Long Term Outcome Goals

This section contains a status report on FDA's progress in developing and measuring long-term, quantifiable outcome goals that will improve the health and well-being of the American Public. FDA is tracking progress towards accomplishment of eight long-term outcome goals in the following areas:

- Reduce the average time to marketing approval for safe and effective new drugs and biologics.
- Reduce the average time for marketing approval for safe and effective new devices
- Reduce the average time to marketing approval for safe and effective new generic drugs
- Increase consumer understanding of diet-disease relationships (dietary fats and CHD)
- Reduce adverse drug events related to medication dispensing and administration errors by requiring bar codes on drugs and biologics used in hospitals
- Increase the patient population covered by active surveillance of medical product safety
- Increase FDA's capacity to effectively analyze food samples for biological, chemical and radiological threat agents in the event of a terrorist attack
- Reduce administrative overhead at FDA by reducing the number of administrative staff

Detailed information on each of these goals is provided in the material that follows.

In each of these areas, FDA is strengthening outcome measurement and achievement capability by taking the following steps:

Examine the linkage between FDA program efforts and ultimate health and safety outcomes; and evaluate possible performance indicators for these end outcomes, which may be relevant for FDA.

Explore of intermediate outcome measures which may serve as good leading indicators of ultimate health outcomes. Many of these intermediate measures are more proximate to FDA efforts and therefore may be more within the influence of Agency actions.

Identify data sources that will serve as valid and reliable sources of information on the selected intermediate and end outcome measures. In some cases these data sources have been identified; in many other cases the search for such sources is still underway.

Formulate data strategies to make databases more accessible and useable for FDA. In some cases data sources are in place, but are not collecting information in categories that would be relevant for FDA. In other cases, data must be purchased from outside sources; and in still other instances, such as adverse event reporting systems, the databases have to be constructed. This takes time and considerable investment of resources.

Analyze and evaluate, as appropriate, to strengthen our understanding of the relationship between FDA program efforts and both intermediate and end health outcomes. We have identified studies that have already been completed, which contributes to our understanding of these relationships.

A discussion of progress in outcome measurement and achievement follows for each of the areas identified above.

> The names of FDA's strategic goals have been changed to reflect revised titles as shown in FDA's Progress and Priorities in FY 2004 (see http://www.fda.gov/oc/initiatives/reports/priorities2004.html.)

FDA Proposed Long-term Outcome Goals for Strategic Goal 1: Using Risk-Based Management Practices

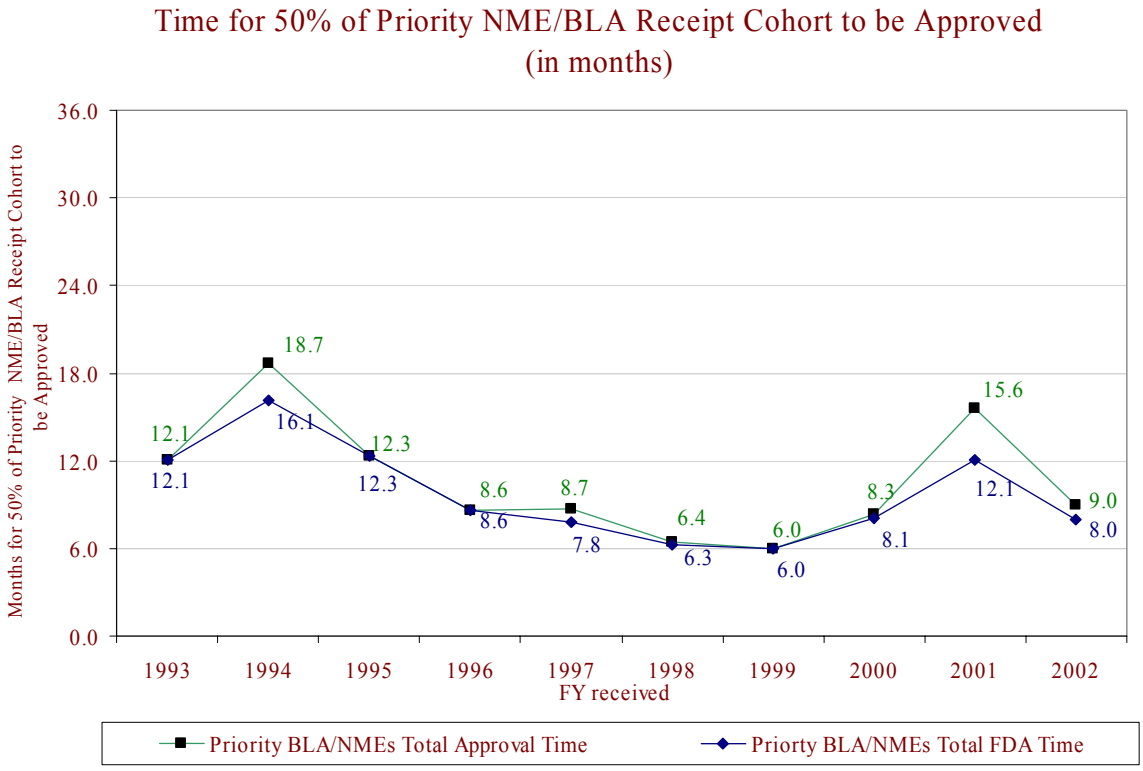
Marketing Approval for New Drugs and Biologics

1. What is the proposed long-term outcome goal? The goal is to ***reduce the average time to marketing approval for safe and effective new drugs and biologics.***

2-3. What are the proposed targets and the proposed data for full accomplishment? The proposed targets will differ for priority applications versus standard drug and biologics licensing applications.

The proposed target calls for a reduction in average FDA approval time by 30 days for the fastest 50 percent of priority New Molecular Entities/ Biologics Licensing Applications approved, using the 3-year submission cohort for FY 2005-2007.

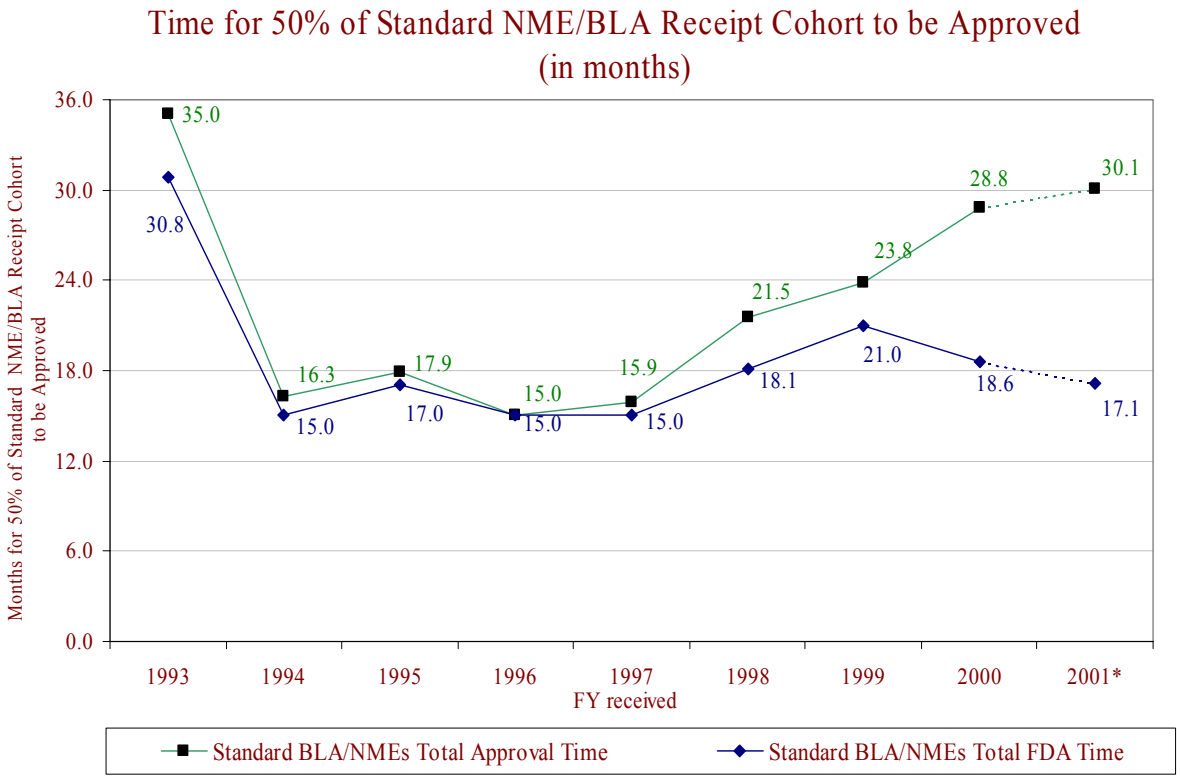
The baseline used for this goal is the average FDA approval time for the fastest 50 percent approved for the FY 2000-2002 submission cohort. The baseline average FDA marketing approval time for priority NME and biologics applications is 9.4 months. [see chart below]



[3] Tufts CSDD quantifies savings from boosting new drug R&D efficiency, *Tufts Center for the Study of Drug Development Impact Report*, Vol. 4 No. 5 September/October 2002

The proposed target calls for a reduction in average FDA approval time by 2 months for fastest 50 percent of standard New Molecular Entities/ Biologics Licensing Applications approved, using the 3-year submission cohort for FY 2005-2007.

The baseline used for this goal is the average FDA approval time for the fastest 50 percent approved for the FY 1999-2001 submission cohorts. [*Note: FY 2001 applications for the baseline measure are not all done so the reduction target is provisional. FDA has projected the average time based on the applications submitted in FY2001 approved so far.*] The baseline average FDA marketing approval time for standard NME and biologics applications is 18.9 months. [see chart below]



* Currently, 38% of the FY 2001 Standard cohort have reached approval. FY 2001 figures are projected based on approvals to date and current status of unapproved applications. Because of the sensitivity of the 50% approval statistic, these figures could change significantly depending on the outcome of applications currently under review.

FDA will have the data to measure and assess accomplishment of these goals in FY2008.

On an intermediate basis, FDA will track and analyze time to approval and look at a rolling 3 year average for the fastest 50 percent of NMEs and biologics approved for the interim years, and the Agency will track the timeliness of implementation and evaluate the impact of a variety of program initiatives that are intended to improve the quality and effectiveness of FDA review and interactions with sponsors, and to improve the quality of applications submitted by sponsors. These factors are expected to impact the time to marketing approval. The target cohort FY 2005-2007 submissions is chosen because the Agency expects to see a return on these efforts by that point in the future.

Long Term Outcome Goals

To progress toward this long-term performance goal for FY2005-2007, FDA will:

a. Review and act on 90 percent of standard original NDA and BLA submissions filed during the fiscal year within 10 months of receipt, and will review and act on 90 percent within 6 months of receipt for priority applications. [reference **PDUFA III goal letter**]
b. Implement the Continuous Marketing Application (CMA) pilot review programs in FY 2004, enabling sponsors to submit portions of applications for Fast Track drugs for early review and feedback, in advance of a full application submission. As part of this initiative FDA will work to the following goals:
    - Complete discipline review team review of a "reviewable unit" for a Fast Track drug or biologic, and issue a Discipline Review Letter within 6 months of the date of the submission for 50 percent of "reviewable units" in FY 2005; for 70 percent of "reviewable units" in FY 2006 and for 90 percent of "reviewable units" in FY 2007.
c. Implement the First Cycle Review initiative. As part of this premarket review initiative, for original NDA/BLA applications FDA will report substantive deficiencies identified in the initial filing review to the sponsor by letter, telephone conference, fax, secure email or other expedient means, within 14 calendar days after the 60-day filing date. FDA will provide a notification of deficiencies prior to the goal date for 70 percent of applications submitted in FY 2004; and for 90 percent of applications submitted in FYs 2005, 2006 and 2007.
    - FDA will also retain an independent expert consultant to conduct an evaluation to assess the first cycle review history of all NDAs for NMEs and all BLAs submitted in FY 2003-2007 including a detailed evaluation of the events that occurred during the review process with a focus on identifying best practices by FDA and by industry that facilitate the process. This should result in better-quality applications and more effective interactions, helping reduce unnecessary delays in time to marketing approval.
d. As part of FDA's **Strategic Action Plan** Goal 1, the Agency will, during FY 2003-2005:
    - Perform root cause analysis to address causes of unnecessary delay in application approval.
    - Initiate quality systems for human drug review process.
    - Work collaboratively with the National Cancer Institute and other government agencies, academic researchers, health care providers and patients to clarify regulatory pathways for targeted disease areas and new technologies, through joint workshops and conferences to address key clinical and scientific issues, to provide clear guidance to product innovators, improving the efficiency and anticipated quality of submitted applications. ***The targeted disease areas include cancer, diabetes and obesity. The targeted technologies include cell and gene therapy, pharmacogenomics and novel drug delivery systems.*** The quality and completeness of submitted applications are key determinants of the time required for FDA approval.

4. What FDA Centers are covered by this goal? The Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER)

5. Why achieving this goal is important? Reducing unnecessary delays in the approval time for safe and effective drugs that truly represent new therapies [i.e., NMEs and biologics] means earlier patient access for these medicines. Reducing unnecessary delays in drug approval also helps to both control the cost of new drug development, cited as a factor affecting the cost to consumers, and supports market competition among innovators. This is both good for the drug industry and good for consumers. New drug development presents uncertainties that increase the business risk and costs to the innovator. Higher costs can create barriers to competition both from new drugs with therapeutic value – but not blockbuster potential, and new innovators that don't have access to the capital available to more established pharmaceutical companies. Although some scientific and technical uncertainties are inherent and unavoidable in drug innovation, others can be reduced or eliminated, helping speed patient access to new drugs, and reducing the cost of drug development. FDA has begun major initiatives to reduce those

sources of uncertainty. See paragraph 4.(d) above. These are included in the Agency's Strategic Action Plan

Sponsors, for example, may be uncertain about what FDA expects to see in a high quality new drug application, because of a lack of interaction with FDA during development, or lack of clear, timely or consistent FDA-sponsor communication during review. As a result, the submitted application may have deficiencies that could have been avoided or addressed quickly, but instead create unnecessary delays as they are identified by FDA and then addressed by the sponsor. Although FDA has found that applications can often contain deficiencies that are not so readily addressed, clear understandings of FDA expectations and timely communication between FDA and application sponsors can increase the likelihood that the submitted application contains the necessary information for timely approval on the first round.

The targeted reductions in this FDA outcome goal represent approximately 10.5 percent reductions in total FDA review times for priority and standard NMEs and BLAs. Using Tufts estimates of potential cost reductions by phase of drug development[3], a 10 percent reduction in regulatory review time yields a 1.6 percent reduction in total capital costs, now estimated at $802 million, translating to a savings of $12.8 million per NME approved.

6. How does this long-term outcome goal relate to achieving ultimate outcomes of reducing mortality and morbidity?

To obtain marketing approval, the new drug application must provide the scientific evidence needed to demonstrate safety and effectiveness in treating the disease indication identified in the labeling. The degree of net impact on mortality and morbidity will vary according to disease indication and the availability and efficacy of alternatives already on the market.

FDA has targeted reduced time to approval for priority applications and has focused the new CMA initiatives [intended to speed development and review] on Fast Track products to increase the expected mortality and morbidity impact of the new approvals in the target years.

The following rapid drug approvals resulting from earlier PDUFA review performance goals illustrate the type impact that can be achieved:[4]

- The new biologic for the treatment of breast cancer (Herceptin®/ trastuzumab) was approved by FDA in less than 5 months. This drug took 18 months to be approved in Europe. There were an

[4] Sources:

- Surveillance Epidemiology and End Results Program, National Cancer Institute
- IMS HEALTH, National Prescription Audit *Plus*™ Years 1997-2000
- IMS HEALTH, National Disease and Therapeutic Index™ Years 1997-1998
- IMS HEALTH, Retail & Provider Perspective™ Years 1997-2001
- Birth cohort in 1999 and 2000, National Vital Statistics Report Vol 49, No. 5 July 24, 2001
- Physicians Desk Reference
- Teerlink JR and Massie BM Am J Cariol 1999 Nov 4;84(9A):94R-102R.
- Zangwill KM, Vadheim CM, Vannier AM, et al. Epidemiology of invasive pneumococcal disease in Southern California: implications for the design and conduct of a pneumococcal conjugate vaccine efficacy trial. J Infect Dis 1996; 174:752-9.
- Pastor P, Medley F, Murphy T. Invasive pneumococcal disease in Dallas County, Texas: results from population-based surveillance in 1995. Clin Infect Dis. 1998; 26:590-5.
- Hofmann J, Cetron MS, Farley MM, et al. The prevalence of drug-resistant Streptococcus pneumoniae in Atlanta. N Engl J Med. 1995; 333:481-515.
- Slamon DJ et al. Use of Chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancere that overexpresses HER2. N Engl J Med 344: 783-792.

estimated 10,000 American patients with advanced breast cancer who received this new treatment (Herceptin®/ trastuzumab) during the time that FDA might have still been reviewing the application, had it not been for the improvements made possible with the additional funds under PDUFA. This added an estimated 2300 years of life to the population who had access to the new treatment (Herceptin®/trastuzumab) following its market approval in May of 1998.

- Earlier access to a new drug for congestive heart failure (Coreg®/carvedilol) is estimated to have prevented up to 2,800 deaths during the period that FDA might have been reviewing the application had it not been for FDA's goal-driven reviews.

- The 6 month review and approval of a new treatment for osteoporosis (Fosamax®/alendronate sodium) is estimated to have allowed thousands of women access to treatment, when compared to the average review time for similar drugs prior to PDUFA. This earlier access to Fosamax prevented as many as 3,000 hip and wrist fractures.

- Compared to the average review time for vaccines prior to PDUFA, the faster review and approval of a new vaccine [Prevnar®/Pneumococcal 7-valent Conjugate Vaccine] for life threatening infections in children, allowed earlier access to the vaccine and prevented an estimated 14,000 cases of serious infections in infants and young children.

In the future, the Agency will demonstrate the impact that reduced approval times have on morbidity and mortality using similar methods. Pharmaceuticals and biologicals approved in the FY 2005-2007 submission cohort that significantly impact morbidity and mortality will be identified by the respective review divisions. For each product identified, the approval time would be compared to the average approval time for the relevant therapeutic category from earlier submission cohorts. This difference in time would represent the average additional time period in which eligible patients had access to new breakthrough treatments. The health benefits related to these breakthrough treatments administered during these time periods would be the primary endpoints.

For each product from the FY 2005-2007 submission cohort judged to have a significant impact on morbidity and mortality, the size of the eligible patient populations and the corresponding product utilization post approval would be determined through IMS data along with other publicly available data sources such as the published literature, data bases, and disease registries. Efficacy and/or effectiveness measures would be taken from either Phase III studies or the most recent published studies demonstrating the products' effects. Health outcomes measures such as events avoided, live years saved, or deaths avoided would be calculated based on the point estimates for effectiveness and product utilization. If healthcare resource utilization and costs are readily available from in-house data sources these estimates would be obtained and analyzed in addition to the health outcomes.

7. What types of data already exist for measuring this long-term outcome goal? FDA maintains a PDUFA application/review tracking system that can provide the data to measure the long-term goal. Because there is a delay from the time of submission to approval of 50 percent of the submission cohort, the Agency anticipates that the data will be available to evaluate performance for these long-term goals in FY 2008.

8. What types of new data sources would be needed to measure progress on this long-term outcome goal? Progress toward achievement of the goal will be tracked through existing review tracking and newly established tracking elements for new FDA initiatives under PDUFA III and under the FDA Strategic Action Plan.

9. Why is this target a stretch? Whether or not a product can be approved in a shorter time period (e.g., a single review cycle of 6 months for priority or 10 months for standard) depends on whether the application contains sufficient, scientifically valid information on safety and effectiveness to meet the Agency's standards for approval (i.e., that there is evidence that the demonstrated benefits of the product outweigh its known risks.) The basic premise at the time of the submission of the application to the FDA is that the application is complete and contains the data needed to support the claims the company wishes to make for the product and that the company is prepared to manufacture the product in a consistent, quality manner in compliance with good manufacturing practices.

As deficiencies are noted during the review of an application, the Agency attempts to work with the company to address these deficiencies during the time allowed for the review cycle. Minor deficiencies can often be so corrected without having to resort to a second review cycle. However, major deficiencies usually need substantial time between cycles for companies to develop the data necessary to address adequately the deficiencies noted during the review.

FDA believes that reducing deficiencies to a minimum prior to application submission would result in the most efficient use of Agency and company resources and would facilitate getting scientifically-substantiated, well-manufactured products to patients as quickly as possible. But the Agency cannot guarantee that sponsors will follow FDA guidances or advice, or respond quickly and completely to noted deficiencies. Achieving this goal requires not only that FDA improve its own performance, and work more efficiently and effectively, but essentially work to improve the performance of the drug sponsors as well.

10. How does this target serve Department priorities and goals? This Agency goal and target measures support the Department priorities of preventing disease and illness and promoting positive life styles, and improving the quality of health care.

11. What measurable progress have we made toward this goal?

Reduction in Review Time

- The FDA approval time for the fastest 50 percent of priority NME and biologics licensing applications (BLAs) approved for the FY 2001-2003 cohort is 265 days as compared to 286 days for the baseline FY 2000-2002 submission cohort. *This is a reduction of 21 days versus the FY 2005-2007 target of 30 days.*

- The FDA approval time for the fastest 50 percnet of standard NME/BLA applications approved for the FY 2000-2002 cohort is 520 days as compared to 575 days for the baseline FY 1999-2001 submission cohort. *This is a reduction of 55 days versus the FY 2005-2007 target of 61 days.*

Overall PDUFA Review Performance

FDA exceeded all PDUFA review performance goals for FY 2002 and appears to be on track to meet the review performance goals for the FY 2003 submission cohort.

- *For the FY 2002 submission cohort, the Agency has exceeded its goals for reviewing and acting on 90 percent of standard original NDA and BLA submissions filed during the fiscal year* within 10 months of receipt, and reviewing and acting on 90 percent of priority applications within 6 months of receipt.

- Based on applications approved by September 30, 2003, the estimated *median approval times for FY 2002 submissions are 7.5 months for priority applications and 12.8 months for standard applications.*

This is a substantial decrease from 15.6 months for priority applications and 22.1 for standard applications in FY 2001. FY 2001 appears to have been a statistical aberration.

- *For 2002, 47 percent of priority applications and 36 percent of standard applications were approved on the first review cycle. This performance was a substantial increase* over FY 2001, when 15 percent of priority applications and 19 percent of standard applications were approved on the first cycle.

This progress was made possible by a number of activities, initiatives, and projects which are detailed below.

Implement the First Cycle Review Initiative – The PDUFA III First Cycle initiative for notification of substantive deficiencies identified during the initial filing review for original NDAs and BLAs was implemented on October 1, 2002. The *goal is to report substantive deficiencies* (or lack of same) identified in the initial filing review to the sponsor within 14 days of the 60 day filing date for original BLAs, NDAs, and Efficacy Supplements. Performance levels progress from *50 percent on time for FY 2003* submissions to 90 percent for FY 2005 to FY 2007 submissions. *As of the end of FY 2003, the Agency met the goal with 84 percent of notifications done on time.*

The draft Good Review Management Principles (GRMP) guidance was published on July 28, 2003. FDA received extensive comments and expects to publish the final GRMP guidance by July 2004.

Retrospective and Prospective Analyses of Applications – *A task order contract was awarded to Booz/Allen/Hamilton on April 30, 2004 to conduct the retrospective and prospective analyses related to the PDUFA III First Cycle Initiative.* The contractor will identify the root causes of multiple cycle reviews and the best practices of FDA and industry for eliminating problems with applications that cause delays. The contractor will evaluate performance for both the First Cycle and CMA initiatives.

Implement the Continuous Marketing Application (CMA) pilot review programs – *Final guidances were published on October 6, 2003, and the pilot programs became effective as of that date.* In CDER, there are seven firms in Pilot two and four in Pilot one. At least two more are in the offing for Pilot one, but have not officially submitted requests to participate. No firms are currently participating with CBER.

Quality Systems for human drug review process – *A request for proposals (RFP) was published on April 21, 2004 to solicit a contractor to implement a quality system for the new drug review process in CDER and CBER.* The contract will provide expert technical assistance to FDA to develop a quality system. FDA expects that the quality system will result in a more efficient and effective review process. Quality systems training will also be provided to senior review managers and review staff.

Independent Consultants – *Draft guidance was published on May 7, 2003*. Final guidance is expected to be published by September 2004.

Postmarketing Initiative – Three concept papers were published in March 2003. Risk management public meetings were held in April 2003. *Draft guidances were published in May 2004.* FDA expects to publish final guidances by September 2004. In FY 2003, CDER was involved in the review of 32 risk management plans and participated in 30 pre-NDA meetings and 11 pre-approval safety conferences. CBER participated in pre-approval safety conferences for two vaccines.

Electronic Applications and Submissions Goals – FDA developed a PDUFA III 5-year IT plan in FY 2003 to meet electronic submission goals. *In FY 2003 FDA published the Electronic Common Technical*

Document (eCTD) guidance, released eCTD specifications, released the initial eCTD software, and has received and is reviewing the initial eCTD submissions.

Collaboration with NCI and other government agencies – In April 2004, FDA clarified for NCI when INDs are required for studies of approved drugs by modifying the "Guidance for Industry: IND Exemptions for Studies of Lawfully marketed Drugs and Biological Products for Treatment of Cancer." Guidance is posted on CDER's website: http://www.fda.gov/cder/guidance/6036fnl.pdf

Communication/Guidance and Meetings

Guidance: In FY 2002, CDER and CBER issued 30 draft guidance documents and 25 final guidance documents. In FY 2003, CDER and CBER issued 44 draft guidance documents and 54 final guidance documents.

Meeting Requests: The PDUFA goal is to notify the requestor of a formal meeting in writing within 14 days of the request 90 percent of the time. In FY 2003, the Agency met this goal 90 percent of the time.

In FY 2003, there were 1,597 meetings with sponsors scheduled in CDER, and 398 meetings scheduled in CBER.

Reviewer Training – Training for reviewers is a high priority. For example, in support of the implementation of the First Cycle and CMA initiatives under PDUFA III and for an introduction to new guidances for the End of Phase 2A Meetings and Drug Dose Exposure-Response relationships, training was offered to all CDER and CBER review staff. In FY 2003, 1,183 employees attended the Agency's training on these topics.

Fast Track Initiative – By 1997, the five-year-old accelerated approval regulations had resulted in about 20 approvals, mostly for AIDS and cancer treatments. In comparison, within its first five years the fast track program led to 200 fast track product development designations and another two dozen approvals. Since 1998 there have been a total of 35 fast track approvals.

12. The following references show the link between our activities and the long term goal.

- **Fast Track Initiative** – Tufts Center for the Study of Drug Development Impact Report; (November/December 2003)
- **Popularity of U.S. Market for First Time Submissions** – CMR International R&D Briefing No. 35; October 2002
- **Effect of FDA Guidance and Advice** – Drug Information Journal, Volume 37, p. 370; 2003
- **Effect of PDUFA on Drug Review Times** – Health Affairs – Perspective, "Explaining Reductions in FDA Drug Review Times: PDUFA Matters by Mary K. Olson, January 30, 2004
- **Effect of Communications/ Guidance and Meetings** – Office of Inspector General Report; "FDA's Review Process for New Drug Applications, A Management Review"; OEI-01-01-00590; March 2003
- **Effect of Training** – GAO-02-058; PDUFA User Fees

FDA Proposed Long-term Outcome Goals for Strategic Goal 1: Using Risk-Based Management Practices

Premarket Approval for New Devices

1. What are the proposed long-term outcome goals? The long-term PART goal is to ***reduce the average time for marketing approval for safe and effective new devices.***

FDA needs to make these improvements to implement MDUFMA successfully. FDA is beginning to implement MDUFMA, and is committed to meeting the ambitious 5-year MDUFMA goals summarized below. Both the PART and the MDUFMA goals assume FDA will get the funding outlined in the statute.

2. What are the proposed targets and the proposed target dates for full accomplishment?

Expedited PMAs

The proposed target calls for a reduction in FDA's total approval time by 30 days for the fastest 50 percent of expedited PMAs approved, using the submission cohort for FY 2005-2007. The baseline for this goal is the three year average of total FDA approval time for the fastest 50 percent approved for the applications filed during FY 1999-2001. The baseline FDA marketing approval time for expedited PMAs is 360 days (see attached chart). MDUFMA's decision goals call for FDA to decide on 90 percent of expedited PMAs within 300 days for applications received in FY 07. In order to achieve this decision goal, and the relevant cycle goals, FDA estimates it would need an average approval time of about 270 days. This will be a stretch with the funding outlined in the statute.

Standard PMAs

The proposed target also calls for a reduction in FDA's total approval time by 30 days for the fastest 50 percent of standard PMAs approved, using the submission cohort for FY 2005-2007. The baseline for this goal is the three year average of total FDA approval time for the fastest 50 percent approved for the applications filed during FY 1999-2001. The baseline FDA marketing approval time for standard PMAs is 320 days (see attached chart). MDUFMA's decision goals commit FDA to decide on 90 percent of standard PMAs within 320 days for applications received in FY 2007. In order to achieve this decision goal and the relevant cycle goals, FDA estimates it would need an average approval time of about 290 days. This is consistent with the long term goal above, and doable with the funding outlined in the statute. But, it will be a stretch. The approval of some key PMAs has been delayed, for example in the cardiac area, because CDRH doesn't have sufficient staff to handle simultaneous reviews that required the same review expertise. MDUFMA resources will be used both for new hires and to expand external expertise.

3. Why is the achievement of this long-term outcome goal important? MDUFMA overall commits FDA to significant improvements in device review performance. This is important overall to the entire device industry, which is expanding in size and technical complexity. The industry is relying on FDA to take a leadership role in regulating a rapidly emerging frontier of medical device technology with timeliness, quality, scientific consistency, and international harmonization. Most of the device industry is small and rapidly changing. Many small and new start-up firms rely heavily on FDA for guidance and outreach, and the reviews take extra FDA time and energy.

- About 25 percent PMAs are for breakthrough technologies; and
- Over 25 percent of PMAs are from first-time submitters.

The area of expedited devices is particularly important because they are the most complex, raise new medical and scientific issues, and FDA often works with first time or small device sponsors. These devices are for uses that haven't been approved yet, and therefore expediting their safe and effective

approval will have great clinical impact. Our expedited program is the area where we have the most improvements to make.

Standard PMAs are also for the most complex (Class III) devices, and also have significant clinical impact For example, a recent drug-eluting cardiac stent could, if used properly, reduce repeat angioplasty of by-pass surgery, by 15-30 percent.

FDA will take steps to improve its device review program by analyzing and taking action to reduce multi-cycle reviews. MDUFMA requires more pre-submission meetings, especially for expedited products. CDRH will use these interactions with sponsors to clarify requirements and improve the quality of applications. FDA is also taking steps to improve the quality of reviews. CDRH will develop an after the fact quality review system to review a sample of reviews to assess the quality of the review and the scientific consistency of the review process and the review decision. This information will be shared with reviewers to improve reviews.

4. How does the long-term goal relate to reducing morbidity or mortality Working with sponsors to reduce product development time and FDA total approval time for expedited devices and standard PMAs by 30 days for applications received in FY 2005-2007 will bring safe and effective expedited devices to market sooner, promoting and protecting public health. FDA will also test ways to assess the clinical impact of the expedited devices approved.

5. What kinds of data already exist? FDA has modified its device review tracking systems to report MDUFMA device categories and decisions.

6. What types of new data sources will be needed? FDA is testing ways to assess the clinical impact of expedited devices at time of approval.

MDUFMA Goals for Expedited Review Original PMA Submissions (These are excerpts from the MDUFMA commitment letter signed by the Secretary.)

1. The following goals apply to PMA submissions where:

    a. FDA has granted the application expedited status;
    b. The applicant has requested and attended a pre-filing review meeting with FDA;
    c. The applicant's manufacturing facilities are prepared for inspection upon submission of the application; and
    d. The application is substantively complete, as defined at the pre-filing review meeting.

2. The following cycle goals apply to:
    FY 2005 – 70 percent of submissions received
    FY 2006 – 80 percent of submissions received
    FY 2007 – 90 percent of submissions received

    a. First action major deficiency letters will issue within 120 days.
    b. All other first action letters (approval, approvable, approvable pending GMP inspection, not approvable, or denial) will issue within 170 days.
    c. Second or later action major deficiency letters will within 100 days.
    d. Amendments containing a complete response to major deficiency or not approvable letters will be acted on within 170 days.

3. FDA decisions:

a. Of submissions received in FY 2005, 70 percent will have an FDA decision in 300 days.
b. Of submissions received in FY 2006, 80 percent will have an FDA decision in 300 days.
c. Of submissions received in FY 2007, 90 percent will have an FDA decision in 300 days.

4. For amendments containing a complete response to an approvable letter received in FYs 2003-2007, 90 percent will be acted on within 30 days.

MDUFMA Goals for Review of Original Premarket Approval (PMA), Panel-PMA Track Supplements, and Premarket Report Submissions

1. The following cycle goals apply to: 75 percent of submissions received in FY 2005; 80 percent of submissions received in FY 2006; 90 percent of submissions received in FY 2007;
   a. First action major deficiency letters will issues within 150 days.
   b. All other first action letters (approval, approvable pending good manufacturing practices (GMP) inspection, not approvable, or denial) will issue within 180 days.
   c. Second or later action major deficiency letters will issue within 120 days.
   d. Amendments containing a complete response to major deficiency or not approvable letters will be acted on within 180 days.

2. Decision Goals:
   a. Of submissions received in FY 2006, 80 percent will have an FDA decision in 320 days.
   b. Of submissions received in FY 2007, 90 percent will have an FDA decision in 320 days.

3. Subject to the following paragraphs, 50 percent of submissions received in FY 2007 will have an FDA decision in 180 days. This goal will be reevaluated following the end of FY 2005. FDA will hold a public meeting to consult with its stakeholders and to determine whether this goal is appropriate for implementation in FY 2007. If FDA determines that the goal is not appropriate, prior to August 1, 2006, the Secretary will send a letter to the Committee on Health, Education, Labor and pensions of the Senate and to the Energy and Commerce Committee, Subcommittee on Health of the House of Representatives stating that the goal will not be implemented and the rationale for its removal.

4. Of amendments containing a complete response to an approvable letter, received in FY 2003-2007, 90 percent will be acted on within 30 days.

— CDRH Original PMA Approval Cohorts —
(As of 16-May-2003)

Expedited

Fiscal Year	Total Filed	Filed Cohort				
		Number Approved	Time to 50 percent Approval		Number With Other Final Action*	Number Pending
			Total FDA Days	Total Elapsed Days		
1999	7	7	382	491	0	0
2000	8	8	341	482	0	0
2001	9	8	358	418	1	0
3 Year Summary	24	23	360 (avg.)	464 (avg.)	1	0

Regular

Fiscal Year	Total Filed	Filed Cohort				
		Number Approved	Time to 50 percent Approval		Number With Other Final Action*	Number Pending
			Total FDA Days	Total Elapsed Days		
1999	48	42	341	372	6	0
2000	60	39	333	399	20	1
2001	58	38	286	327	8	12
3 Year Summary	166	119	320 (avg.)	363 (avg.)	34	13

*****Includes PMAs with a final action other than approval, such as withdrawal, conversion, denial, or other final actions.

How is "**Time to 50 percent Approval**" calculated?

- Separate calculations are performed for expedited PMAs and regular PMAs.
- The first step in calculating "FDA time to 50 percent approval" is to count the number of PMAs filed in a given fiscal year, and divide this number by two. (If the result is not a whole number, it is rounded up to the next highest whole number.) This determines how many PMAs make up 50 percent of the filed cohort.
- Next, the approved PMAs in the cohort are ranked in ascending order based on each application's total elapsed time from filing to approval. The "fastest 50 percent" of the cohort is identified from the ranked list of approved PMAs by selecting applications representing 50 percent of the filed cohort (i.e., the number of PMAs determined in the previous step), starting with the application having the lowest total elapsed time to approval.
- The PMA with the highest FDA review time is identified from the PMAs that represent the "fastest 50 percent" of the filed cohort. This FDA review time is the "FDA time to 50 percent approval" for the filed cohort.

7. What measurable progress have we made toward this goal?

Last year CDRH calculated the baseline data for this goal, time to approval for the fastest fifty percent of expedited PMAs, for the time period of FY 1999 – 2001. This year CDRH has calculated the time to approval for the fastest fifty percent for the time period FY 2000 – 2002. The results are

provided in the following table. Please note that when this long-term goal was created it was based on a specific resource allocation. *Although the full allocation was not realized, the Center was able to decrease the average review time of the fastest fifty percent for expedited PMAs by 33 days versus the FY 2005 –2007 target of 30 days.*

— CDRH Original PMA Approval Cohorts —
Expedited

Fiscal Year	Total Filed	Filed Cohort				
		Number Approved	Time to 50 percent Approval		Number With Other Final Action*	Number Pending
			Total FDA Days	Total Elapsed Days		
2000	8	8	341	482	0	0
2001	9	8	358	418	1	0
2002	9	7	282	306	1	1
3-Year Summary (2000 – 2002)	**26**	**23**	**327 (avg.)**	**402 (avg.)**	**2**	**1**
Previous 3-Year Summary (1999 – 2001)	24	23	360 (avg.)	464 (avg.)	1	0

- Last year CDRH calculated the baseline data for this goal, time to approval for the fastest fifty percent regular PMAs, for the time period of FY 1999 – 2001. This year CDRH has calculated the time to approval for the fastest fifty percent for the time period FY 2000 – 2002. The results are provided in the following tables. Please note that when this long-term goal was created it was based on a specific resource allocation. Last year those resources were not allocated as expected. To compensate, resources were moved into expedited products since they are the most important in terms of public health impact. *The result of moving resources into expedited PMA review adversely affected the review time for regular PMAs increasing average review time to 18 days.* Full results are reported on in the following table.

Regular

Fiscal Year	Total Filed	Filed Cohort				
		Number Approved	Time to 50 percent Approval		Number With Other Final Action*	Number Pending
			Total FDA Days	Total Elapsed Days		
2000	60	39	333	399	20	1
2001	58	38	286	327	8	12
2002	32	20	395	427	3	9
3-Year Summary (2000 – 2002)	**150**	**97**	**338 (avg.)**	**384 (avg.)**	**31**	**22**
Previous 3-Year Summary (1999 – 2001)	166	119	320 (avg.)	363 (avg.)	34	13

*****Includes PMAs with a final action other than approval, such as withdrawal, conversion, denial, or other final actions.

It is important to remember that the decrease in approval time of the fastest 50 percent of expedited PMAs is not the result of a single event, rather the decrease is the product of several initiatives CDRH is undertaking in an effort to meet the long-term outcome goal's target. The accomplishments of these initiatives include:

- CDRH met all of the Center's performance targets for Device review in FY 2003.
- Eleven guidances were published in FY 2003 and 3 guidances were published in the first quarter of FY 2004.

- There were 18 completed hires as of February 21, 2004. (MDUFMA FY 2004 1st Qtr. Report)

- CBER has substantially (approximately 25 percent) increased device related effort in the last year -In addition to increased device effort from employees, new hiring has allowed recruitment of individuals with specialized experience/expertise and diverse backgrounds. (MDUFMA FY 2004 1st Qtr. Report)

- Forty three (43) professionals participated in the CDRH Medical Device Fellowship Program. (MDUFMA FY 2004 1st Qtr. Report)

- Instituted quality system initiatives involving peer review and balanced scorecard. To help FDA reviewers keep up with the latest relevant developments, to provide high quality safety review, to improve efficiency, and to attract and retain the best possible scientific talent, FDA is committed to the implementation of a continuous learning/ quality systems approach to medical product reviews. This is needed to address inconsistencies in the review process; a lack of consensus on what constitutes "quality review"; opportunities to provide training for review staff and review managers; institution of peer review of the review process and content, and support for rigorous scientific review through better analytic tools.

[5] Mitchell JB et al. Impact of the Oregon Health Plan on access and satisfaction of adults with low income. Health Serv Res 2002 Feb;(37(1):33-42.

Goals for Strategic Goal 1: Using Risk-Based Management Practices

Marketing Approval for Generic Drugs

1. What is the proposed long-term outcome goal? The goal is to ***reduce the average time to marketing approval or tentative approval for safe and effective new generic drugs.***

2-3. What are the proposed targets and the proposed date for full accomplishment? The proposed target calls for a reduction in average FDA time to approval or tentative approval by 1.5 months for the fastest 70 percent of original generic drug applications approved or tentatively approved of those submitted using the three year submission cohort for FY 2005 - 2007.

The baseline used for this goal is the average FDA time to approval or tentative approval for the fastest 70 percent of applications approved for the FY 1998 - 2000 submission cohort. The table below provides the analysis of current approval time statistics, and shows that the mean and median times have remained relatively flat for the 60 percent and 70 percent approval cohorts. Using the mean for the fastest 70 percent approved cohort yields a baseline average of 17.9 months to FDA marketing approval or tentative approval.

Approval Time Statistics
Based on Fastest XX% Approval Times
Fiscal Years 1998-2000

		<-----50%------>			<-----60%------>			<-----70%----->		
Year	**Subs Appd**	**n**	**mean**	**median**	**n**	**mean**	**median**	**n**	**mean**	**median**
1998	320 264	160	14.3	14.0	192	15.8	15.3	224	17.6	16.9
1999	316 244	158	15.5	16.0	189	17.2	16.9	221	19.4	17.7
2000	313 250	156	13.9	14.3	187	15.2	15.7	219	16.8	16.8
1998-2000	**949 758**	**474**	**14.6**		**568**	**16.1**		**664**	**17.9**	

On an intermediate basis, FDA will track and analyze time to approval and look at a rolling three year average for the fastest 70 percent of original generic drug applications approved for the interim years, and the Agency will track the timeliness of implementation of a variety of program activities intended to improve the quality and efficiency of FDA review and interactions with sponsors, and to improve the quality of applications submitted by sponsors. These factors are expected to impact the time to marketing approval or tentative approval. The target cohort FY 2005 - 2007 submissions is chosen because the Agency expects to see a return on these efforts by that point in the future.

4. What FDA Centers are covered by this goal? CDER and ORA

The baseline and target both consist of a three year cohort of original generic drug application submissions using the fastest 70 percent approved per year.

How are FDA activities linked to achievement of this goal?

FDA will achieve this goal through enhancements to the generic review program made with increased resources to speed generic drug application review. In FY 2003, FDA received a $5.3 million increase to improve review times for product applications within six months and decrease the median time to full approval on generic drug applications. FDA will do this by using the resources to:

- Hire additional reviewers and staff that support the Office of Generic Drugs to accelerate the review and approval of Abbreviated New Drug Applications-ANDAs.
- Make technology upgrades needed to meet the expected increase in generic drug applications.
- Hire additional inspectors to increase inspections of domestic and foreign firms by 15 percent, and provide for team inspections, with both a reviewer and inspector, to increase efficiency.

This will allow the Agency to set a more challenging goal of reviewing 85 percent of ANDAs within 6 months after submission, and increase inspectional coverage of imported generic drugs by 10 percent so that FDA can better monitor the quality of finished drug products and bulk drug substances entering the U.S. from overseas in FY 2004. Activities for FY 2004 include:

- Some efforts to develop manufacturing monographs and methods for demonstration of bioequivalence, so that generic drug products can be developed in additional product areas e.g., for topical and inhalation dosage forms and complex drugs.
- A few additional staff were hired to complete review and action on 85 percent or better of original applications within 180 days and decrease the median time to full approval.
- Hire more field investigators for inspections of generic manufacturing firms to allow for faster action on generic drug applications.
- Some efforts to enhance Office of Generic Drugs IT capabilities to support electronic submissions for generic drug applications and expansion of electronic review efforts.

In addition to the review process changes, on December 8, 2003, the President signed as part of the Medicaid Bill the “Access to Affordable Pharmaceuticals Act” which limits the number of 30-month stays of approval that can be imposed upon the ANDA. FDA’s new rule regarding 30-month stays was superceded by the Act. However, FDA’s revisions to the patent listing process will remain and should decrease the number of patents that are submitted to FDA for listing which may result in an overall decrease in the time to effective approval for ANDAs. The Act was signed on December 8, 2003 and applies to ANDAs pending as of August 18, 2003

- FDA's proposal and the Act should speed generic drugs to market, achieving billions of dollars of savings for American consumers. When implemented, consumers should save approximately $35 billion over ten years.

- Specifically, the Act permits, in most instances, one thirty-month stay per generic drug application for patents that were listed at the time the ANDA was submitted if the ANDA applicant challenges the validity or states it does not infringe the patents. FDA’s rule, clarifies that certain patents can't be listed, and beefs up the declaration innovators must make about the patents they submit to FDA for listing in the Orange Book.

- Currently, FDA regulations allow multiple and successive 30-month stays on each application. Under the Act FDA will impose one 30-month stay per Abbreviated New Drug Application. However, there may be some instances when more than one 30 month stay will be applicable. One 30-month stay will speed up approval of applications for generic drugs.

- The rule clarifies that certain types of patents may not be submitted to FDA for listing in its "Orange Book."

- The rule strengthens the signed declaration accompanying the patent submissions to cut down on patents that should not be listed in the Orange Book. The detailed declaration would ensure that the listing is appropriate from the "face" of the declaration without FDA having to review the patent.

- The rule was published on June 18, 2003 and was effective on August 18, 2003.

8. Why is achievement of this long-term outcome goal important? FDA achievement of this goal will create earlier access to lower cost drug alternatives for patients. The high cost of drugs limits patient access to treatment. The lower income and uninsured populations are particularly affected.[5,6] Research has shown that 42 percent of the uninsured do not fill prescriptions because of financial reasons. While all state Medicaid programs provide outpatient prescription drug coverage, slightly more than one in four Medicaid patients ages 18-64 could not afford to fill at least one prescription, according to a study by the Center for Studying Health System Change (HSC). Increasing the availability of generic drugs will make many important treatments more affordable to the poor and the elderly and significantly improve access to treatment.

Prescription drug expenditures remain one of fastest-growing segments of the U.S. health care system. In 2001, a 13.8 percent increase in drug spending accounted for one-fifth of the overall increase in health care spending. State Medicaid programs are particularly challenged with controlling escalating cost of pharmacy benefits and are in serious need of more generic alternatives to high cost brand name drugs to both reduce costs and increase access to treatment. Medicaid spending on outpatient drugs has increased by 18 percent a year from 1997 - 2000, which is close to three times greater than increases in medical care spending.[7]

Optimal access and use of generic drugs will enable policy decision makers to contain costs in both the Medicare and Medicaid programs. This will only become more important as more of the top selling brand name drugs go off patent over the next few years and if legislation for a Medicare drug benefit is passed by Congress. The National Institute for Healthcare Management has estimated that Medicaid programs could save $1 to $1.5 billion over the next few years if they were to increase their share of generic drug use to 55 percent of their total drug spending. According to researchers at Brandeis University, if a Medicare drug benefit were to be implemented and the use of generic drugs represented 50 percent of the total prescriptions, approximately $250 billion would be saved over 10 years.[8]

Generic drugs are typically priced between 20 – 50 percent lower than brand name competitors, which represent a significant cost saving to consumers.

9. How does this long-term outcome goal relate to achieving ultimate outcomes of reducing mortality and morbidity? Greater access to generic drug alternatives will have a positive impact on public health, both on direct outcomes and more cost-effective allocation of health care resources. Research has shown that when patients have to spend more out-of-pocket on prescription drugs, they decrease their use of essential drugs and cost the health care system more by increasing use of other services. One study showed that elderly and welfare recipients reduced their use of essential drugs following a policy that required them to spend more on prescription drugs. This resulted in a significant increase in serious adverse events associated with poor disease control and an increase in emergency room visits.[9]

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[6] Stuart B, Grana J. Ability ot pay and the decision to medicate. Med Care 1998 Feb;36(2):202-11.

[7] A Primer: Generic Drugs, Patents, and the Pharmaceutical Marketplace. National Institute for Health Care Management Research and Educational Foundation, June 2002.

[8] Greater Use of Generics: A Prescription for Drug Cost Savings. The Schneider Institute for Health Policy, Brandeis University, January 2002.

[9] Tamblyn R et al. Adverse events associated with prescription drug cost-sharing among poor and elderly persons. JAMA. 2002 May 9;285(4):421-9.

Drug prices also have a substantial effect on the amount of health that can be purchased with a certain budget, especially among elderly people with several health conditions. For example, $1 million spent on a generic statin yields 90 years of life for patients aged 75 to 84 with a history of myocardial infarction, assuming the cost of a generic statin is 40 percent below the average wholesale price (AWP) of a brand name statin. At the AWP of the brand name statin, the number of life-years for $1 million spent results in 48 years of life.[10]

7. What types of data already exist for measuring this long-term outcome goal? FDA maintains a tracking system for generic drug applications and FDA review times; this data will be used to measure the accomplishment of the long-term goal. Because there is a delay from the time of submission to approval of 70 percent of the submission cohort, the Agency anticipates that the data will be available to evaluate performance for these long-term goals in FY 2009.

8. What types of new data sources would be needed to measure progress on this long-term outcome goal? Progress toward achievement of the goal will be tracked through existing review tracking and enhancements associated with the activities outlined above.

9. Why is this target a stretch? Whether or not a product can be approved in a shorter time period depends on whether the application contains sufficient, scientifically valid information on safety and effectiveness to meet the Agency's standards for approval.

As deficiencies are noted during the review of an application, the Agency attempts to work with the company to address these deficiencies. FDA believes that reducing deficiencies to a minimum prior to application submission would result in the most efficient use of Agency and company resources and would facilitate getting scientifically-substantiated, well-manufactured products to patients as quickly as possible.

The Agency cannot guarantee that sponsors will follow FDA guidances or advice, or respond quickly and completely to noted deficiencies. Achieving this goal requires not only that FDA improve its own performance, and work more efficiently and effectively, but essentially work to improve the performance of the drug sponsors as well. Achievement of the goal is also impacted by the rate of submission of new applications for review by the Office of Generic Drugs which has been increasing.

Achieving this goal will effectively shift the approval cohort so that average time to approval for 70 percent of the submission cohort in FY 2005 - 2007 will be accomplished in basically the same time frame achieved today for only 50 percent of the submission cohort.

10. How does this target serve Department priorities? This FDA goal supports the DHHS priorities of preventing disease and illness and promoting positive life styles, increasing access to health services, improving the quality of care and closing the health disparities gap by making available more affordable therapy alternatives.

11. What measurable progress have we made toward this goal?

Last year CDER calculated the baseline data for this goal, time to approval for the fastest seventy percent of applications approved for FY 1998 – 2000. This year CDER has calculated the time to approval for the fastest seventy percent for the time period FY 1999 – 2001. *The results, provided in the following table, show that the mean approval time for the fastest 70 percent of applications reviewed was reduced by 0.2 months.*

[10] Russell LB, Wolff N. The impact of drug pricing policies on the health of the elderly. Am J Prev Med 2002; Apr(3):151-5.

Long Term Outcome Goals

Approval Time Statistics
Based on Fastest 70 Percent Approval Times

Fiscal Years 1998 - 2003

(As of March 31, 2004)

Year	Sub-missions	Currently Approved	First 50% Approved			First 60% Approved			First 70% Approved		
			N	Mean	Median	N	Mean	Median	N	Mean	median
1998	320	264	160	14.3	14.0	192	15.8	15.3	224	17.6	16.9
1999	316	244	158	15.5	16.0	189	17.2	16.9	221	19.4	17.7
2000	313	250	156	13.9	14.3	187	15.2	15.7	219	16.8	16.8
2001	298	221	149	13.3	13.2	178	14.8	14.5	208	16.7	15.9
2002	339	221	169	12.4	11.9	203	13.8	13.5			
2003	425	96									
1998-2000	949	758	474	14.6		568	16.1		664	17.9	
1999-2001	**927**	**715**	**463**	**14.3**		**554**	**15.8**		**648**	**17.7**	

Performance Goals

- FDA exceeded its goal for FY 2003 acting on 90 percent of original applications.
  - The office has engaged in several activities to refine the overall review process to assist in dealing with the record numbers of applications submitted and approving products more rapidly.
  - Reviewers are increasing their use of the telephone to clarify points such as location of data, typographical errors, etc., in applications to allow more timely completion of reviews.
  - Some recommendations from a consultant hired in 2003 to do process mapping are being incorporated into the review process. For example, several recommendations involved more extensive use of Project Managers in the chemistry review process. Procedures have been developed to change the process.

- Increased staff:
  - Director of Science, several chemistry reviewers and managers, a Medical Officer, and regulatory management officers have been hired.
  - Compliance and legal support to the Office of Generic Drugs (OGD) was expanded. The increased staff was critical in reducing review times for ANDAs/ generic drug applications and granting approval as quickly as possible.
  - For further details see Marking Approval for Generic Drugs Update and Appendix A of the Performance Plan.

- Research conducted:
  - A contract has been let in April of 2004 for a Phase II study on the development of system to assess the therapeutic equivalence of topical products.
  - Also in April of 2004, a contract has been let to investigate novel clinical methods for bioequivalence studies of inhaled corticosteroids.

  - For further details see Marking Approval for Generic Drugs Update and Appendix A of the Performance Plan.

- Technology upgrades:
  - OGD continues to provide PC hardware enhancements to support for electronic submissions (e.g., dual monitors).
  - OGD is included in the current development of the electronic Common Technical Document (CTD) review tool and provided training to industry on the CTD in a workshop in April of 2004.
  - For further details see Marking Approval for Generic Drugs Update and Appendix A of the Performance Plan.

Quality Systems
To help FDA reviewers keep up with the latest relevant developments in the biomedical, statistical, and risk assessment sciences, to provide the highest quality of safety review, to continue to improve efficiency in its operations, and to attract and retain the best possible scientific talent, FDA is committed to the full implementation of a continuous learning/ quality systems approach to medical product reviews. This is needed to address identified and potential inconsistencies in the review process within review organizations and across review organizations; a lack of consensus among expert reviewers on what constitutes "quality review"; opportunities to provide better and more relevant training for review staff and review managers; institution of peer review of the review process and content, and better support for rigorous scientific review through better analytic tools.

Advanced scientific education
- The program grew from seven activities offered in 1997 to more than 40 in science and science policy.
- We offer 44 courses in job skills, research tools, leadership and management.
- All CDER reviewer participants, including generics reviewers, increased six-fold, from about 250 in 1997 to 1,500 currently.

Long-term Outcome Goals for Strategic Goal 2: Empowering Consumers for Better Health

Increase Consumer Understanding of Diet-Disease Relationships

1. What is the proposed long-term outcome goal? The goal is to ***increase consumer understanding of diet-disease relationships, and in particular, the relationships between dietary fats and the risk of coronary heart disease (CHD), the leading cause of death in the U.S. and one that disproportionately affects African-Americans and Hispanics.***

2. What are the proposed targets and the proposed date for full accomplishment? The proposed target for this goal calls for the following:

- Between 2004 and 2007, FDA will increase, by 40 percent, the percentage of American consumers who correctly identify that trans fat increases the risk of heart disease.

- Between 2004 and 2007, FDA will increase, by 10 percent, the percentage of American consumers who correctly identify that saturated fat increases the risk of heart disease.

- Between 2004 and 2007, FDA will increase, by 10 percent, the percentage of American consumers who correctly identify that omega-3 fat is a possible factor in reducing the risk of heart disease.

Little data are available at present to provide baseline information that clearly demonstrates the current levels of consumer understanding of the relationship between the risk of coronary heart disease (CHD) and consumption of saturated, trans, and omega-3 fats[17]. FDA proposes to develop baseline performance indicators of consumer understanding of the relationships between saturated fat, trans fat, and omega-3 fat). The baseline indicators will come from a near-term nationally representative telephone survey in 2004. The performance indicators will be obtained again in 2007 via the periodic Health and Diet Survey (HDS) conducted by FDA. By comparing the 2004 and 2007 indicators, FDA will be able to identify and measure an incremental improvement in consumer understanding,

3. Which FDA Centers are covered by this long-term goal? CFSAN has responsibility for food labeling and is most directly involved in achieving this goal.

4. Why is achievement of this long-term outcome goal important? CHD is the leading cause of death among Americans, accounting for more than 1 in 5 deaths annually. CHD is also the leading cause of premature, permanent disability in the labor force. Dietary factors, especially fats, play a significant role in CHD risk.

5. How does this long-term outcome goal relate to achieving ultimate outcomes of reducing mortality and morbidity? One modifiable factor that is important for reducing mortality and morbidity associated with heart disease is consumer understanding of the consequences of dietary choices with respect to CHD. Increased understanding will strengthen motivation to adopt and to maintain recommended healthy dietary behavior and to make informed dietary choices.

6. What types of data already exist for measuring this long-term outcome goal? CFSAN has collected data on consumer understanding of diet-health relationships for more than a decade as part of its

HDS. The HDS is a random-digit-dialing telephone survey of nationally representative samples of English speaking non-institutionalized adult Americans.[18]

The only data that already exist for measuring the long-term outcome goal come from consumer responses to a pair of questions in the 2002 HDS. The first question specifically asks consumers about awareness of trans fat:

Q: Have you heard of trans fatty acids, also called trans fat?

There is a follow-up question to this question concerning the relationship between trans fat and blood cholesterol:

Q: Do trans fatty acids raise blood cholesterol, lower blood cholesterol or have no effect on blood cholesterol?

The responses to these questions in 2002 indicated that only 34 percent (+/- 1.8 percent) of Americans had heard of trans fats; of that 34 percent, only 37 percent (+/- 2.9 percent) (i.e., 13 percent of all Americans) were able to correctly identify that trans fatty acids raise blood cholesterol.

The 2002 HDS provides a less clear picture concerning saturated fat, because of the wording of the questions. The response to the question "have you heard about different kinds of fat, like saturated fat and polyunsaturated fat" suggested 88 percent (+/- 1.2 percent) of Americans had heard of these fats. A follow-up question further suggested that, between saturated and polyunsaturated fats, 59 percent (+/- 2 percent**)** of the Americans thought saturated fat is "more likely" to raise blood cholesterol, 5 percent (+/- 0.9 percent**)** polyunsaturated is "more likely," and 24 percent (+/- 1.7 percent**)** both are likely.[19] However, because both saturated and polyunsaturated fats are mentioned in these questions, it is more difficult to generate comparable information on saturated fat as on trans fat.

There are no specific questions on omega-3 fat in the 2002 HDS. Thus, with the exception of the questions on trans fatty acids, there are no data that can be used as a baseline for the purposes of this exercise, i.e., for saturated fat and Omega 3 fatty acids.

7. What types of new data sources would be needed to measure progress on this long-term outcome goal? FDA needs to conduct a near-term survey in 2004 to establish baseline indicators. The indicators will be developed from consumer responses to a series of questions on the respective fat-cholesterol relationships. The questions asked about each fat will mirror the existing questions on trans fat in the 2002 HDS. Answers to these questions should be available in late 2004.

[17]We are discussing further the possibility of including in the survey instrument questions about mono- and polyunsaturated fats. The substantive reason to include these questions is to give FDA an understanding about consumer knowledge of the role of mono- and polyunsaturated fats in heart-healthy diets. In the absence of understanding of the beneficial effects of mono- and polyunsaturated fats, consumers only know to eat less trans and saturated fats. How such understanding would improve their diet is a matter of conjecture. Although there is currently no mandatory FDA labeling or specific educational action concerning mono- and polyunsaturated fats, FDA regulations require declaration of saturated fat in nutrition labels, and a recent final rule allows for the declaration of trans fat now, making it mandatory by January 1, 2006. Levels of omega-3 fatty acids may not be included in nutrition labeling, but may be stated outside the Nutrition Facts box.

[18] As is typical with telephone surveys, the response rates have been declining and are now 40.8 percent. FDA and OMB worked together to develop a series of measures used by FDA to maximize the response rate for the 2002 HDS.

[19] The follow-up question asks "which kind of fat is more likely to raise people's blood cholesterol level, saturated fat, polyunsaturated fat, both, or neither?"

8. Why is this target a stretch? FDA anticipates a reasonable gain in the percentage of consumers who correctly identify that trans fat increases blood cholesterol, in light of the new rulemaking and ANPR. With saturated fat, the gain will be more modest because consumer awareness of the saturated fat-cholesterol relationship is already relatively high; increasing this awareness will depend in part on preventing consumers' confusion about saturated fat following the new trans fat rulemaking and ANPR. Consumer groups have raised concerns, based on limited data, that when consumers are informed about the health risks associated with trans fats, they may come to think trans fats pose a greater risk than saturated fats, which are more prevalent in U.S. diets and are also unhealthy. In addition, there are multiple public and private sources of nutrition information; these sources may have different priorities for consumer nutrition education in competition with FDA. FDA also anticipates a modest gain in the number of consumers who correctly identify that omega 3 fats are a possible factor in reducing blood cholesterol. Increases in consumer awareness will result in part from industry's adoption of the voluntary FDA qualified health claim for omega 3. This gain will be limited because the qualified claim for omega 3 will appear on a relatively small number of foods.

9. How does this target serve Department priorities and goals? The target is directly in line with several of the Department's priorities and strategic goals. First, improving the American diet through informed choice about fats that increase or reduce the risk of heart disease is one of several important steps toward reducing the enormous morbidity and mortality burden of CHD. This burden is borne disproportionately by minority populations, including African-Americans, Hispanics, and Native Americans. As the leading cause of death and a significant cause of illness and disability, CHD also imposes substantial costs on the U.S. health care system.

10. What measurable progress have we made toward this goal?

Obtaining Baseline Measures

A primary and critical initial action is to obtain baseline indicators against which we can measure our progress toward achieving the long-term goal. While we have years' worth of periodic survey data about consumers' understanding of the relationship between saturated fats and health, we do not have consumer data concerning the specific fats-cardiovascular health relationship.

- To collect these more specific baseline data, we have drafted a random-digit-dial telephone survey that measures consumers' awareness of trans, saturated, and omega-3 fatty acids and knowledge about their relationships with cardiovascular disease. This will survey a nationally representative sample of English-speaking non-institutionalized adult Americans.

  - FDA received OMB clearance to conduct this survey in September, 2004. Consequently, we are on track to have the survey results available by the end of 2004 or beginning of 2005.

  - This will provide us with data about consumers' specific perceptions from 2004. However, these data will already be affected by Agency actions taken in 2003 - 2004. We also have some data from a 2002 national survey that we hypothesize will run parallel to the 2004 data and will provide an earlier baseline measure.

Improving Nutritional Information in Labeling

Regulatory Framework. In July 2003, FDA issued the Task Force report "Consumer Health Information for Better Nutrition Initiative" (CHIBN). This report provides an overall draft regulatory framework that we expect will contribute to achieving the long-term goal by optimizing information on food labeling regarding the value of a food's nutrients in improving cardiovascular health. Specifically, this framework

expands the range of allowable statements on labeling about the benefits of specific nutrients, by permitting claims even when the evidence is not conclusive. The framework is consistent with FDA's decision in February 2002, to accept a qualified claim about the relationship between omega-3 fats and cardiovascular disease: "Consumption of omega-3 fatty acids may reduce the risk of coronary heart disease. FDA evaluated the data and determined that, although there is scientific evidence supporting the claim, the evidence is not conclusive."

As part of the Task Force report, FDA described a consumer studies research agenda to provide guidance to FDA and industry about consumers' understanding of qualified claims and how to optimize the communication effectiveness and wording disclaimers about the level of scientific evidence supporting a claim.

Rulemaking. In July 2003, in addition to issuing the CHIBN Task Force report discussed above, FDA took the following actions.

- Published a final rule requiring, by January 1, 2006, that manufacturers list trans fat content on their products' Nutrition Facts Panels (NFP) for foods, and also on relevant Supplement Facts Panels (July 11, 2003).

- Published an advance notice of proposed rule-making (July 11, 2003) asking for comments and data to inform decisions on whether to establish additional food label requirements
  - about trans fat content, both alone and in conjunction with saturated fat information; and
  - about claims to enhance consumer understanding and use of labeled information to make healthy food choices.

Consumer Research. As planned in the CHIBN Task Force report, FDA is in the process of examining consumer perceptions about qualified health claims and how best to present these to optimize consumer understanding.

- FDA is in the process of analyzing and interpreting the data from an experiment that examined consumer perceptions of formats for displaying qualified health claims. These data, along with data from private sector research are being prepared for internal dissemination to guide decision-making concerning the interim framework set up in the CHIBN report.

- FDA has also obtained OMB clearance for two experimental consumer studies to evaluate selected options for labeling statements on consumers' abilities to understand and use trans fat information and claims on foods' NFP and on other parts of the food label. We expect to begin data collection for these studies starting in November 2004. The results from these 2 studies will be used to guide disclosure requirements in future rulemaking concerning trans and saturated fats disclosures.

- The results from all 3 of these studies will help FDA improve its development of nutritional information and optimize the understandability of food labeling for usefully and accurately communicating product benefits and risks.

Educational Activities. FDA has already engaged, and plans to continue engaging, in directed activities to educate the public on the dangers of trans and saturated fats, and to encourage manufacturers to provide qualified claims regarding the value of omega-3 fats in possibly reducing the risk of heart disease. In this vein, FDA has done the following.

Long Term Outcome Goals

- Extensively publicized its July 2003 Trans Fat final rule issuance and Task Force Report through an HHS News Release and other press activities. By doing so, FDA precipitated extensive front page and health section newspaper coverage.

  - **The message that often-hidden trans fatty acids in foods contribute to heart disease risk** was reported in the *Associated Press* and across the country in major papers like the *Washington Post, USA Today, NY Times, Wall Street Journal, Boston Globe, LA Times,* and *San Francisco Chronicle*. It also appeared in the *Detroit News, Detroit Free Press, News Observer (Warsaw, NC),* the *Tennessean,* the *Orlando Sentinel,* and the *Houston Chronicle*. Altogether, FDA's Clipping service, which looks for mentions of FDA only, in the time period from July 9-23 identified 27 articles concerning the trans fat final rule.

  - Another 8 articles focused on **FDA's framework for allowing qualified health claims**; these appeared in the *Associated Press, Washington Post, NY Times, Wall Street Journal, USA Today, Reuters, LA Times,* and *Detroit Free Press*.

  - Other coverage that did not mention FDA or was only in very small media outlets is likely to have been missed. Further, we are unable to assess radio and television coverage.

- Established an FDA web site that highlights and provides extensive information about these regulatory actions and proposals: http://www.fda.gov/oc/initiatives/transfat/. The site includes the press release and FDA backgrounder; information for consumers, examples of food labels with trans fat information, extensive Questions and Answers on trans fats and the regulation, and a trans fat radio spot and transcript. **Since July 2003, the home page for this site has received at least 60,000 visits. During this same time period, the Qs & As page (which can be reached through different paths) has received almost 82,000 visits.**

- Established an FDA/CFSAN web site article to show consumers in graphic format what the new label will look like, to provide educational information about trans and other fats, and how to use the label to make heart-healthy food choices. Since debuting in mid-January, this web document (http://www.cfsan.fda.gov/~dms/transfat.html) **has received over 36,000 visits**. Notification of the availability of this article was publicized in FDA's *Dietary Supplement/Food Labeling Electronic Newsletter*, which has between 14,000 and 15,000 subscribers.

- Published an article on trans fats in the September/October 2003 issue of the *FDA Consumer*. Also provided the article on FDA's web site: http://www.cfsan.fda.gov/~dms/fdatrans.html. Between subscriptions to the print magazine and visits to the FDA web page with this article, **more than 25,000 people were exposed to this information**.

- Published an article on trans fats in the Winter 2004 "*FDA and YOU*" newsletter. In the third week in April 2004, 62,000 postcards were sent to health educators publicizing *FDA and YOU*, and sending them to FDA's web site, where the Winter issue is the first issue they would see. Currently, FDA directly notifies 500 people when an issue is published, but expects to be expanding that number.

- Also produced an FDA "Patient Safety News" video webcast, designed for health care professionals, that addresses the new rules (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/psn/transcript.cfm?show=19#10). As medical product-focused outlets, the webcast and newsletter channels are designed to reach different audiences than those likely to be reached through normal "food-related" channels.

- Provided FDA field Public Affairs Specialists (PASs) with a slide show, script, and related educational materials about the new trans fat labeling requirements to help them reach their stakeholders. The PASs report use of the slide show and/or trans fat materials at a multitude of meetings, ranging from small groups of dietitians and food science students, bakers, high school and college students, drug rehabilitation attendees, Girl Scouts, community leaders, legislators, diabetics, native Americans, Mexicans, and Latinos to larger groups of company employees and at national meetings. The number of people exposed in this face-to-face interactive manner adds up to the thousands.

Long-term Outcome Goals for Strategic Goal 3: Patient and Consumer Protection

Reducing Adverse Drug Events

1. What is the proposed long-term outcome goal? ***By 2008, FDA will aim for an 11 percent reduction in adverse drug events related to medication dispensing and administration errors in 50 percent of hospitals in the U.S. by requiring bar codes on drugs and biologics used in hospitals which will increase the uptake and use of bar code scanners in hospitals.***

2. What are the proposed targets and date for full accomplishment? By 2008, reduce adverse drug events related to medication dispensing and administration errors by 11 percent in 50 percent of hospitals, as measured by bar code scanner adoption in the hospital marketplace.

3. Which FDA Centers are covered by this long-term goal? In an effort to improve patient safety in the hospital setting by reducing medication errors, the Food and Drug Administration (FDA) has published a proposed rule titled, Bar Code Label Requirements for Human Drug Products and Blood. FDA's regulation proposes to require bar codes on prescription drugs, over-the-counter drugs packaged for hospital use, vaccines, blood, and blood components. Therefore, this goal pertains to CDER and CBER, since they both regulate products impacted by the bar code rule.

4. Why is achievement of this long-term outcome goal important? In November 1999, the Institute of Medicine released a report estimating that as many as 98,000 patients die from medical errors in hospitals alone. Many of these deaths, as well as additional non-fatal illnesses, are associated with errors involving FDA regulated medical products, especially medications. A significant percentage of drug related mortality and morbidity results from errors that are preventable. In addition to their human cost, these errors impose significant economic costs on the U.S. health care system.

The Secretary of Health and Human Services has directed FDA to promulgate the bar coding regulation to reduce preventable errors from medical products. This rule is anticipated to enable the uptake and use of bar code scanners that will allow a health professional to compare the bar code on a human drug product to a specific patient's drug regimen and then verify that the right patient is receiving the right drug, at the right dose, via the right route, at the right time. Research to date has demonstrated the ability of bar code scanners at the point of care to intercept errors in dispensing and administration of medication and prevent related adverse events. The implementation of this rule will be a big step forward for FDA in improving patient safety. The total cost of preventable adverse events has been estimated at $17 Billion.[20] Preventing 11 percent of adverse drug events related to medication errors in half of all the hospitals in the U.S. will significantly reduce the related morbidity, mortality and health care costs.

5. How does this long-term outcome goal relate to achieving ultimate outcomes of reducing mortality and morbidity? Adverse drug events (ADEs) result in more than 770,000 injuries and deaths each year and cost up to $5.6 million per hospital.[21,22,23] Over 7,000 died from medication errors in 1993

[20] The Institute of Medicine report: *To Err is Human, Building a Safer Health System.*

[21] Bates DW, Spell N, Cullen DJ, et al. The costs of adverse drug events in hospitalized patients. *JAMA* 1997;277(4):307-11.

[22] Bates DW, Cullen DJ, Laird N, et al. Incidence of adverse drug events and potential adverse drug events. *JAMA* 1995;274(1):29-34.

[23] Raschke RA, Collihare B, Wunderlich TA, et al. A computer alert system to prevent injury from adverse drug events. *JAMA* 1998;280(15):1317-20.

alone as evidenced by a review of U.S. death certificates.[24] Although the incidence of ADEs and their effect on costs have been investigated in only a few hospitals in the United States, the implications are clear from published results that ADEs constitute a widespread problem that causes injuries to patients and disproportionately increases expenses. On average, ADEs increase the length of stay by as much as 4.6 days and increase costs up to $4,685 per patient.[25]

About 45 percent of the ADEs are caused by errors that occur in dispensing or administering pharmaceuticals. According to published reports and consultants, bar code point of care systems have interception rates of between 20 and 80 percent (current interception rates are between 0.3 and 4.5 percent). We expect that 50 percent of currently unintercepted dispensing and administration errors will be identified with a bar code system. FDA estimates that the bar code rule, once implemented, will enable the adoption and use of bar coding scanners at the point of care and result in 413,000 fewer adverse events over the next 20 years.

6. What types of data already exist for measuring this long-term outcome goal? The American Society for Health Systems Pharmacists conducts a national survey of pharmacy practice in acute care settings that pertain to drug dispensing and administration practices which also captures point of care systems such as bar coding scanners. The 1999 survey was the basis for the impact analysis for the bar code rule. The 2002 ASHP national survey was based on a stratified random sample of pharmacy directors at 1,101 general and children's medical-surgical hospitals in the United States surveyed by mail. SMG Marketing Group, Inc., supplied data on hospital characteristics; the survey sample was drawn from SMG's hospital database. The response rate was 46.7 percent. Despite widespread recommendations to use barcode technology to check and document doses administered, only 1.5 percent of hospitals used this technology in 2002, an increase from 1.1 percent in 1999.[26]

As summarized above, the published literature provides baseline estimates on unintercepted medication dispensing and administration errors as well as the percent of ADEs caused by them. In addition, studies to date have reported interception rates use to project the impact of bar coding scanners on preventing errors and ADEs, although these rates are highly variable and highlight the need for additional research.

7. What types of new data sources would be needed to measure progress on this long-term outcome goal? FDA plans to partner with the Agency for Healthcare Quality and Research (AHRQ) to evaluate the impact of the bar coding rule. We need to obtain reliable estimates of medication error interception rates at various hospitals, with and without bar coding technology, to extrapolate results with greater certainty and external validity.
FDA will also plan to supplement the ASHP survey with data from manufacturers and other stakeholders that will allow for a more reliable estimate of bar code scanner adoption and use.

[24] Phillips et al. Increase in US Medication-Error Deaths between 1983 and 1993. Lancet. 1998 351:643-644.
[25] Bates, DW et al. The Costs of Adverse Drug Events in Hospitalized Patients. JAMA 1997 277:307-311.
[26] Pedersen CA, Schneider PJ, Scheckelhoff DJ. ASHP national survey of pharmacy practice in hospital settings: dispensing and administration--2002. Am J Health Syst Pharm 2003 Jan 1;60(1):52-68.

8. What measurable progress have we made toward this goal? Though only around 125 hospitals in the country (2 to 3 percent) currently use bar code technology, the Institute for Safe Medication Practices (ISMP), an independent, internationally recognized expert organization dedicated to the prevention of medication errors, found in a recent survey that "almost half of the respondents reported that they are actively engaged in discussing possible implementation of bar code technology, or have partially implemented this technology into some part of the drug use process (*ISMP Medication Safety Alert!* March 6, 2002, http://www.ismp.org/MSAarticles/Calendar/Mar02.htm)." ISMP found that, the "lack of machine readable code… was one of biggest barriers to starting BPOC [Bar code point of care] (http://www.ismp.org/rtb/documents/barcodetele1.ppt, 2003)." Further, they found that (ISMP bar code study of 350 Hospitals, March 6, 2002 issue, http://www.ismp.org/MSAarticles/Calendar/Mar02.htm):

- Nearly 50 percent of participants in the study said they are actively discussing the acquisition of bar code systems.
- Hospital Corporation of America (HCA) intends to have all of their 200 hospitals equipped with bar coding technology by 2005 (4 percent of U.S.).
- Veterans Affairs intends to have all of its 162 acute care facilities equipped with bar coding technology (3 percent of U.S.).
- Many major group purchasing organizations (GPOs), such as Premier, Novation, VA, are now demanding bar codes on medication packages

A recent leadership survey conducted by the Healthcare Information Management System Society reports that 42 percent of hospital chief information officer respondents named bar coding a top IT priority for the next two years (http://www.himss.org/2004survey/ASP/healthcarecio_final.asp). The University of Wisconsin started deploying a medication management system, which incorporates bar codes, in December 2001. The hospital reports an 87 percent reduction in the number of medication errors (http://infosolutions.mckesson.com/himsspatient/survey.asp).

To advance the implementation of bed side bar coding technology, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) has proposed that hospitals would have to develop a plan for implementing bar code technology at the bedside, to be operational by January 2007. Under a proposed expansion to the JCAHO patient safety goals, which hospitals must meet as part of the accreditation process, adopting bar code readers would become part of an overall goal of improving patient identification (http://www.jcaho.org/accredited+organizations/patient+safety/05_hap_npsg.pdf). Since the FDA published regulations in February 2004 requiring drug manufacturers to add bar codes to medication, the JCAHO felt that they had the authority to now "mandate" the use of bed side bar coding technology to help prevent medication errors.

The American Society for Health Systems Pharmacists conducts a national survey of pharmacy practice in acute care settings every three years that pertains to drug dispensing and administration practices. This survey captures point of care systems, such as bar coding scanners. The 1999 survey was the basis for the impact analysis for the bar code rule. The survey is conducted on a three year cycle. The 2002 ASHP national survey found that, despite widespread recommendations to use barcode technology to check and document doses administered, only 1.5 percent of hospitals used this technology in 2002, an increase from 1.1 percent in 1999. The next survey to include information on bar coding will be conducted in 2005.

Long-term Outcome Goals for Strategic Goal 3: Patient and Consumer Protection

Increase the Patient Population Covered by Active Surveillance

1. What is the proposed long-term outcome goal? ***Increase by 50 percent the patient population covered by active surveillance of medical product safety by 2008.***

2. What are the proposed targets? 50 percent increase in the patient population covered by active surveillance

3. What is the proposed target date for full accomplishment? 2008

4. Which FDA Centers are covered by this long-term goal? All Centers that regulate medical products with planned or ongoing active surveillance programs are covered by this goal – specifically, this includes CDRH, CDER, and CBER.

5. Why is achievement of this long-term outcome goal important? Historically, FDA has relied on spontaneous reporting systems to ascertain risks associated with regulated medical products, and more recently dietary supplements and foods. However, there is considerable evidence that the spontaneous reporting systems for adverse events and medical product problems do not allow for an adequate characterization of the true safety profile for these products. These systems largely depend on health care providers taking time away from the delivery of health care to complete reports, which means there are many adverse events that go unreported. In addition, many events that are reported may be coincidental, not causally related to the use of the product. However, these systems can provide valuable information, particularly on rare, serious adverse events that may be caused by the product.

The Agency needs to maximize the efficiency and effectiveness of the spontaneous reporting systems, and at the same time increase active surveillance through prospective data collection through hospitals participating in MedSun, CDC surveillance systems and direct access to safety data through health care providers' information systems. Active surveillance will allow FDA to better ascertain risks associated with medical products and focus its resources on the highest impact problems.

6. How does this long-term outcome goal relate to achieving ultimate outcomes of reducing mortality and morbidity? Active surveillance will allow for more rapid identification and analysis of adverse events which are two important objectives in the Agency's strategic plan. If we want to speed up the process of risk assessment and control, we need to build our capability to actively monitor a greater proportion of the patient population in the U.S. One of the most important new strategic directions for the Agency in this area involves speeding access to data that will allow us to understand risks and prevent adverse health outcomes. It is not easy to quantify or project how specific active surveillance programs will result in a reduction in morbidity and mortality, but the more patients using medical products FDA actively monitors the better able the Agency will be to warn and caution health care providers and patients about serious safety problems and minimize risks.

7. What types of data already exist for measuring this long-term outcome goal? Our primary active surveillance program is MedSun. CDRH can obtain an estimate of the population covered by MedSun but we currently do not have an estimate on the size of the patient population admitted to health care facilities participating in MedSun. To increase the population covered by active surveillance by 50 percent we will also have to expand active surveillance of drugs and biologicals through other programs or partnerships. In our strategic plan we included the addition of drug and device modules to ongoing

active surveillance systems and we also plan to launch an automatic data collection project with select health care providers across the country.

8. What types of new data sources would be needed to measure progress on this long-term outcome goal? To determine the size of the population covered by active surveillance, FDA will calculate the number of health care encounters at the health care facilities that actively or automatically collect data on medical product safety. Specifically the Agency will need to:

- Obtain the annual number of admissions for each healthcare facilities participating in MedSun.
- Determine the number of patients monitored in hospitals participating in the National Electronic Injury Surveillance System, once drug and device modules have been added to the system.
- Determine the number of patients in health care facilities during automatic data collection projects.

9. What measurable progress have we made toward this goal? To determine the size of the population covered by active surveillance, FDA calculates the number of health care encounters at the health care facilities that actively collect data on medical product safety. Specifically the Agency:

- Obtains the annual number of admissions for each of our active data collections programs, particularly for the healthcare facilities participating in MedSun.

- Determines the number of patients monitored in hospitals participating in the National Electronic Injury Surveillance System.

- Determines the number of patients in the Medicare Patient Safety Monitoring System.

In **MedSun**, the number of admissions covered increased significantly. The number of admissions reported for the beginning of FY 2003 was 16,645,345. The number of admissions for the beginning of FY 2004 is 53,198,046. The increase is 36,552,701 admissions covered – **an increase of over 200 percent.**

Additionally, the Connecting for Health project is a pilot collaborative project among three large, urban tertiary care facilities. Through this project, FDA receives signals generated from the participating site's electronic medical record data when certain criteria are met (e.g., pregnant female taking isotretinoin). **Last year, the sites had a combined 150,000 discharges.**

The National Center for Injury Prevention and Control (NCIPC), Centers for Disease Control and Prevention (CDC) is collaborating with the U.S. Consumer Product Safety Commission (CPSC) to expand the National Electronic Injury Surveillance System (NEISS) to collect data on all types and causes of injuries treated in a representative sample of U.S. hospitals with emergency departments (ED). NEISS is a statistically valid injury surveillance and follow-back system operated by CPSC. The primary purpose of NEISS has been to provide timely data on consumer product-related injuries occurring in the U.S. In the year 2000, CPSC initiated an expansion of the system to collect data on all injuries. With the expansion, NEISS becomes an important public health research tool, not just for CPSC, but for users throughout the U.S. and around the world. NEISS comprises 63 participating sites, representing a random sample of US hospitals with 24-hour emergency departments. Thus, NEISS data are representative of the entire US. **Last year, the system covered 535,000 emergency room visits** – which, with the addition of drug and device modules, represent an entirely new active surveillance population for the Agency.

Moreover, CDC administers the National Hospital Ambulatory Medical Care Survey, **with a sample size of 37,337 patient visits from 396 emergency departments. Approximately 36 percent** of the **injuries were related to medical products**. Of these, approximately 7.1 percent involved an adverse event to a

single drug, and another 1.2 percent involved an adverse event to multiple drugs. Thus, approximately 1,100 of the 37,337 patient records involved an adverse drug event. Further, vaccines are a subset of these 1,100 drug adverse events – which allows CBER to identify potential signals.

The Agency has begun to use CMS's Medicare Patient Safety Monitoring System, which reviewed 40,620 randomly selected charts being evaluated to calculate payment errors under the Payment Error Prevention Program (PEPP). This is an additional source of information not previously available to us (the entire number is an increase).

Long-term Outcome Goals for Strategic Goal 4: Counterterrorism

Increased Analytic Surge Capacity in the Event of Terrorist Attack on Food

1. What is the proposed long-term outcome goal? The goal is to ***increase FDA's capacity to effectively analyze food samples for biological, chemical and radiological threat agents in the event of a terrorist attack.***

2. What are the proposed targets and the proposed date for full accomplishment?
FDA will need to develop laboratory testing capacity for biological, chemical and radiological threat agents. The determination of the number of Food Emergency Response Network (FERN) Laboratories needed to respond to a terrorist event involving foods was based on the development of a plausible scenario in which food was contaminated with a threat agent. Based on this scenario, FDA estimated that 50 state laboratories would be required to provide the needed surge capacity to respond to the attack. These 50 laboratories reflect laboratory capabilities for chemical and microbiological analysis rather than actual laboratory locations because some state laboratories will have capability to analyze samples for both types of agents at one location. If fully funded, these laboratories will be added incrementally between 2005 and 2008. Laboratories will need to have the ability to be operational 24/7, including two working shifts of trained personnel. Laboratories will use validated methods and have satisfactorily completed proficiency test samples. FERN laboratories will be geographically distributed by region according to the five proposed FERN Regional Coordination Centers. Funds provided in the Administration's FY 2005 Budget will initiate the effort. The goal is to have the following laboratory surge capacity by 2008:

Biological Samples (Known Analyte) 12,500 per week
Chemical Samples (Known Analyte) 6,250 per week
Radiological Samples 12,500 per week

3. Which FDA Centers are covered by this long-term goal? ORA and CFSAN have the responsibility for food safety and security and are directly involved in achieving this goal.

4. Why is achievement of this long-term outcome goal important? A critical component of controlling threats from deliberate food-borne contamination is the ability to rapidly test large numbers of samples of potentially contaminated foods for the presence of contaminants. Once the contaminant and food vehicle have been identified through food surveillance or outbreak investigation, FDA has primary responsibility for distinguishing contaminated food products from safe food products as quickly as possible to protect public health and mitigate disruption in distribution of important foods. Typically, laboratory analysis for a contaminant may involve two types of methods: screening methods, which are sensitive but which may also identify a number of false positives; and confirmatory assays, which can better confirm the presence of a contaminant. In some cases, samples are presumed positive and bypass the screening step. The use of screening or confirmatory methods requires time and labor and use of equipment. Increasing the number of samples that can be appropriately analyzed in a given period of time – the aim of this goal – can be accomplished in a range of ways including:

- Increase the number of laboratories capable of such analysis. For example, there are currently 8 FDA laboratories capable of doing a rapid screen of foods for approximately 50 toxic chemical compounds, and a handful of state laboratories with comparable capacity.
- Enhance the sharing of sampling results among laboratories through the use of eLEXNET (Electronic Laboratory Exchange Network).
- Develop new rapid screening and confirmatory methods.

The importance of surge capacity is illustrated by past experience with respect to a deliberate contamination event involving a non-food – the introduction of anthrax into the postal system in Washington, D.C. in 2001 – and the accidental contamination of orange juice in Arizona.

Testing would likely be necessitated under at least the following circumstances:

- Finished product testing of foods implicated in human illness;
- Finished product testing of food of the same lots as those implicated in human illness at various points in the production and distribution system;
- Finished product testing of food of lots produced in close time proximity to those implicated in human illness;
- Ingredient testing of lots of food implicated in human illness and lots produced in close time proximity to those implicated in human illness; and,
- Environmental testing in the various manufacturing and distribution facilities, including supermarkets, through which the ingredients and products passed, for purposes of assessing contamination and clean-up efforts.

5. How does this long-term outcome goal relate to achieving ultimate outcomes of reducing mortality and morbidity? Speed in identifying whether food is contaminated is critical to reducing the risk of death and illness resulting from human exposure. It is also critical to economic stability (recovery) in that news of contamination may lead to virtual boycotting of classes of products unless consumers can be assured that certain products are safe. Improvements in surge capacity will have public health value even in non-deliberate food contamination events.

6. What types of data already exist for measuring this long-term outcome goal? FDA knows the number of current laboratories capable of performing such analysis.

7. What types of new data sources would be needed to measure progress on this long-term outcome goal? The FERN infrastructure includes establishing a FERN National Program Office (NPO) to support FERN Programs (methods development/ validation, training, proficiency testing, national laboratory sampling, and electronic communication/ reporting) and establishing regional coordination centers to coordinate and manage FERN laboratory surveillance and response capacity/ capabilities. FDA is developing data to measure baseline performance.

8. Why is this target a stretch? At the present time, a limited number of detection methods have been developed for the detection of threat agents in foods. However, these methods have not yet been subjected to the robust inter-laboratory validation procedure necessary to assure their accuracy, reproducibility, and reliability. Accepted validation procedures require that for each agent and food, multiple analyses be done in a minimum number of individual laboratories. This performance goal would employ FERN laboratories to conduct the appropriate validation trials needed to certify the analytical methods that would be used by FERN laboratories to analyze foods for threat agents. In addition, the complexities of foods and their various compositions make it difficult to assume the method can be applied to a broad range of food commodities. Therefore, it is essential to validate food testing methods for additional food commodities to ensure that all performance criteria are satisfactory.

9. How does this target serve Department priorities and goals? This FDA long-term goal directly supports the Department's strategic goal to enhance the ability of the Nation's health care system to effectively respond to bioterrorism and other public health challenges. This goal further supports the first sub-goal: to build the capacity of the health care system to respond to public health threats in a more

timely and effective manner, especially bioterrorism threats by upgrading the Nation's laboratory capacity to quickly identify and characterize suspected biological threat substances and respond to actual incidents. In addition, this long term outcome goal supports the second sub-goal: to improve the safety of food, drugs, biological products, and medical devices by assuring the safety of the US food supply to protect consumers at the least cost for the public.

10. What measurable progress have we made toward this goal? FDA has made progress towards the goal in a number of areas.

- Established the FERN Steering Committee (federal, state representation) in September 2003. The FERN Steering Committee serves as an advisory and policy-recommending body for the FERN. It is composed of representatives from FDA, USDA, Centers for Disease Control and Prevention: Laboratory Response Network, National Animal Health Network, State Public Health Laboratory, State Agriculture Laboratory, State Veterinary Diagnostic Laboratory, Department of Defense, Environmental Protection Agency, and Department of Homeland Security.

- Established the FERN National Program Office to direct five Regional Coordination Centers, coordinate the FERN Support Programs, and manage the laboratory response in the event of a food related emergency.

- Brought 10 FDA laboratories for biological and/or chemical agents and 3 USDA laboratories into FERN. If fully funded, beginning with FY 2005, FDA will begin adding 50 state laboratories, and an additional 50 USDA laboratories to complete the network of 113 laboratories in FERN.

- Ninety-three (93) laboratories representing 43 States and Puerto Rico have satisfactorily completed the FERN Laboratory Qualification Checklist. The FERN Laboratory Qualification Checklist provides the FERN National Program Office (NPO) with vital information to determine if a laboratory meets the criteria for participation in FERN.

- A short-term surveillance sampling activity was conducted in April of 2004. It included 18 federal (FDA and USDA) and State laboratories collecting and analyzing specific food/analyte combinations. The primary objective of this FERN surveillance activity was to evaluate the current organizational infrastructure and test its communication, coordination and electronic reporting capabilities based on the issuance of two check samples to selected laboratories. This surveillance activity will also provide the necessary infrastructure for a national surveillance sampling program.

- The FERN Surveillance Assignment was issued on September 8, 2004 to 40 FERN Laboratories. This assignment assessed and demonstrated the effectiveness and capabilities of the FDA FERN Chemistry/Microbiology and Radiology laboratories and tested the operating mechanisms and protocols of the network.

- Created Standard Operating Procedures (SOPs) for the FERN Proficiency Testing Program which will evaluate the capability of laboratories to detect contaminants and ensure FERN laboratories can demonstrate ability to successfully conduct the analysis of CT samples. Proficiency test samples for *Bacillus anthracis* and Cesium were issued in the first quarter of FY 2005.

- Established an SOP for FERN Methods Evaluation and posted Interim Counterterrorism Methods on eLEXNET. The Method Evaluation process ensures, based on minimum standards, methods will provide consistent, repeatable results in food matrices.

- FDA and USDA are holding Regional Coordination Center (RCC) meetings to establish operational/communication guidelines within each FERN regional hub, communicate FERN objective, policies and current activities, enhance collaboration between FERN laboratories within a region, and provide an opportunity for individual regions to tailor response plans to their state policies and regional needs for interaction. The Northeast RCC Meeting was held in Amherst, MA on July 27-28. The Southwest RCC Meeting was held September 13-16 in Denver, CO. The Southeast RCC Meeting was held September 28-29 in Athens, Georgia. The Pacific and Central RCC meetings are targeted for early within FY 2005 as funds permit.

- Two FERN training courses were given in August 2004. A Real-Time PCR training was held in San Francisco, CA with 35 attendees from Federal, State, and local laboratories. A *Bacillus Anthraces* and *Salmonella* training was held in Athens, GA with 13 laboratory personnel from 13 International, Federal, State, and Local laboratories attending.

- Created FERN Journals on eLEXNET as a communication tool. The FERN Journals allow the FERN NPO to share current information, meeting minutes, documentation, and guidance information; FERN Subcommittees to conduct discussions, disseminate information, and develop documentation; and, FERN Participants to have a central location to check for information regarding activities

- Employed eLEXNET to communicate laboratory information. eLEXNET is an integrated secure system designed for federal, state and local agencies involved in food-safety activities. It is a critical system, adding a necessary infrastructure to provide an early warning system, to identify potentially hazardous foods and possibly, to identify or assess risks and analyze trends. There are 113 laboratories participating in eLEXNET, representing 50 states of which 79 laboratories are actively submitting data.

11. The following references show the link between our activities and the long term goal.

- **Increase the Number of Laboratories Capable of Detecting Microbiological, Chemical and Radiological Agents** – A Recipe for Stronger Food Safety Testing Programs; Association of Public Health Laboratories, Food Safety Laboratory Capacity Assessment Project; April 2003.
  − National Governors Association website, http://www.nga.org/nga/legislativeUpdate
  − "Will the Nation Be Ready for the Next Bioterrorism Attack? Mending Gaps in the Public Health Infrastructure," National Health Policy Forum, George Washington University, June 12, 2002.

- **Enhance the Sharing of Sample Data and Results Among Laboratories Through Partnering and Leveraging** – National Governors Association website, http://www.nga.org/nga/legislativeUpdate

- **Develop New Rapid and Confirmatory Methods for Detecting Agents** – "Will the Nation Be Ready for the Next Bioterrorism Attack? Mending Gaps in the Public Health Infrastructure," National Health Policy Forum, George Washington University, June 12, 2002.
  − Biological Threats and Terrorism: Assessing the Science and Response Capabilities, IOM, Jan 2002.

Long-term Outcome Goal for Strategic Goal 5: Improving FDA's Business Practices

Increase Efficiency and Effectiveness

1. What is the proposed long-term outcome goal? The goal is to reduce administrative overhead at FDA by reducing the number of administrative staff.

2. What are the proposed targets and the proposed date for full accomplishment? FDA proposes to ***reduce the number of administrative staff by 7.5 percent by the end of FY 2004 and further reduce [from current FY03 levels] by 15 percent by the end of FY 2005.***

Supporting data
FDA administrative/ HR system provides the data on the number of staff currently in administrative positions. The following are the series that the Agency counts as administrative versus non-administrative

Administrative positions include positions in the following series:
0000 – Miscellaneous[27], 0200 – Human Resources, 0300 – General Administration[28], 0500 – Budget and Finance, 1000 – Arts and Information, 1100 – Business, 1200 Copyright, Patent and Landmark, 1400 – Library and Archives, 1600 – Equipment and Facilities, 1700 – Education, 1900 – Quality Assurance and Inspection, 2000 – Supply, 2100 – Transportation, and 2200 – Information Technology

In addition to the mission/non-administrative positions identified by the Department which include positions in series: 0100 – Social Science, 0400 – Biological Science, 0600 – Medical and Public Health, 0700 – Veterinary Medicine, 0800 – Engineering and Architecture, 1300 – Physical Sciences and 1500 – Mathematics and Statistics, the following positions are also considered non-administrative and FDA mission-critical: Economists, Consumer Science Specialists, Consumer Science Specialists, Regulatory Counsels, Attorneys and Criminal Investigators

FDA used a FY 2003 baseline of 3,086 administrative positions.
Thus to achieve the percentage targets above, FDA will need to make the following reductions:

- By FY 2004 – reduction of 231 administrative positions = 2855
- By FY 2005 – reduction of 463 administrative positions = 2623

3. What strategies/activities will be used to achieve these reduction targets?

- Early out and buyout plan for administrative positions including positions affected by A-76, human resources consolidation and shared services migration. (Approximately 10 percent in FY 2004 and 2005)
- Attrition (approximately five percent in FY 2004 and 2005)
- Institute a partial freeze on administrative positions
- A-76 (350 FTE combined for FY 2004 and FY 2005)
- Stand-up of shared services

4. What is the proposed target date for full accomplishment? 2005

[27] A total of 40 non-administrative Economists and Consumer Science Specialists positions are also classified in the 0100 series.
[28] All of our 181 Regulatory Counsels are non-administrative and classified in the 0301 series.

5. Which FDA Centers are covered by this long-term goal? Each FDA Center, the Office of Regulatory Affairs and the Office of the Commissioner will work to accomplish this goal.

6. Why is achievement of this long-term outcome goal important? In order to ensure that we do not assign valuable resources to duplicative administrative functions, we need to reduce administrative expenses and redirect any dollar savings to program areas.

7. How does this long-term outcome goal relate to achieving ultimate outcomes of reducing mortality and morbidity? N/A

8. What types of data already exist for measuring this long-term outcome goal?

- Number of administrative and non-administrative positions
- Projected number of A-76 positions to be competed in FY 2004 and FY 2005

9. What types of new data sources would be needed to measure progress on this long-term outcome goal?

- Number of people who participate in early out/buyouts from FY 2004 – 2005
- Attrition rate for FY 2004 – 2005
- Number of positions actually competed in FY 2004 – 2005

10. Why is this target a stretch? ***Reaching this goal is a stretch because FDA already has low administrative overhead and has an extensive field operation that requires logistical support –provided by staff with positions classified as administrative—in order to effectively perform its public health protection function. In fact, FDA already has the second lowest percentage of administrative positions to mission critical positions in the Department: FDA at 29.6 percent compared to CMS – 46.4 percent, NIH – 46 percent and CDC – 42.2 percent.***

11. How does this target serve Department priorities and goals? This FDA long term goal supports the Department's priority of strengthening management, and it is part of FDA's implementation of the President's Management Agenda.

12. What measurable progress have we made towards this goal?

- FDA studied the following commercial activities for outsourcing in FY 2002: graphic arts/visual information services, medical/scientific library services, web publishing, and a television studio in the Center for Devices and Radiological Health. These activities represented 5 percent of FDA's commercial FTE which totaled 64 positions.
- FDA studied the following commercial activities for outsourcing in FY 2003: general accounting in the Office of Regulatory Affairs field components, biological technician and physical science technician services, and facilities/real property management services. The number of positions competed for these series totaled 167 FTE.
- The formal clerical support services study was announced in February 2004. This study will include 350 FTE of work.
- FDA exceeded its performance target for FY 2004 by 89 administrative positions. FDA reduced the number of administrative positions by 320 positions from its baseline of 3,086 positions. The actual number was 2,766 or approximately 9% reduction.