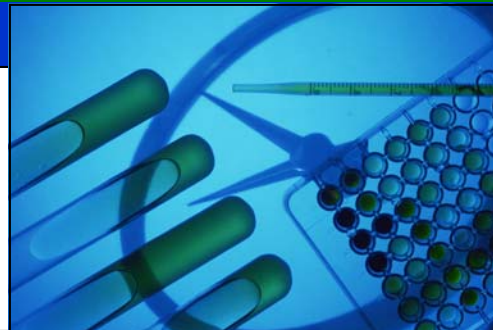


Life Sciences Report

► Volume 3, Issue 1
July 2008



The **Life-Sciences Report** will update clients and colleagues about issues of relevance in the life-sciences and related fields. The Report will cover a range of topics including new, or amendments to existing FDA law and regulation; the potential impact of these changes on the development and marketing of regulated products; human subject research issues including the conduct and monitoring of clinical trials; related patent matters; and relevant litigation.

This issue of the Report will highlight the following:

- **The Food and Drug Administration Amendments Act of 2007**.....pg. 1
 - Prescription Drug User Fees
 - Medical Device User Fees
 - FDA Advisory Committees and Conflicts of Interest
- **BEWARE: You Could Be Considered a Medical Device Manufacturer If You Store and Package Device Components**pg. 4
- **Physician Alert - Clinical Trials**.....pg. 4
- **Case Report - Terminally-ill Patients and Access to Experimental Drugs**.....pg. 5

► IMPORTANT NEW LEGISLATION AFFECTING FDA-REGULATED INDUSTRIES: **The Food and Drug Administration Amendments Act of 2007**

On September 27th, 2007, President Bush signed a major FDA reform initiative, amending the Federal Food, Drug, and Cosmetic Act. The new legislation includes a reauthorization of and amendments to the Prescription Drug User Fee Act (PDUFA), the Medical Device User Fee and Modernization Act (MDUFMA), the Best Pharmaceuticals for Children Act, and the Pediatric Research Equity Act.

The provisions of the **Food and Drug Administration (FDA) Amendments Act of 2007 (FDAAA)**, organized into eleven Titles or Chapters, will have an impact on many aspects of the development and marketing of prescription drugs, medical devices, and food products. The provisions address, among other issues, conflict of interest waivers for members of FDA advisory committees, the public posting of clinical trial results for both drugs and devices, mandated labeling changes, and requirements related to post-marketing studies.

Consistent with earlier user fee legislation, the FDA has agreed to performance and procedural goals to be achieved over the next five years. The final document includes specific provisions geared to the following issues: expediting application review times; making interactions with industry more efficient and responsive; extending oversight of drug safety, including timely review of proprietary names for drugs and biologics in an effort to reduce medication errors; review of internal agency management procedures and information technology capabilities; and establishing standards and goals for the review of direct-to-consumer television ads. A complete compilation of the performance and procedural goals is available at <http://www.fda.gov/oc/pdufa4/pdufa4goals.html>.

In this issue of Damon & Morey's *Life Sciences Report*, we provide highlights of two areas covered in the 2007 legislation: amendments to the user fee scheme for drugs and medical devices; and the expansion of conflict-of-interest provisions relevant to FDA Advisory Committee members.

In subsequent issues of the *Life Sciences Report*, we'll review other important features of the legislation.

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Title I. Prescription Drug User Fee Amendments of 2007

Of particular interest to: [Prescription Drug Manufacturers; Companies Involved in Direct- to- Consumer Advertising for Prescription Drugs; Non-Profit Medical Centers](#)

Reauthorizes and expands the user fee program through fiscal year (FY) 2012;

- Increases the total annual user fees to be collected for FY 2008 to \$392.8 million, \$87.4 million over the current level. The three basic categories of fees, first established in 1992, are human drug application and supplement fees; prescription drug establishment fees, and prescription drug product fees, each accounting for one-third of the total to be collected. Here are two examples of fees established for FY 2008: for a new drug or biologic application requiring clinical data - \$1,178,000; and for an application not requiring clinical data or a supplemental application with clinical data - \$589,000.
- Allows for significantly reduced establishment fees to be paid by non-profit medical centers holding approved applications for positron emission tomography drugs;
- Creates a new category of fees to be dedicated to post-marketing drug safety measures; this additional \$225 million in user fees will be collected over five years and will be phased in beginning with \$25 million in FY 2008, and increased by \$10 million annually through 2012;
- Initially established an interesting new user fee program for what was termed “advisory review of direct-to-consumer (DTC) prescription- drug television advertising”; “advisory review “ was intended to be a voluntary process initiated by manufacturers seeking FDA review of and commentary on DTC ads prior to public dissemination to ensure compliance with FDA standards and statutory requirements. However, the program has been delayed due to non-appropriation of the fees as required by the provisions of FDAAA. A future attempt to reestablish this component of user fees is anticipated.
- Companies must provide annual notice to the FDA stipulating the number of advisory reviews to be requested during the subsequent FY. This notice will constitute a legally binding commitment by participating companies to pay on or before October 1st of the FY the annual advisory review fee for the stipulated number of intended submissions. No refunds or exceptions are permitted.

Title II. Medical Device User Fee Amendments of 2007

Of particular interest to: [Medical Device Manufacturers, Single-use Device Reprocessors, Medical Device Distributors or Specifications Developers, and Hospitals](#)

- Reauthorizes medical device user fees through 2012;
- Stipulates the FDA filings that will trigger application fees, including filing of a premarketing application (PMA), a premarket report, a supplement, and a request for device classification information; the PMA filing fee for FY 2008 will be calculated from a base of \$185,000, taking into account a range of factors;
- Reduces significantly PMA and 510(k) fees, but introduces two new categories of device user fees: 1) an annual establishment fee; and 2) an annual fee for the filing of periodic reports related to design and manufacturing changes for Class III devices approved under a PMA or for reports on new studies involving these products;

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- Establishes the following Four New Standard (S) and Small Business (SB) Fees for FY 2008:
 - Submission of a 30-day notice - \$ 2,960 (S) \$ 1,480 (SB)
 - Submission of a 513(g) request for classification information - \$ 2,498 (S) \$ 1,249 (SB)
 - Annual fee for periodic reporting on a class III device - \$ 6,475 (S) \$ 1,619 (SB)
 - Annual fee for registration of a medical device establishment that is a manufacturer, a single-use device reprocessor, or a specification developer - \$1,706
- Amends provisions dealing with fee reductions available to a “small business”. A company may qualify as a small business if it reported gross receipts or sales of no more than 100 million in all affiliates, partners, and parent firms in the most recent tax year;
- Defines with more specificity those responsible for payment of establishment fees: device manufacturers; single-use device reprocessors; and device specifications developers, who do no manufacturing but distribute devices under their company names.
- Appropriates annual sums for FY 2008 – 2012 funding for the collection, review, and evaluation of post-marketing safety information on medical devices, with \$7,100,000. stipulated for FY 2008;
- Calls for a study on the number and causes of nosocomial infections (acquired during a hospital stay) attributable to new and reused medical devices.

Title VII. FDA Advisory Committees and Conflicts of Interest – More Transparency

Of particular interest to: [Physicians and Other Experts Who Serve or Are Considering Membership on an FDA Advisory Committee](#)

The FDA relies on outside expertise for independent advice on a range of pre- and post marketing issues. In the biologics, blood products, human drugs, and medical device areas alone, 43 Advisory Committees are called on to make recommendations to the Agency.

A confluence of issues served as the incentive for the provisions in Title VII (discussed in part below): the FDA's need for independent review by outside experts; the limited pool of experts in specific therapeutic areas; concern that the financial holdings of FDA Advisory Committee members had the potential to affect the independence of their review; and a perceived lack of transparency by the FDA in those instances when the Agency granted a waiver permitting a Committee member to be involved in a Committee deliberation and vote when the member (or immediate family - spouse, or minor children) had a financial interest that could be affected by the Committee's recommendation.

Here are some of the ways Title VII attempts to address these concerns:

- Specifies and broadens methods used to identify and recruit qualified experts to serve on FDA Advisory Committees;
- Calls for specific disclosure, prior to a Committee meeting, of all financial interests that could be affected by the Committee's recommendation;

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- Sets out a formula to reduce over five years the number of waivers granted by the FDA in those instances where a conflict exists, but the individual's specific expertise is required for the Committee's deliberations; the waiver may specify whether the individual may participate as a voting or non-voting member;
- Establishes measures to increase the transparency of waivers, including posting on the FDA's Web site at least 15 days prior to a Committee meeting the type, nature and magnitude of the financial interest involved and the reasons for granting the waiver.
- Requires the inclusion of the waiver disclosure in the public record and transcript of the Committee meeting.

▶ **BEWARE: YOU COULD BE CONSIDERED A MEDICAL DEVICE MANUFACTURER IF YOU STORE & PACKAGE DEVICE COMPONENTS**

The components of unapproved medical devices from other countries are finding their way into the United States and innocent companies are taking the heat when the FDA discovers these components.

The scheme involves contracts with United States storage, warehousing or light manufacturing companies by foreign entities. Components of the devices are shipped, often through Canada, to the U.S. entities where they are "assembled" and re-shipped. Although the "assembly" is limited to placing two or three components into a box, this constitutes the "manufacture" of a medical device and subjects the U.S. entity to FDA regulations for manufacturing and labeling of the device. In addition, since the device has not been approved by the FDA for marketing in the United States, it is considered an adulterated and misbranded device, and its importation and distribution by the U.S. entity represents violations of FDA's statute and regulations and subjects the entity to penalties.

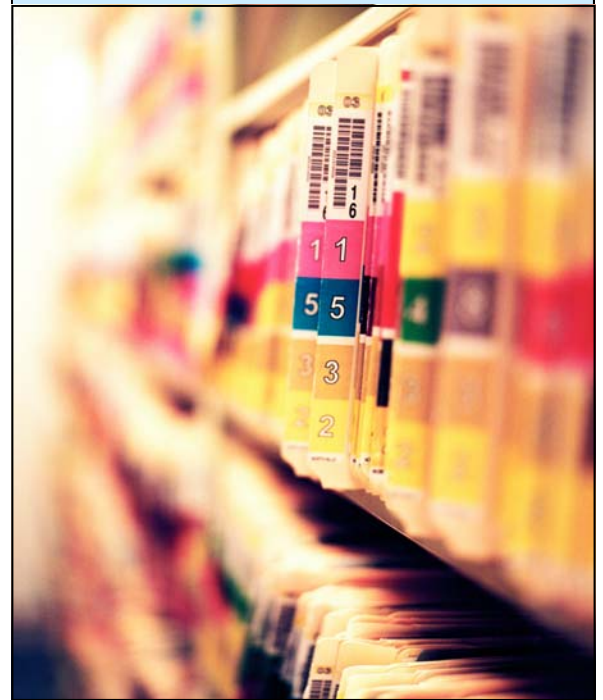
▶ **PHYSICIAN ALERT**

Know the Risks!

- Are you conducting clinical trials of either drugs or devices through your office practice?
- Are you protected from claims of lack of informed consent by end users?
- Are you protected from medical malpractice claims?

Be certain your contract with the pharmaceutical or medical device company protects your interests. Regular contract review can help determine any liability risks you might face.

For more information, contact Barbara Schifeling or Mary Raymond.



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▶ CASE REPORT: The Terminal Illness and Access to Experimental Drugs - Affirming the FDA's Role

Do competent, terminally-ill adults who have exhausted all other potential therapies have a constitutional right to access experimental drugs that have completed Phase I clinical trials? At this point the answer to that question is "no".

In a case followed closely by drug manufacturers, patients' advocacy groups, and physicians, the U.S. Court of Appeals for the District of Columbia refused to recognize a constitutional right of access for the terminally ill. The Court, relying on a Supreme Court precedent, rejected the argument that the Food, Drug, Cosmetic Act's safety requirement does not apply to the terminally ill: "for the terminally ill, as for anyone else, a drug is unsafe if its potential for inflicting death or physical injury is not offset by the possibility for therapeutic benefit." (*United States v. Rutherford*, 442 U.S. 544 at 555).

The case had been filed against the Food and Drug Administration (FDA) by **The Abigail Alliance for Better Access to Developmental Drugs**, which argued that "forcing patients to wait years for a drug to go through the process of clinical trials deprived dying patients of their right to self-defense, and violated the Fifth Amendment clause stating that people cannot be deprived of life, liberty or property without due process of law."

The FDA has had in place for a number of years several regulatory pathways through which patients and their physicians may seek access to drugs during Phase 2 and 3 of clinical trials. More recently, in an apparent response to the Abigail Alliance lawsuit, the FDA has proposed a clarification and an expansion of these options that seem to contemplate permitting access to investigational drugs under circumstances similar to those claimed by the plaintiffs.² The critical difference, of course, is that the FDA retains the authority to determine when, to whom, and under what circumstances early access will be permitted.

Congress has delegated to the FDA the responsibility to determine when a drug is safe and effective, and what evidence must be presented prior to commercial marketing. Recognition of a constitutional right to access experimental drugs in the absence of FDA oversight clearly would undermine the FDA's role, and given the highly toxic nature of many of these drugs, would shift largely unknown risk to desperately ill patients and their families.

Little is known about new drugs at the end of Phase I trials. To permit access outside of formal clinical trials suggests a therapeutic option that is illusory. An exclusion of the FDA's oversight role under these circumstances would constitute an amendment of the FDA's governing statute. This is a job for Congress not the Courts.

On Monday, January 14th, 2008, the U.S. Supreme Court rejected an appeal of the D.C. Circuit's decision in the case.

¹ Abigail Alliance for Better Access to Developmental Drugs and Washington Legal Foundation v. Andrew von Eschenbach, Commissioner, Food and Drug Administration and Michael Leavitt, Secretary, Dept. of Health and Human Services (US Court of Appeals, District of Columbia, Aug. 7, 2007)

² Expanded Access to Investigational Drugs for Treatment Use. Fed Reg Vol 71, No 240, 75147 Dec. 14, 2006.

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Ms. Shulman serves on several editorial boards, including the board of the Food and Drug Law Journal and the Journal of the Drug Information Association. She has authored many articles on legal, regulatory, and policy issues of relevance to the pharmaceutical and biotechnology industries, as well as on broader healthcare and malpractice law issues. Her current research work examines the role of pharmaceutical buying groups, and regulatory oversight of drug promotional activities.



Mary Raymond is Special Counsel practicing in the firm's Business and Corporate Department. A member of the Health Care, FDA and Medical Device and Pharmaceutical Practice Groups. Chair of the firm's FDA Practice Group, she advises clients on matters involving FDA petitions, HACCP, product recalls, regulatory compliance, retail establishments, clinical drug trials, NDAs, OTC drug issues, drug labeling/marketing, medical device approvals and recalls, biotechnology/safety, import/export issues.

She is a member of the American Health Lawyers Association, the Association of Food and Drug Officials. She lectures frequently on FDA and health care issues.

Mrs. Raymond is a former regional liaison to the Cornell statewide Food, Diet and Health Program Committee and chairperson of the Cornell Cooperative Extension Marketing Committee.



Barbara Schifeling is a Partner at Damon & Morey LLP, practicing in the firm's Litigation Department, concentrating in the areas of medical malpractice defense and environmental coverage litigation.

Ms. Schifeling devotes a significant portion of her practice to defending medical professionals who are the subject of litigation, is a frequent lecturer on medical/legal issues to members of the health care community and has presented mock trials to hospital risk managers and nursing groups. She is co-chair of the firm's Health Care Practice Group.

She has conducted classes at the Nursing School of the State University of New York at Buffalo, and has presented at a joint medical/law school seminar. Ms. Schifeling has been an adjunct faculty member at SUNY at Buffalo School of Law where she taught a course on depositions.

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