

Department of Health and Human Services  
Food and Drug Administration  
Fiscal Year 2006

**Significant Items from FY 2005 House, Senate, and Conference Reports ~  
FY 2006 Congressional Justification**

The following section represents FDA's response to Congressional requirements or directives derived from House Report 108-584, Senate Report 108-340, and House Report 108-792.

HOUSE REPORT 108-584

**Item**

*Prior Notice and Facility Registration* — The Committee expects FDA to fully consider all comments received during the open comment period regarding the Interim Final Rule for Prior Notice of Imported Food Shipments. The Committee understands that a final rule will be issued in March 2005. The Committee is concerned about FDA's requirement—based in part on the statutory language in section 305 of the Bioterrorism Act—that all prior notices contain the registration number of the facility where the food was produced. This may impede the importation of certain foods, including wine and products imported into the U.S. for analytical testing or research and development (not for consumption), without materially adding to the security of the food supply. Alternatives when a person filing a prior notice cannot reasonably obtain the registration number of the facility in which the item to be imported was produced should be considered. (Page 85)

**Action taken or to be taken**

The Center for Food Safety and Applied Nutrition (CFSAN) has received and are considering all comments to the Interim Final Rule for Prior Notice of Imported Food Shipments as part of the rule making process. The Office of Regulatory Affairs (ORA) is providing feedback and providing any assistance that is needed to accomplish this. The current Compliance Policy Guide (CPG) - Guidance for FDA and CBP Staff Prior Notice of Imported Food under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 was updated on November 4, 2004 (<http://www.cfsan.fda.gov/~pn/cpgpn4.html>) to provide guidance to FDA and CBP staff when they encounter the prior notice situations described above. The policy contains several references which offer different scenarios related to what should be provided for the manufacturer's identity and registration. There are also scenarios whereby if after making a good faith effort, the submitter is unable to determine the manufacturers' registration they are allowed to transmit the manufacturers name and address in lieu of the registration. The submitter must also transmit a reason why the information is not being transmitted. The current CPG offers alternatives when a person can't determine the registration number of a manufacturer. The CPG also currently provides for broad enforcement discretion related to shipment of personal household goods, gifts, and samples of foods for analytical testing. We anticipate issuing the final rule later this year. The original publication goal of March 2005 was extended by 3 months when we extended the full enforcement compliance date from August 2005 to November 2005.

**Item**

*Testing food products* — The Committee expects FDA to establish a mechanism for providing prior notice without a manufacturer's facility registration number for food products that are imported for analytical testing or research and development activities that do not involve consumption by humans or animals. (Page 86)

**Action taken or to be taken**

The current Compliance Policy Guide (CPG) - Guidance for FDA and CBP Staff Prior Notice of Imported Food under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 was updated on November 4, 2004 (<http://www.cfsan.fda.gov/~pn/cpgpn4.html>) to provide guidance to FDA and CBP staff when they encounter the prior notice situations described above. The policy contains several references which offer different scenarios related to what should be provided for the manufacturer's identity and registration. There are also scenarios whereby if after making a good faith effort, the submitter is unable to determine the manufacturer's registration they are allowed to transmit the manufacturer's name and address in lieu of the registration. The submitter must also transmit a reason why the information is not being transmitted. The current CPG offers alternatives when a person can't determine the registration number of a manufacturer. The CPG also currently provides for broad enforcement discretion related to shipment of personal household goods, gifts, and samples of foods for analytical testing.

FDA is also considering all of the comments we received on the prior notice interim final rule during the open comment period as we develop the final rule, including comments on the issue identified above. Until we consider the comments in light of the statutory language, we will not be able to conclude that we will definitively will "establish a mechanism for providing prior notice" for such samples in the final rule, but we will consider this issue fully. We anticipate issuing the final rule later this year. The original publication goal of March 2005 was extended by 3 months when we extended the full enforcement compliance date from August 2005 to November 2005.

**Item**

*Women's health* – The Committee recommendation includes an increase of \$325,000 above the budget request for the Office of Women's Health, for a total of not less than \$4,000,000. Part of this office's mission is to determine if we are designing systems and collecting data to find the crucial differences between women and men's diagnoses, treatment, and outcomes for a given disease. Coronary heart disease is a predominant cause of mortality in women in the United States, and studies have shown that women differ from men in the symptoms they present, the effectiveness of diagnostic testing, success of treatment regimens, and their prognoses.

The Committee directs that, in addition to base resources for that purpose, \$250,000 of the increase amount is to be used for research, data analysis, and outreach related to cardiovascular disease in women. The Committee provides \$75,000 of the increase amount for continuation and expansion of the hormone therapy education program. (Page 86)

### Action Taken or To Be Taken

The Office of Women's Health has identified heart disease in women as its priority for current and future initiatives in FY05. In FY 2004, OWH issued a solicitation for research projects to address important issues related to FDA products and heart disease in women. In response to this solicitation, OWH funded three projects: 1) Use and Outcomes of Coronary Stents in Women: Use of a National Medicare Database, 2) Reduced Efficacy of Ace Inhibition in women with Chronic Heart Failure, 3) Transmission Attenuation Correction for Female Patients undergoing Myocardial Perfusion Imaging: Correction for Confounding Breast Tissue Artifact. OWH will monitor the progress of these research projects and fund additional intramural or extramural research to help prevent heart disease in women. In addition, OWH will review the results of funded research and generate consumer-friendly information for women.

### Item

*Spending for the Generic Drugs Program* — The Committee commends the Agency for making progress over the past several years in expediting the review of generic drug applications. In order to ensure that this success continues, the Committee directs FDA to maintain spending for this program at not less than \$56,000,000. (Page 87)

### Action taken or to be taken

FDA has made significant progress in recent years in expediting the review of generic drug applications and will strive to maintain that progress. To that end, we intend to maintain spending for the Generic Drug Review Program at a level not less than \$56,000,000.

### Item

*Rare Diseases Clinical Trials and Drug Evaluation* — The Committee supports rapid access to therapeutics for children and adults with rare diseases. The Committee encourages the FDA to make the best possible use of FDA's Advisory Committee members in FDA's considerations of clinical trial design and allow the same panel to participate in final review meetings, when feasible. The Committee supports utilization of qualified independent consultants as reflected in the draft guidance document "Independent Consultants for Biotechnology Clinical Protocols" issued in May 2003. The Committee encourages exploration of potential surrogate endpoints and use of the fast-track process, where appropriate, to make drugs available as early as possible for serious and life-threatening orphan diseases. (Page 87)

### Action taken or to be taken

FDA supports development of drugs to treat rare diseases and we have a very good track record for prompt assessment of such drugs. Regarding the issue of clinical trial design, FDA has, through the provisions of the Orphan Drug Act, an ongoing program for orphan product protocol and product development assistance that has helped many sponsors develop appropriate clinical trials. The FDA also welcomes pre-IND, end of phase 2 and pre-NDA meetings. It should be noted that sponsors usually consult with recognized experts in the orphan disease and bring them to meetings with FDA. Indeed, such experts usually conduct the studies.

In addition, FDA supports the use of advisory committees to provide advice on approaches to clinical trial design and analysis for Orphan and Rare diseases, particularly where there is

uncertainty over the appropriate course of action and/or likely disagreement between company and FDA.

We will continue to work with sponsors and outside experts to ensure that development programs for rare diseases are based on sound science and focus on increasing the availability of treatment options to patients while also ensuring that patients are not put at unnecessary risk of harm. To that end, we support the use of surrogate markers provided that they have biological and medical plausibility. Reliance on a surrogate endpoint must be determined case by case. Under our accelerated approval rule and FDAMA, for serious diseases with no good treatment, FDA can rely on surrogate endpoints considered reasonably well developed to lead to a clinical benefit as a basis for approval, with definitive clinical data to be obtained after the drug is marketed.

### **Item**

*Labeling of Genetically Modified Foods: Final Rule* — In January 2001, FDA issued a proposed rule concerning food developed through biotechnology. As proposed, the rule would require food developers to notify FDA at least 120 days in advance of their intent to market a food or animal feed developed through biotechnology and to provide information to demonstrate that the product is as safe as its conventional counterpart. The comment period ended April 3, 2001. The Committee expects the Agency to make this matter a high priority, and finalize both the pre-market notification rule as well as the related guidance document that assists manufacturers who wish to label their food products as being made with or without ingredients developed through biotechnology. (Page 87)

### **Action taken or to be taken**

FDA utilizes a process under which any firm that intends to market a food developed through biotechnology is encouraged to consult with FDA and to submit to the Agency a summary of the firm's safety and nutritional assessment. This process is working well; companies have continued to appropriately consult with the Agency. In addition, FDA has provided advice to developers and marketers on labeling foods and food ingredients as being made with or without bioengineered products. FDA believes that these practices fully protect the public health. In view of these existing protections, we are focusing our limited resources on those other high priority areas where protections need to be enhanced. We are continuing to monitor the success of these actions, and will consider additional action if it becomes necessary.

### **Item**

*Shellfish safety* — The Committee expects that FDA will continue its work with the Interstate Shellfish Sanitation Commission (ISSC) to promote educational and research activities related to shellfish safety in general, and *Vibrio vulnificus* in particular. The Committee directs the use of not less than \$250,000 for this effort. In addition, the committee expects that FDA will continue its work with ISSC through a memorandum of understanding, and that FDA will devote not less than \$200,000 to that work. The Committee is concerned that some states are taking actions outside the ISSC process and expects the FDA to urge all states to work cooperatively in conformity with the National Shellfish Sanitation Program implemented by the ISSC. (Page 88)

#### Action taken or to be taken

In FY 2004, CFSAN/FDA continued to work with the Interstate Shellfish Sanitation Conference (ISSC) to implement a control strategy for *Vibrio vulnificus* in raw oysters that was developed in July 2001. Accomplishments this year include: (1) a 28% reduction in *V. vulnificus* illnesses in the core reporting states reported for 2002 compared to the baseline data and a 25% reduction reported for 2003. It is too early to assess whether this will continue as a trend in the future; (2) completion of research on the effectiveness of on-board or dockside refrigeration at reducing *V. vulnificus* levels in oysters, with a demonstration of positive effects on risk reduction; (3) continuation of ISSC funding for research to study the effectiveness of “dockside” controls, including publication of a study on “dockside” icing by University of Florida; (4) continuation of research by FDA on virulence markers in *V. vulnificus* and *V. parahaemolyticus*, useful in epidemiology and risk assessment; and, (5) continued efforts by the ISSC and by the principle *V. vulnificus* illness reporting states to educate at-risk consumers and health professionals on the risks of consuming raw oysters.

#### Item

*Test method evaluation* — The Committee directs that the agency continue its contract to conduct method evaluation of rapid test methods of fresh fruits and vegetables for microbiological pathogens with New Mexico State University’s Physical Science Laboratory at the fiscal year 2004 level. (Page 88)

#### Action taken or to be taken

Through a Department of Defense contract, FDA continues to support New Mexico State University’s Physical Science Laboratory in evaluating rapid test kits for microbiological analyses. Physical Science Laboratory (PSL) continues to assess potential rapid methods for particular analyte/food combinations which are essential before implementation in the regulatory arena. PSL will also be evaluating test methods for chemical analysis. In FY 05, FDA will maintain funding with PSL at the FY 2004.

#### Item

*WERC* – The Committee expects the FDA to continue its support for the Waste Management Education and Research Consortium [WERC] and its work in food safety technology verification and education at no less than the fiscal year 2004 level. (Page 88)

#### Action taken or to be taken

In FY 2001 FDA awarded a five-year grant to the Waste Management Educational Research Consortium. Funding of the grant in FY 2005 will be at no less than the fiscal year 2004 level.

#### Item

*Antibiotics in shrimp imports* — The Committee continues to have serious concerns regarding seafood safety issues posed by banned antibiotic contamination in farm-raised shrimp imports. The Committee recommends that the FDA, in cooperation with any state testing programs, continue testing of farm-raised shrimp imports for chloramphenicol and other related harmful antibiotics used in the aquaculture industry and ensure that any adulterated shrimp that tests

positive for chloramphenicol or other banned antibiotics will be destroyed or exported from the United States. (Page 88/89)

Action taken or to be taken

FDA continues to sample and test for chloramphenicol in shrimp. The Agency has validated, and is employing, the most current test methods for chloramphenicol. As a result of this routine use of best available technology as it reaches maturity and is validated, the limit of detection for chloramphenicol was reduced from 5.0 parts per billion (ppb) down to 1.0 ppb over a year ago and has recently been further reduced to 0.3 ppb. FDA has also validated a commercially available, rapid immunodiagnostic test kit.

Samples are now being analyzed at the lower limit of detection of 0.3 ppb, with 420 shrimp samples collected and analyzed between 8/19/03 to 8/20/04. Fourteen of these were found to be positive, with corresponding shipments refused entry, and subsequent shipments from these firms to be detained without physical examination.

Recently a method for detection of nitrofurans residues in shrimp, another aquaculture drug of concern, has been developed and validated with a detection limit of 1ppb. The Agency has included this drug in the current sampling program of imported and domestic shrimp.

Item

(BSE) *FDA rule* – On January 26, 2004, in response to the BSE case in Washington state, FDA announced it was issuing new rules banning various bovine-derived material from human food and cosmetics, prohibiting feeding mammalian blood products and several other substances to ruminants, and requiring separation of the production of ruminant and non-ruminant feed. In announcing the new rules, Secretary Thompson said, 'this is the time to make sure the public is protected to the greatest extent possible.' The Committee is very concerned that FDA has still not published these rules nearly five months later. In the absence of the new rules, compliance with the proposed new safeguards is not required. The Committee directs FDA to issue these rules at the earliest possible time. (Page 89)

Action taken or to be taken

On July 14, 2004, FDA published an Interim Final Rule, effective immediately, banning use of specified risk materials (SRMs), and other prohibited cattle materials in foods and cosmetics. Prohibited cattle materials include SRMs from cattle 30 months of age and older, small intestine of all cattle, materials from nonambulatory disabled cattle, material from cattle not inspected and passed for human consumption, and mechanically separated beef. At the same time, the agency also published a companion proposed rule to require records, to be made available to FDA, documenting that prohibited cattle materials were not used in these products. The agency is in the process of finalizing this proposed rule.

Also on July 14, 2004, FDA and USDA published a joint Advanced Notice of Proposed Rulemaking seeking comments on feed controls recommended in the International Review Team's (IRT) February 4, 2004 Report. In the July 14, 2004 ANPRM, FDA also announced that the agency had tentatively decided to implement the IRT's main recommendation, which was to

prohibit the use of specified risk materials (SRMs) in all animal feed. FDA is currently working on a proposed rule to address the use of SRMs in animal feed.

**Item**

*Recall Improvement* - The committee directs FDA to list on all FDA recall press releases the website address of the manufacturer of the recalled product--if any-- and, when it will assist consumers and the media in identifying it, a photograph of the recalled product and/or product label. The Committee further directs FDA to ask the manufacturer to voluntarily provide information on retail outlets of the product for inclusion on the FDA press release. (Page 89)

**Action taken or to be taken**

FDA continues to revise and improve its recall alert processes and its automated Recall Enterprise System. Currently, the public is notified of all Class 1 Recalls, with few justified exceptions, through media coverage of a press release issued to the proper media outlet by either the recalling firm or the FDA. This includes, when appropriate, listing the website of the firm recalling a product in the FDA press release, including photographs or label of recalled products when it is available to FDA, and when it will assist consumers and the media, and where practical and permitted under the information disclosure provisions of the law, provide information on retail outlets of the recalled product in the FDA press release.

SENATE REPORT 108-340

**Item**

*Codex Alimentarius* – Within the total funding available, at least \$2,500,000 is for FDA activities in support of Codex Alimentarius. (Page 149)

**Action taken or to be taken**

In FY 2005, FDA will devote no less than \$2,500,000 in resources (e.g., pay costs, travel, materials) in order to continue Agency activities in support of Codex Alimentarius. These total expenditures for Codex Alimentarius are based upon the dealings of FDA's Center for Food Safety and Applied Nutrition, the Center for Veterinary Medicine, the Office of International Programs and other organizations within the Office of the Commissioner.

**Item**

*Agricultural Products Food Safety Laboratory*- The Committee provides an increase of \$250,000 above the FY 2004 funding level for the FDA to expand its contract with New Mexico State University's Physical Sciences Laboratory to operate the Food Technology Evaluation Laboratory, which conducts evaluation and development of rapid screening methodologies, technologies, and instrumentation; and to provide technology deployment modeling and data analysis for food safety and product safety in order to facilitate FDA's regulations and responsibilities in food safety, product safety, homeland security, bioterrorism, and other initiatives. (Page 149)

**Action taken or to be taken**

Through a Department of Defense contract, FDA continues to support New Mexico State University's Physical Science Laboratory in evaluating rapid test kits for microbiological

analyses. Physical Science Laboratory (PSL) continues to assess potential rapid methods for particular analyte/food combinations which are essential before implementation in the regulatory arena. In FY 2005, PSL will also be evaluating test methods for chemical analysis.

**Item**

*WERC* - The Committee expects the FDA to continue its support for the Waste Management Education and Research Consortium [WERC] and its work in food safety technology verification and education at no less than the fiscal year 2004 level. (Page 149)

**Action taken or to be taken**

In FY 2001 FDA awarded a five-year grant to the Waste Management Educational Research Consortium. Funding of the grant in FY 2005 will be at no less than the fiscal year 2004 level.

**Item**

*Alaska Food Inspection Contract* - In addition, the funding provided for food safety will ensure the continuation of food contract inspections in the State of Alaska. Specifically, it will allow the FDA to renew its contract with the State of Alaska for inspections of food and seafood processors operating in Alaska. The current contract became effective on June 12, 2003. It will fund at least 292 inspections, approximately 272 seafood/HACCP inspections and 20 other food inspections, at a cost of approximately \$269,000. The establishments to be inspected will be mutually agreed upon by FDA and the State of Alaska. (Page 149)

**Action taken or to be taken**

FDA continues its contract with the State of Alaska for inspections of food and seafood processors operating in Alaska. The current contract became effective on June 12, 2003. The contract consisted of approximately \$269,000 to fund approximately 272 seafood/HACCP inspections; and, 20 other food inspections. In FY05, the proposal for Alaska will be for 386 total inspections (346 Seafood and 40 Food). Once we achieve this level of inspections, the numbers of inspections and funding will remain stable for the foreseeable future to allow for better annual planning for the State and FDA.

**Item**

*Seafood Safety* – General Accounting Office [GAO] reports on the safety of seafood have documented the inadequacy of the FDA efforts to address foodborne hazards in seafood, including shellfish. GAO found FDA's seafood inspection system provides consumers with inadequate protection for seafood-related foodborne illness. The Committee urges FDA to promote the development of new food safety technologies such as irradiation, flash freezing, high-pressure processing, or others that can cost-effectively reduce the incidence of pathogens, and technologies that can ensure constant safe temperatures of seafood throughout the food chain.

The Committee supports the ongoing work of the Interstate Shellfish Sanitation Conference and its joint efforts with the FDA and the shellfish industry to formulate shellfish safety regulations through the National Shellfish Sanitation Program. The Committee recommends no less than the fiscal year 2004 level be directed through the Office of Seafood Inspection to continue these activities, and directs that \$200,000 be directed to the Interstate Shellfish Sanitation Conference for the *Vibrio Vulnificus* Education Program.



The Committee is concerned that FDA has not taken effective action to address foodborne illness risks from the consumption of raw shellfish. In particular, the Committee is concerned that the ISSC proposed steps to reduce the rates of death and illness due to consumption of *Vibrio vulnificus*-contaminated raw shellfish may not effectively address public health concerns. (Page 149/150)

Action taken or to be taken

FDA's policy specifically encourages the use of new technologies that are effective in controlling human food safety hazards but does not promote any specific technology. For seafood, FDA is always interested in understanding new technologies and the extent to which they succeed in controlling food safety hazards. FDA occasionally engages in research on the effectiveness of new technologies to control certain hazards. Where new technologies are known to work, FDA might make reference to them in hazards and controls guidance that it develops for seafood processors. FDA takes new technologies into account in various other ways. For example, FDA recently worked with the Interstate Shellfish Sanitation Conference to develop a national control plan for *Vibrio vulnificus*. That plan relies substantially on the existence of emerging new post harvest treatment technologies to kill this organism.

Item

*Chloramphenicol* – The Committee continues to have serious concerns regarding seafood safety issues posed by banned antibiotic contamination in farm-raised shrimp imports. The Committee encourages FDA to use any available funding, in cooperation with State testing programs, to substantially increase the percentage of farm-raised shrimp imports tested for chloramphenicol and other related harmful antibiotics used in the aquaculture industry. Further, FDA is encouraged to develop a program for testing existing U.S. cold-storage inventories of farm-raised shrimp originating from countries known to use chloramphenicol or other banned antibiotics, and to ensure that any shrimp that tests positive for these substances will not be subsequently consumed. (Page 150)

Action taken or to be taken

FDA continues to sample and test for chloramphenicol in shrimp. The Agency has validated, and is employing, the most current test methods for chloramphenicol. As a result of this routine use of best available technology as it reaches maturity and is validated, the limit of detection for chloramphenicol was reduced from 5.0 ppb down to 1.0 ppb over a year ago and has recently been further reduced to 0.3 ppb. FDA has also validated a commercially available, rapid immunodiagnostic test kit.

Samples are now being analyzed at the lower limit of detection of 0.3 ppb, with 420 shrimp samples collected and analyzed between 8/19/03 to 8/20/04. Fourteen of these were found to be positive, with corresponding shipments refused entry, and subsequent shipments from these firms to be detained without physical examination.

Recently a method for detection of nitrofurans residues in shrimp, another aquaculture drug of concern, has been developed and validated with a detection limit of 1ppb. The Agency has included this drug in the current sampling program of imported and domestic shrimp.

### **Item**

*HACCP* – The Committee also continues its concern with the agency's failure to bring FDA-regulated seafood into compliance with HACCP. However, the Committee is aware that special or unique circumstances may exist for particular seafood processors. While ultimate HACCP compliance is not in question, the Committee is specifically aware of Hawaii's lengthy and culturally important history of hook-and-line fisheries, auction markets, and the high consumption of raw tuna and other pelagic fish in Hawaii, and strongly encourages the Agency to take into account both the history and the industry's practical experience in approving a plan that is consistent with healthy seafood products and national standards for seafood safety. (Page 150)

### **Action taken or to be taken**

FDA's seafood HACCP program is designed to allow for unique processing situations. Processors may design one-of-a-kind HACCP systems to accommodate their own circumstances so long as they meet minimum national standards for safety. It is not realistic, however, to expect or allow for gradations of safety in products sold for profit in interstate commerce based on culturally based processing practices at the point of origin.

The longstanding issue to which the Senate language applies involves proper handling practices on board fishing vessels to insure that tuna do not form scombrototoxin as a result of time/temperature abuse. Scombrototoxin is one of the three most frequently reported illnesses from seafood in the United States and is completely avoidable. In this case, the issue involves what constitutes proper handling of fish that are allowed to die and remain in the water for some time before they are landed on the boat. Once a tuna dies, it can begin to decompose and form scombrototoxin if not properly chilled. FDA's Office of Seafood has engaged in a continuing dialog with the auction house in Hawaii on how it can most effectively and practically ensure the control of scombrototoxin as a result of the death of tuna and other species while still on the line. Agreement has been reached on the overall mechanism for control, and it is expected that the details will be resolved in the very near future. The Office of Seafood will continue to conduct complementary research in this area this year. Such research was delayed last year as a result of extensive hurricane damage in the Caribbean.

### **Item**

*Farmed Salmon* – The Committee has been advised that farmed salmon imported from overseas is fed feed with chemical additives to change the color of its flesh or the flesh is artificially dyed. A lawsuit was recently filed against national grocery chains alleging they do not adequately label the fish which are dyed. The Committee directs the Food and Drug Administration to continue to monitor information concerning the safety of the use of such additives and dyes in seafood and to more aggressively enforce the clear and conspicuous disclosure of such additives and dyes to consumers on consumer packaging. (Page 150)

### **Action taken or to be taken**

Under the Federal Food, Drug and Cosmetic Act, retailers are required to label salmon that has been colored by the use of astaxanthin or canthaxanthin to clearly denote that the food has had

color added. The FDA will continue to monitor information concerning the safety of the use of such additives in seafood.

**Item**

*Chloramphenicol* – The Committee continues to have serious concerns regarding seafood safety issues posed by banned antibiotic contamination in farm-raised shrimp imports. The Committee recommends that the FDA, in cooperation with any state testing programs, continue testing of farm-raised shrimp imports for chloramphenicol and other related harmful antibiotics used in the aquaculture industry and ensure that any adulterated shrimp that tests positive for chloramphenicol or other banned antibiotics will be destroyed or exported from the United States. (Page 150)

**Action taken or to be taken**

FDA continues to sample and test for chloramphenicol in shrimp. The Agency has validated, and is employing, the most current test methods for chloramphenicol. As a result of this routine use of best available technology as it reaches maturity and is validated, the limit of detection for chloramphenicol was reduced from 5.0 ppb down to 1.0 ppb over a year ago and has recently been further reduced to 0.3 ppb. FDA has also validated a commercially available, rapid immunodiagnostic test kit.

Samples are now being analyzed at the lower limit of detection of 0.3 ppb, with 420 shrimp samples collected and analyzed between 8/19/03 to 8/20/04. Fourteen of these were found to be positive, with corresponding shipments refused entry, and subsequent shipments from these firms to be detained without physical examination.

Recently a method for detection of nitrofurans residues in shrimp, another aquaculture drug of concern, has been developed and validated with a detection limit of 1ppb. The Agency has included this drug in the current sampling program of imported and domestic shrimp.

**Item**

*Mercury* – In March 2004, the FDA and the Environmental Protection Agency released a revised joint dietary advisory on mercury in seafood. During the development of the advisory, the Committee understands that significant information gaps were found in what consumers, especially sensitive populations such as women who are or may become pregnant and young children, know about mercury levels in various seafood species. The Committee encourages FDA to implement an outreach and education effort with physicians and other appropriate outlets in order to increase awareness among potentially affected consumers, and to measure the effectiveness of the efforts on target group behavior and impact on their overall consumption of seafood. (Page 150)

**Action taken or to be taken**

FDA and EPA are jointly sponsoring a public education campaign to reach women planning on becoming pregnant, pregnant women, nursing mothers, and parents of young children about the methylmercury advisory. An extensive outreach effort to over 9,000 print and electronic media outlets, including outlets that specialize in reaching women, has been conducted.

Information about the advisory has been sent to over 50 organizations of health care providers to women and children, such as the American Academy of Pediatrics; the American Academy of Family Physicians; the American College of Obstetricians and Gynecologists; the American College of Nurse Midwives; directors of the Women, Infant, and Children (WIC) program; and all local health departments. The advisory has also been distributed through exhibits at medical professional association meetings that took place in 2004 and will be distributed at similar meetings scheduled during 2005.

Brochures about the methylmercury advisory have been sent to all practicing pediatricians, obstetricians and gynecologists, nurse midwives, and nurse practitioners and physician assistants specializing in pediatrics or obstetrics throughout the country for distribution through their offices. These health professionals are able to order additional copies of the brochure as needed from FDA and EPA to provide to their patients. In November and December of 2004, EPA and FDA were filling additional requests for these brochures at a rate of approximately 35,000 brochures per week.

An educational program for pregnant women on food safety for use by health educators will be launched in spring 2005 that will highlight information from the methylmercury advisory. This program will include an educational video and a curriculum and will be sent to 35,000 health educators working with pregnant women. A special web page for pregnant women will be part of the program.

Special funding has been set aside for community outreach efforts in several different geographic locations to ensure that the message reaches women in special populations at greater risk for illness. Examples include Native Americans and certain Hispanic and Asian groups who have high fish consumption practices. Some of these projects are already underway; others will begin during 2005.

A Federal-State Working Group on the Coordination of Methylmercury advisories has been established to examine ways to join the federal advisory with the state advisories as much as possible.

This outreach campaign will be evaluated through the FDA-USDA consumer survey on food safety knowledge, attitudes, and behaviors that will be completed in 2005.

**Item**

*Dietary Supplements* – The Committee believes that the potential for dietary supplements to have positive health benefits has been realized in many cases. However, it is essential that FDA continue its efforts to ensure their safety, and to fully enforce the prohibition of false, misleading or unsubstantiated claims regarding dietary supplements implemented in the Dietary Supplement and Health Education Act [DSHEA] of 1994. The budget request includes total funding of approximately \$5,360,000 for the CFSAN Adverse Events Reporting System [CAERS], of which approximately \$1,500,000 is for dietary supplements. (Page 151)

Action taken or to be taken

FDA will continue efforts to ensure the safety of dietary supplements and, consistent with resources and priorities, to effectively implement the Dietary Supplement and Health Education Act (DSHEA) of 1994. As described in FDA's November 2004 announcement on the Regulatory Strategy for the Further Implementation of DSHEA, FDA will allocate resources to regulate dietary ingredient and product safety, quality, and labeling in the interests of public health and consumer use of dietary supplements. The Agency is committed to spending no less than \$5,360,000 for CAERS related work in FY 2005.

**Item**

*Natural Center for Natural Products Research* – FDA has indicated that the ability to identify and analyze specific components in ingredients, including botanical ingredients, is an essential component of research and regulatory programs directed at ensuring the safety and effectiveness of dietary supplements. The Committee expects the same level of review of botanicals in dietary supplements to continue in fiscal year 2005. This work is being carried out by FDA in collaboration with the National Center for Natural Products Research, Oxford, MS. (Page 151)

Action taken or to be taken

The work performed by the National Center for Natural Products Research in Oxford, Mississippi to identify and analyze specific components in dietary supplement ingredients, including botanical ingredients, has become an essential component of FDA's research and regulatory programs directed at ensuring the safety and effectiveness of dietary supplements. FDA will continue with the same level of review of botanicals in dietary supplements in fiscal year 2005.

**Item**

*Standards of Identity* - The Committee is aware of the ongoing debate surrounding increased importation and use of milk protein concentrate. A [Government Accountability] Office investigation highlighted a dramatic increase in milk protein concentrate imports. The Committee remains concerned with FDA's current lack of enforcement of standards of identity as it relates to the potential illegal use of milk protein concentrate in standardized cheese. (Page 151/152)

Action taken or to be taken

In FY 2002/2003, the Center for Food Safety and Applied Nutrition (CFSAN)/FDA (1) conducted inspections at specific cheese manufacturing sites to determine compliance with the cheese standards and to document the use of Milk Protein Concentrate in standardized cheeses and, as a result, issued warning letters to some cheese manufacturers using MPC in standardized cheese; (2) conducted a thorough review of the two petitions requesting the use of filtered milk in standardized cheeses and, subsequently, closed the petition submitted by the American Dairy Products Institute and converted it to a comment to the petition submitted by the National Cheese Institute; and (3) developed a proposed rule to provide for the use of fluid ultrafiltered milk in standardized cheeses.

In FY 2004, CFSAN/FDA issued reports to Congress on the status of petitions regarding the use of ultrafiltered milk, casein, or MPC in standardized dairy products. CFSAN/FDA did not receive any new petitions in FY 2004.

In FY 2005, CFSAN/FDA intends to publish a proposed rule to amend the definition of “milk” and “nonfat milk” in cheese standards to provide for the use of fluid ultrafiltered milk.

### **Item**

*Tissue Safety* – In 1997, the FDA proposed rules that would regulate human cells, tissues, and related products. As of May 2004, the FDA has finalized the first two of the three proposed rules. The Committee remains concerned that the third rule, which would provide guidelines for current good manufacturing practices for establishments that produce human cells, tissues, and related products, has not yet been finalized. (Page 152)

### **Action taken or to be taken**

The Food and Drug Administration (FDA) announced on November 18, 2004, the issuance of a final rule on current good tissue practice (GTP), the last of three rules to be finalized as part of the Agency's overall plan to make human cells and tissues even safer. GTP includes the methods, facilities and controls used to manufacture these products. With this final rule, FDA's efforts to establish a new, comprehensive, and risk-based approach to this promising and innovative field of medicine can be realized. The new approach will be fully implemented on May 25, 2005.

The new rule, entitled "Current Good Tissue Practice for Human Cell, Tissue, and Cellular and Tissue-Based Establishments; Inspection and Enforcement," requires manufacturers to recover, process, store, label, package and distribute human cells, tissues and cellular and tissue-based products (HCT/Ps) in a way that prevents the introduction, transmission, or spread of communicable diseases. The regulations apply to a broad range of these products including musculoskeletal tissue, corneas, human heart valves, dura mater (lining of the brain) and cellular therapies.

The final GTP rule follows the earlier publication of FDA's final regulations on registration of human tissue establishments and the eligibility of human tissue donors. The rule also includes a requirement for manufacturers to report certain adverse reactions and HCT/P deviations, to have labeling that contains accurate and complete information, and to allow FDA inspections to ensure compliance with regulations.

### **Item**

*Rare Diseases Clinical Trials and Drug Evaluation* – The Committee supports rapid access to therapeutics for children and adults with rare diseases. It is the view of the Committee that improvements can be made with respect to clinical trial design and FDA Advisory Committees. The Committee encourages the FDA to make the best possible use of FDA's Advisory Committee members in FDA's considerations of clinical trial design and allow the same panel to participate in final review meetings, when feasible. The Committee supports utilization of qualified independent consultants as reflected in the draft guidance document 'Independent Consultants for Biotechnology Clinical Protocols' issued by CBER/CDER on May 12, 2003. The Committee encourages enhanced exploration of potential surrogate endpoints and use of

FDAMA's fast-track provision, where appropriate, to make drugs available as early as possible for serious and life-threatening orphan diseases that have no treatment. The Committee believes these policy enhancements will lead to more efficient and timely evaluation of rare disease therapeutics and further stimulate private sector investment in rare disease research. (Page 153)

Action taken or to be taken

FDA supports development of drugs to treat rare diseases and we have a very good track record for prompt assessment of such drugs. Regarding the issue of clinical trial design, FDA has, through the provisions of the Orphan Drug Act, an ongoing program for orphan product protocol and product development assistance that has helped many sponsors develop appropriate clinical trials. The FDA also welcomes pre-IND, end of phase 2 and pre-NDA meetings. It should be noted that sponsors usually consult with recognized experts in the orphan disease and bring them to meetings with FDA. Indeed, such experts usually conduct the studies.

In addition, FDA supports the use of advisory committees to provide advice on approaches to clinical trial design and analysis for Orphan and Rare diseases, particularly where there is uncertainty over the appropriate course of action and/or likely disagreement between company and FDA.

We will continue to work with sponsors and outside experts to ensure that development programs for rare diseases are based on sound science and focus on increasing the availability of treatment options to patients while also ensuring that patients are not put at unnecessary risk of harm. To that end, we support the use of surrogate markers provided that they have biological and medical plausibility. Reliance on a surrogate endpoint must be determined case by case. Under our accelerated approval rule and FDAMA, for serious diseases with no good treatment, FDA can rely on surrogate endpoints considered reasonably well developed to lead to a clinical benefit as a basis for approval, with definitive clinical data to be obtained after the drug is marketed.

Item

*Self-Contained Modular Facilities* – The Centers for Disease Control [and Prevention] (CDC) has incorporated self-contained modular facilities [SCMF] and modular specimen triage units [STU] in the development and implementation of its 50 State public health laboratories and facilities comprising the Laboratory Response Network [LRN]. The Committee encourages the FDA to consult with CDC to evaluate the benefits of incorporating self-contained modular facilities. (Page 153)

Action taken or to be taken

The purpose of the CDC/LRN self-contained modular facilities and modular specimen triage units is to provide a screening mechanism for chemical, biological, and radiological contamination in unknown samples and facilitate triaging of unknown samples before the samples are brought into a laboratory facility. FDA representatives currently participate in the LRN Partnership Group as well as in LRN working groups addressing laboratory triage issues. Additionally, the FDA currently has two self contained mobile laboratory facilities developed by Edgewood Chemical and Biological Warfare Center that provide screening and analytical capability for chemical and microbiological threat materials in food samples. These mobile

laboratories will be deployed at US ports of entry or other locations where there is a temporary need for heightened analytical capabilities. This, of course, includes being deployed in the event of a terrorist incident to provide screening and triage capabilities. FDA/ Food Emergency Response Network (FERN) will continue to work with CDC/LRN to assess the benefits of incorporating additional self contained modular facilities and/or expanding the screening and triage capability of existing modular facilities for FERN and LRN laboratories.

### **Item**

*Animal Drug Compounding* – The Committee is aware that in 2003, the FDA issued a Compliance Policy Guideline [CPG] regarding animal drug compounding. The Committee is concerned that the CPG represents a shift in policy, and does not clearly explain how the FDA's enforcement priorities have changed, particularly with respect to compounding from bulk drug substances for non-food producing animals. Further, the Committee is concerned that the FDA did not seek public comment prior to issuing the CPG, although public input is currently being gathered from the animal drug compounding community and other interested parties. Therefore, the Committee strongly encourages the FDA to work closely with all interested parties to ensure that the reasons for issuing the CPG, as well as changes that will result from it, are well understood, and to seriously consider all public comments made regarding this CPG. (Page 154)

### **Action Taken or To Be Taken**

On September 1, 2004, FDA publicly announced its intention to draft and publish for public comment a revised Compliance Policy Guide (CPG) on veterinary pharmaceutical compounding.

FDA is basing its action on the numerous letters from veterinarians, pet owners, compounding pharmacists, and associations the Agency received expressing concern that the CPG lacks sufficient clarity on the circumstances in which veterinary compounding, particularly from bulk drugs, would be permitted. Many of the letters also disagreed with the current policy, stating that it was not within FDA's legal authority, and complained about the lack of prior public comment. FDA has met with many interested groups and has reviewed the comments received in the letters.

When it is available, the draft CPG will be posted on FDA's Center for Veterinary Medicine (CVM) Website and a notice of availability will be published in the Federal Register.

### **Item**

*Food Labeling* – The FDA Office of Nutritional Products, Labeling and Dietary Supplements [ONPLDS] is responsible for several important public health and consumer protection programs. Responsibilities of ONPLDS include developing policy and regulations for dietary supplements, nutrition labeling and food standards, infant formula and medical foods, and scientific evaluation to support such regulations and related policy development. Further, ONPLDS supports compliance and enforcement actions and is responsible for the clinical review, data summaries, and, as appropriate, follow-up and research related to adverse events associated with dietary supplements and infant formula. The Committee is aware that funding for activities in ONPLDS other than the regulation of dietary supplements has remained level for several years, while the responsibilities relegated to this office have increased. Therefore, the Committee encourages FDA to determine if additional funding is necessary for ONPLDS to more effectively carry out



its important responsibilities, and, if appropriate, increase funding for this office in its fiscal year 2006 budget request. (Page 154)

Action taken or to be taken

FDA's Office of Nutritional Products, Labeling and Dietary Supplements' (ONPLDS) responsibilities continue to grow, including initiatives on infant formula review notifications, better informed consumers, obesity, and allergen labeling. In addition, we have a continuing challenge to protect the safety and security of the food supply from tampering and from counterfeit products. The President's FY 2006 budget request delineates FDA's priorities in this regard. FDA will continue to evaluate if additional funding is necessary for ONPLDS to more effectively carry out its important responsibilities.

**Item**

*Center of Excellence* – The Committee is aware of the important work currently being done at FDA's three Centers of Excellence regarding food safety and dietary supplements. The Committee is also aware of interest in creating a new Center of Excellence at the University of California at Davis (UC-Davis) to address the unique nature and contributions of this region of the country, both in terms of its role as the source of a substantial portion of the domestic food supply and as the gateway for foods arriving from our international trading partners. Due to financial constraints, the Committee is unable to provide funding to establish this Center, but encourages the FDA to consider the development of a Center of Excellence at the University of California at Davis, if it is determined to be an important and appropriate use of Federal dollars. (Page 155)

Action taken or to be taken

The FDA recognizes the potential benefits of a Center of Excellence at the University of California. The FDA also recognizes that funds for the establishment of such a center are not available at the current time. The FDA will continue to work with the university to identify means for establishing such a center in the future.

**Item**

*Canned Tuna* – The Committee encourages the Food and Drug Administration to initiate rulemaking to revise the standard of identity for canned tuna as requested in 'Citizens Petition to Amend Canned Tuna Standard of Identity, 21 CFR 161.190, Docket No. 94P-0286' to replace the current press cake weight requirement with a drained weight requirement and to incorporate any other changes that may be deemed necessary. (Page 155)

Action taken or to be taken

Consistent with Agency priorities and available resources, the Agency will consider whether it should initiate rulemaking to revise the standard of identity for canned tuna as requested in "Citizens Petition to Amend Canned Tuna Standard of Identity, 21 CFR 161.190, Docket No. 94P-0286" to replace the current press cake weight requirement with a drained weight requirement and to incorporate any other changes that may be deemed necessary.

## **Item**

*Implanted Medical Devices* – The Committee acknowledges current FDA regulations designed to improve post-market surveillance for medical devices, and strongly encourages FDA to devote the necessary resources to require registries and monitor well-designed long-term safety studies for implanted devices, including but not limited to jaw implants. As the aging U.S. population becomes more dependent on implanted devices, the Committee believes it is essential that the FDA allocate adequate resources to patient safety activities related to these devices, such as registries, post-market surveillance, and long-term phase IV trials. (Page 157)

## **Action taken or to be taken**

FDA monitors reports through its nation-wide reporting system of adverse events and product problems associated with marketed medical devices, including implants. Of the approximately 115,000 device reports received during CY 2004, implants figured prominently and were noted among the top 10 in reports received (e.g., intraocular lenses and drug-eluting stents). FDA continues to take significant actions based on these reports. In fact, the agency expects to devote more resources toward postmarket surveillance as a result of increased budget authority and medical device user fees in FY 2005 and FY 2006. In 2003, CDRH noted problems with the St. Jude Aortic Connector which led to its recall. The Center put out a public health notification on the Medtronic Intravascular Graft.

FDA is also looking into utilizing registries as a post market tool to monitor device safety. For example, in CY 2003, in anticipation of the rapid diffusion of a break-through technology, FDA worked with the sponsor of the first-of-a-kind drug-eluting coronary stent to establish a nation-wide, multi-center registry to capture detailed information on 2,000 consecutive patients. Based on early reports of thrombosis and hypersensitivity with these implanted devices, FDA updated a public health notification to inform the clinical community of FDA's ongoing assessment. The data from the registry, and other sources, will provide FDA with a more definitive assessment of any safety concern. Similar registries were established in CY 2004 for other coronary stents as well as the first-of-a-kind carotid stents.

Post approval studies are another mechanism by which the agency gains information about marketed devices; the agency may require such studies as a condition of approval of a premarket approval (PMA) application or under its post market surveillance authority. FDA generally imposes a post-approval study requirement for new implants. The registry for drug-eluting stents is an example. One of the main purposes of such studies is to gather long-term safety and effectiveness data for the device. Recognizing the importance of post-approval studies, CDRH has instituted new efforts to strengthen its oversight of these studies. The Center has allocated funds to developing a new system to track the progress of the studies and new procedures to involve epidemiologists more extensively in designing the protocols and evaluating the results sponsors submit. The goal of these efforts is different for sponsors and CDRH. Sponsors need to produce post-approval studies that use good science and high quality methodology in the study design, and provide timely and accurate study results. CDRH needs to manage the information in a timely and accurate manner; provide timely and accurate notification of sponsors regarding their study status; use appropriate public notification; and determine when enforcement action is necessary.

In CY 2004, FDA continued working with the Consumer Products Safety Commission to utilize its nation-wide sample of emergency departments to obtain further information on, and national estimates of, device-related adverse events, including those related to implants. FDA staff published a pilot study that used data collected from these emergency departments. The study indicated that medical device reporting systems significantly underestimate the magnitude of the annual number of adverse events associated with medical devices, and that a relatively high proportion of adverse events involving implanted devices, compared to other types of devices, had outcomes serious enough to require patient hospitalization. FDA's ongoing collection of these data is focused on increasing their specificity to construe how these adverse events occur and how they can be prevented.

Lastly, FDA has contracted with the Institute of Medicine (IOM) for IOM to conduct a study of the adequacy of the postmarket surveillance of devices, particularly implants, used in the pediatric population. The study was called for under Section 212 of Medical Device User Fee and Modernization Act (MDUFMA). CDRH staff has worked closely with the IOM staff to provide them information and public testimony.

**Item**

*SEC. 729.* -- None of the funds made available to the Food and Drug Administration by this Act shall be used to close or relocate, or to plan to close or relocate the Food and Drug Administration Division of Pharmaceutical Analysis in St. Louis, Missouri, outside the city or county limits of St. Louis, Missouri. (Page 73 of S.2803, 108<sup>th</sup> Congress)

**Action taken or to be taken**

FDA has no plans to close or relocate or to plan to close or relocate the FDA Division of Pharmaceutical Analysis in St. Louis, Missouri.

HOUSE REPORT (CONFERENCE) 108-792

**Item**

*Communication with Oversight Committees* – The conferees find it necessary to remind the Food and Drug Administration that the Committees on Appropriations perform critical oversight functions for the agency. The ultimate expression of this oversight is the funding decisions for the agency and accompanying language in the statement of managers. The conferees expect that Members of Congress will be provided requested information from FDA so that the Committees can perform their oversight function. It is insupportable that in some cases FDA has given information about major policy matters to the press before providing the same information to Congress. The conferees expect FDA to be fully cooperative with all Congressional oversight activities.

**Action taken or to be taken**

FDA recognizes the need for Congressional members and their staffs to be fully aware of FDA activities as they relate to Congressional oversight responsibilities and the interests of member constituents. Between November 2004 and February 2005, several offices within FDA met to determine the best approach to providing the Appropriation Committees with significant developments at the Agency involving finance, policy, personnel, and regulatory actions.

Additionally, Agency staff met to discuss a number of possible methods of expediting response times to Congressional inquiries. As a consequence of these meetings and subsequent commitments, the Agency now believes that it has set up greater collaboration amongst those responsible for appropriations, legislative affairs, and external communications, and has developed streamlined communications that will lead to greater responsiveness to all Congressional oversight committees and/or their staffs.

**Item**

*Influenza Vaccine* – The conferees include a \$300,000 increase for the Center for Biologics Evaluation and Research (CBER) and related activities in the Office of Regulatory Affairs for flu vaccine-related activities. The conferees understand that CBER will be undertaking a number of additional activities in fiscal year 2005 to secure additional units of flu vaccine for the 2004-2005 flu season and to ensure an adequate supply of flu vaccine for the 2005-2006 flu season. (Page 708)

Action taken or to be taken

On November 21, 2004, FDA authorized the use of GlaxoSmithKline's (GSK) influenza vaccine, Fluarix, in the United States under an Investigational New Drug (IND) application. On December 7, an agreement was reached by HHS with the company to purchase 1.2 million doses of the vaccine for distribution, if needed, to supplement available licensed vaccine during this year's shortage. To provide for this potential use, FDA reviewed extensive manufacturing and clinical information as well as conducted an inspection of the GSK manufacturing facility in Germany to determine that this vaccine is suitable for use under an IND. FDA reviewed GSK's proposed clinical study plan and informed consent document, as well as the clinical protocol and manufacturing data. These steps, along with the conditions and controls required under the IND are designed to assure the product is safe for use during the current flu season. The FDA is working closely with GSK (e.g., review, consultation, and inspection) throughout FY2005 in an effort to facilitate the licensure of its vaccine product for the 2005-2006 flu season.

FDA has also similarly reviewed extensive manufacturing and clinical information, and conducted several inspections of the manufacturing facilities of additional sponsors of influenza vaccine INDs. These steps are designed both to improve shortage response capabilities and, most important, to expand future manufacturing capacity for influenza vaccine in coming years by encouraging interest in and progress toward US licensure, as well.

FDA (both CBER and ORA) is working closely with the United Kingdom regulatory authority (MHRA) to do all that is possible to facilitate Chiron's remediation of its manufacturing problems at the Liverpool facility. These efforts involve frequent teleconferences, multiple site visits/inspections, and review of manufacturing and facility information. FDA is also interacting closely and proactively with the 2 other currently licensed influenza vaccine manufacturers, Aventis Pasteur and MedImmune on a variety of issues related to their vaccine manufacturing.

Throughout FY2005, FDA will be developing reagents for potency testing and serology necessary for evaluation of influenza vaccines for the 2005-2006 flu season. FDA will continue work to develop high growth reassortants, which will help to ensure timely and adequate supply of vaccine when the influenza strain composition for the 2005-2006 vaccine is determined.

**Item**

*National Center for Food Safety and Technology* – The conferees recognize the contributions with the National Center for Food Safety and Technology (NCFST) is making toward ensuring the security of the nation’s food supply. The conferees direct that the FDA continue to provide \$3,000,000 to NCFST through the cooperative agreement. The \$3,000,000 in funding shall be exclusive of any additional initiative funds that FDA may award NCFST. (Page 709)

**Action taken or to be taken**

The National Center for Food Safety and Technology (NCFST) continues to make contributions toward ensuring the security of the nation’s food supply. A five year renewal of the cooperative agreement with NCFST was completed in FY 2004. FDA will continue to provide total funding of \$3,000,000 to NCFST.

**Item**

*Human Drug Compounding* – The conferees do not include language in the Senate report on human drug compounding. The conferees believe that drugs for human use compounded by pharmacists in response to a practitioner’s prescription or order in conformity with state law should be prepared according to established guidelines on quality, purity, and strength, and preparation-specific monographs when they exist. The conferees also recognize, however, that the nature of compounding and the medical need it serves makes it impossible for all compounded medications to be prepared according to pre-existing monographs, and doing so would infringe on the professional obligation of a medical practitioner to prescribe the optimal medications for their patients.

There are existing state laws and official United States Pharmacopoeia (USP) pharmacy standards which necessitate good compounding practices. However, the conferees believe it is desirable to develop additional formal monographs to provide additional guidance and conformity for doctors, patients and pharmacists.

Presently, the USP, a national drug standard setting organization recognized by Congress, has developed a number of monographs for individual compounded preparations. The conferees believe that a private sector partnership of involved organizations with demonstrated expertise regarding pharmacist compounding of preparations for humans should be expeditiously established to help assure a significant expansion of USP monographs and other relevant guidelines.

The conferees believe that the FDA should assist in the establishment of the private sector partnership to commence the expansion of available monographs relevant to pharmacist compounding of drugs for humans. The conferees encourage the FDA to request adequate funding in the fiscal year 2006 budget request to support this effort at increasing the number of formal monographs. (Page 709)

**Action taken or to be taken**

We do believe that having monograph standards could potentially improve the quality of compounded products with regard to identity, strength, purity and potency. However, unless there was an extensive testing and enforcement program to determine compliance with the monographs and take action in the event of non-compliance, having the monographs would have

virtually no effect on the quality of compounded drugs. Such a testing and enforcement program would require substantial FDA and/or State resources to implement.

The language as originally written would have required FDA to embark on a resource-intensive effort with the USP to develop monographs for compounded products. As there are thousands of compounded drugs on the market, and the number and kinds of drugs change daily, this would be a gargantuan effort. Furthermore, the language would not have ensured that FDA would have the resources to implement an effective testing and enforcement program. In the absence of adequate additional resources, the establishment of a program to develop and enforce monographs would take away resources from other programs, such as surveillance of marketed approved drugs.

**Item**

*Alpha-1 Antritrypsin Deficiency* – The conferees commend FDA for the progress made in bringing two additional plasma based therapies to market for the treatment of the progressive degenerative lung disease Alpha-1. Currently the only treatment for Alpha-1 is weekly infusions of plasma based augmentation therapy that is life sustaining and helps these individuals maintain lung function. Further, the Center for Biologics and Evaluation and Research (CBER) is recognized for meeting with consumer stakeholders in efforts to further the development of next generation therapies. The conferees encourage CBER to facilitate the development of novel and innovative therapies for the Alpha-1 community to treat the entire spectrum of individuals with Chronic Obstructive Pulmonary Disease. (Page 709)

**Action taken or to be taken**

The Center for Biologics Evaluation and Research (CBER) will continue to meet with consumer stakeholders to hear their concerns and to work with manufacturers to facilitate the development of novel and innovative therapies for the Alpha-1 community. With the licensure of three plasma-derived Alpha-1-Proteinase Inhibitor products, there is no shortage of intravenous Alpha-1 PI products at this time. However, assuring the safety and availability of Alpha-1 PI products remains a high priority and CBER will continue to monitor the situation and respond to any reports of shortages. The Center for Drug Evaluation and Review (CDER) will also work with manufacturers to facilitate the development of therapies for the Alpha-1 community to treat the entire spectrum of individuals with Chronic Obstructive Pulmonary Disease.

**Item**

*Biotechnology* – The conferees understand that the FDA frequently receives requests from foreign governments for FDA regulators to visit foreign countries to educate regulators on the evaluation of the safety of biotechnology. Providing information on the soundness of the U.S. regulatory process will promote the understanding of the benefits of biotechnology to human health and the environment and improve the climate for acceptance of U.S. agricultural products abroad. The conferees encourage FDA to allocate adequate funding so that agency representatives may perform this service. (Page 710)

**Action taken or to be taken**

In FY 2004, CFSAN/FDA played a lead role in developing the U.S. position for the Terms of Reference for new work by a second Codex Task Force on Foods Derived from Biotechnology

to be chaired once again by the Government of Japan. CFSAN/FDA in conjunction with Health Canada held a workshop on biotechnology food safety assessment for regulators in Mexico. CFSAN/FDA participated in a similar workshop with Australia for regulators in Jakarta, Indonesia, and neighboring countries. In addition, a CFSAN/FDA scientist served as an Embassy Science Fellow for two months in the Agriculture Office of the U.S. Embassy in Tokyo, Japan working on food biotechnology. CFSAN is also assisting FAO/WHO to prepare information that will assist developing countries in understanding the new Codex guidelines for the safety assessment of biotech foods. In FY 2005, CFSAN/FDA expects to participate in several international workshops and seminars to provide countries with information on FDA's food biotechnology policy and the Codex guidelines. These may include China, India, New Zealand, and the Philippines.

**Item**

*Consolidation and Fees* – The conferees direct the Department of Health and Human Services (DHHS) to include all anticipated consolidations that impact FDA in the President's budget requests submitted to Congress. Further, the conferees direct that none of the funds made available to FDA in this Act be used for any assessments, fees, or charges by DHHS unless such assessments, fees, or charges are identified in the FDA budget justification and expressly provided by Congress, or approved by Congress in the official reprogramming process as required in the General Provisions of this Act. (Page 710)

Action taken or to be taken

DHHS/FDA has included a table in this document, the President's budget request or Congressional Justification, entitled "DHHS Charges and Assessments". This table lists assessments, fees, or charges by DHHS and transferred from FDA.