layers do not exceed four.

During FY 03 CDRH implemented a strategic evaluation of workforce needs and succession planning. This was achieved by prioritizing CDRH's recruitment and retention needs for mission critical positions across the Center by the Center's six product review groups.

Improve Information Technology Management

CDRH's goal is to improve the use of information technologies resources, specifically:

- **Computer Tracking Systems** - Significant work was done to the document tracking systems for the 510k, PMA, and Modular PMA databases.
- New hold statuses were created and the data entry programs were modified to check MDUFMA payment status and to apply holds automatically.
- MDUFMA payment data was linked to the 510k and PMA data entry programs and new programs were written to notify CDRH staff of payments received.
- A new flag was added to the 510k and PMA tracking systems for the Summary Technical Documentation (STED) Initiative. The STED Initiative is a pilot program to assess the feasibility of using an internationally harmonized format in the review of certain submissions for device safety and performance.
- **Video Conferencing** - CDRH has the ability to conduct Room and Desktop Video Conferences with outside parties that have H.320 compliant systems, a standard for video conferencing over Integrated Services Digital Network (ISDN) lines and other narrowband transmission media. In FY 03, ODE held 8 video conferences involving industry and other Federal agencies.
- **Image2000** - The CDRH system for storing copies of past device application submissions was upgraded to provide additional capabilities for CDRH reviewers. Reviewer input played a major role in the redesign of the document repository and the upgraded system has been well-received. The system now stores documents in PDF format and allows for full-text searching, for copying or saving documents and for printing all or part of the submission.
- **E-Room -** Implemented e-Room as a collaborative tool in the review of medical device submissions.
- CDRH also:
    - Hired contract personnel to assist in improved development of IT systems
    - Hired a contractor to perform as a mentor to the IT staff in implementation of improved IT systems development
    - Sent staff members to Project Management certification courses in order to apply newer standard techniques to IT systems development
- **Remote access** – CDRH Implemented secure remote access throughout the Center.
- **E-journals** – CDRH added a significant number of e-Journals to the library services provided to the Center.