

# Modernizing The FDA: An Incremental Revolution

A 1997 law sets the stage for continued scrutiny of the Food and Drug Administration.

*by Richard A. Merrill*

**PROLOGUE:** In November 1997 Congress passed a sweeping reform of one of the nation's oldest public health laws: the Federal Food, Drug, and Cosmetic Act. Unlike past legislation aimed at the Food and Drug Administration (FDA), the Food and Drug Administration Modernization Act (FDAMA) affects most of the products that the agency regulates—foods, drugs, and medical devices. Implementing the new law, in a span of eighteen to twenty-four months, “is one of the most demanding challenges faced by the agency in its 92-year history,” the FDA stated last summer in a Message to FDA Stakeholders ([www.fda.gov/oc/fdama/comm/message.htm](http://www.fda.gov/oc/fdama/comm/message.htm), 22 July 1998). In this paper Richard Merrill, a long-time expert on and former chief counsel to the FDA, assesses the new law's impact on the agency's responsibilities. In his view, the legislation represents a new level of congressional fine-tuning of the agency's charter, giving it new authorities but also detailed instructions as to how it is to carry out its expanded mission. This reflects a more general propensity on the part of Congress to limit agencies' discretion and control their operations more tightly.

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**ABSTRACT:** The U.S. Food and Drug Administration (FDA) is responsible for protecting consumers from unsafe or ineffective drugs and medical devices. The agency's role is defined by a growing and increasingly complex set of statutes, which reflect Congress's desires, on the one hand, to prevent product hazards and, on the other, to expedite FDA review and approval of promising new medical technologies. Congress's latest attempt to calibrate regulation to achieve these goals, the 1997 Food and Drug Administration Modernization Act, endorses certain of the FDA's own innovations and changes in the agency's ways of doing business.

**M**ORE THAN A YEAR AGO Congress enacted the immodestly titled "Food and Drug Administration Modernization Act of 1997" (FDAMA, P.L. 105-115). The act's passage culminated a decade-long debate, which had been rekindled by the Republican victory in the 1994 congressional elections. From this genesis one might assume that the Modernization Act represents a victory for advocates of deregulation of medical product development, marketing, and use. However, the act also contains features that appeal to supporters of regulation. Many of its "reforms" codify initiatives that the Food and Drug Administration (FDA) had initiated before Congress acted.<sup>1</sup>

One is tempted, therefore, to suggest that the Modernization Act contains less than meets the eye. This conclusion would be too cynical, because the act does make some significant changes in the FDA regime. More important, its passage establishes an inescapable framework for congressional debate over future, and more radical, changes in the law regulating medical products: "drugs" and "devices" in the terminology of the Federal Food, Drug, and Cosmetic Act (FDCA).

This paper focuses on the provisions of the Modernization Act that apply to such drugs and medical devices. Many of these reflect a familiar pattern of administrative and legislative reaction that commenced with the most important single set of amendments to the original FDCA: the Drug Amendments of 1962 (P.L. 87-781).

## Regulation And Reaction

Passage of the 1962 drug amendments was triggered by the early discovery of deformities in children born to women, most in Europe, who had taken thalidomide to prevent morning sickness. This "near miss" galvanized Congress to change the law governing new medications.<sup>2</sup> First, and most famously, the 1962 amendments required makers of new drugs to demonstrate that their products were effective as well as safe. Second, they specified that effectiveness had to be proved by "substantial evidence," defined as including "adequate and well-controlled clinical studies"—a requirement that later be-

came known as the FDA “gold standard.” Third, they forbade marketing until the FDA agreed that a drug had been shown to be safe and effective. This meant that the introduction of new drugs would be hostage to the FDA’s ability to process, review, and approve applications—and, perhaps even more important, to Congress’s willingness to provide the agency with the resources necessary to carry out these functions.

The FDA’s drug approval process quickly became the single most important function that the agency performed and, soon, the target of fierce but quite divergent criticisms. For more than a decade the sharpest critics were those who believed that the FDA was slow to address hazards associated with old drugs and careless in guarding against the hazards of new ones.<sup>3</sup> Other critics, increasingly vocal, challenged the FDA for failing to approve, or being slow in reviewing, new medicines. They contended that the agency was preventing or delaying U.S. citizens from gaining access to important new medications that were available to patients and physicians in other countries. Sam Peltzman’s main target was the changes in the law that Congress made in 1962.<sup>4</sup> Others focused on the FDA’s risk-averse administration of the new standards.<sup>5</sup>

Evidence that important medications were taking longer to reach American patients eventually helped to convince FDA officials that the agency’s drug review process required reform.<sup>6</sup> The agency established a “fast-track” review of drugs that promised significant treatment advances.<sup>7</sup> It relied increasingly on outside experts, whose views about the risks and benefits of new drugs were expected to be less cautious than those of career reviewers.<sup>8</sup> And, spurred by the acquired immunodeficiency syndrome (AIDS) crisis, it formalized means by which seriously ill patients could get experimental therapies before they were approved for general marketing.<sup>9</sup>

But even as the FDA sought to respond to the charges that its approval process was too cautious and cumbersome, the cost of developing new drugs continued to rise. Academic standards for the design, conduct, and analysis of clinical trials became increasingly rigorous and elaborate.<sup>10</sup> Clinical trials took longer and involved larger patient populations. Thus, by the early 1990s it was widely believed that mere administrative “reforms” had not made, and perhaps could not make, a major impact on the “drug lag.”

In 1983 and 1984 Congress passed two statutes to restore incentives that critics of the drug approval system claimed had been eroded. Neither the Orphan Drug Act (P.L. 97-414) nor the Drug Price Competition and Patent Term Restoration Act (P.L. 98-417), the latter also known as the Waxman-Hatch Amendments, squarely addressed charges that the FDA was too cautious or its processes

too slow. Both laws focused instead on the incentives for discovery and development of drugs. The Orphan Drug Act sought to spur investment in treatments for “rare” diseases or conditions by providing tax credits for clinical trial costs and guaranteeing some market exclusivity for drugs that gained approval. The Waxman-Hatch legislation employed the same “exclusivity” reward for pioneer formulations, and it also provided for restoration of a portion of the patent life that expired during clinical testing and FDA review.

In 1992 Congress for the first time sought to change the FDA’s drug review process. The Prescription Drug User Fee Act (PDUFA, P.L. 102-571) simultaneously addressed the FDA’s need for resources and the way it conducted drug reviews. By authorizing the agency to charge a fee for processing applications and requiring that most of the proceeds be devoted to hiring and training of additional reviewers, PDUFA confronted the FDA’s claim that any “lag” was largely a result of systematic underfunding. Simultaneously, Congress exacted from the agency a set of staged commitments to speed up decisions on new marketing applications.

FDA Commissioner David Kessler’s bet—that additional resources and reeducation of the review staff could significantly improve the FDA’s performance—paid off.<sup>11</sup> Although manufacturers questioned the FDA’s own accounting, the agency’s claims that the “drug lag” had been erased and that the United States was approving important drugs faster than other countries were never successfully rebutted. Thus, by 1996 most U.S. drug manufacturers had become supporters of the user-fee regime. But continuity of the scheme was not guaranteed, because Congress had provided that it would “sunset” automatically in five years. For the most successful “reform” of the past generation to continue, Congress had to enact a new law. The user-fee law thus became the vehicle for debate about, and enactment of, the other features of the FDA Modernization Act.

## The FDA Modernization Act

■ **Renewal of the prescription drug user-fee program.** Congress’s wish to reauthorize the user-fee program drove the legislative process. FDAMA empowers the FDA to collect fees of up to \$250,000 for processing drug-marketing applications for an additional five years.<sup>12</sup> The total contributed to the FDA budget will exceed \$550 million during the life of the program.<sup>13</sup>

Supporters of the original user-fee law wanted to make sure that this new revenue did not provide an excuse for the White House or Congress to reduce the FDA’s tax-supported budget. Thus, PDUFA established what came to be termed a “waterline” below which the agency’s base budget could not fall. The 1997 law reenacts this fea-

ture and establishes a complicated formula for assuring that the FDA's tax-supported funding for drug regulation is protected during the life of the program.<sup>14</sup>

A second key element of the user-fee scheme is the establishment of FDA performance goals. Neither the FDA nor the Bush White House was willing to make the agency's original commitments part of the statute; they appeared in a "side letter" sent to Congress by the FDA. The FDA met or exceeded all of its initial goals, and it agreed to slightly more ambitious time lines in the 1997 legislation.

■ **Reforms of the FDA's new drug approval process.** Republican proponents of FDA "reform" were determined to make changes in the agency's process for reviewing product applications. Drug manufacturers had their own "wish list," and so did the FDA. The final legislation reflects the desires of all three constituencies.

*Number of studies required.* It had long been the FDA's position that the statutory "substantial-evidence" standard for proof of a drug's effectiveness generally requires at least two "well-controlled" Phase III clinical studies.<sup>15</sup> The agency also acknowledged, however, that it could approve a drug based on a single study, for example, when the drug offered treatment for an otherwise untreatable disease.

FDAMA codifies and expands the FDA's discretion to base approval on a single controlled study, plus what the law terms "confirmatory evidence."<sup>16</sup> Whether to approve a drug based on such a "lesser" showing of effectiveness, however, is essentially up to the FDA. Although it is difficult to envision circumstances in which the agency's insistence on two studies would be overturned by a court, the statutory clarification might strengthen a manufacturer's case before an FDA advisory committee.

*Representativeness.* Two provisions of the Modernization Act address the desire of clinicians and others to make clinical trial populations more representative of the patients who are likely to use drugs. The debate over the inclusion of women in clinical trials is not a new one.<sup>17</sup> Less attention has been given to participation by minorities.<sup>18</sup> Taking a cautious approach, the Modernization Act merely instructs the FDA to consult with the National Institutes of Health (NIH) and industry representatives to develop guidance on the inclusion of women and minorities in clinical trials.<sup>19</sup> Beyond this, the law imposes no obligations on the FDA or drug sponsors.

FDAMA embodies a more proactive approach to studies in pediatric populations. In the past the FDA rarely insisted that a drug be studied in children; its customary posture has been to require labeling that specifies that such studies have not been conducted. As a result, many drugs that are widely used in pediatric populations have gained recognition of their utility and risks through clinical

use. The Modernization Act does not mandate the inclusion of children in clinical trials but does provide incentives for manufacturers to undertake such studies.<sup>20</sup> The primary incentive is the addition of six months to any period of marketing exclusivity or continuing patent protection if a drug sponsor agrees to undertake studies in children. Moreover, the act does not leave the initiative to conduct pediatric studies solely with the companies. It establishes a multi-step procedure by which the FDA is first to determine which drugs should be studied in children and then initiate agreements with manufacturers to conduct such studies. In these ways, the act responds to a controversial initiative that the FDA launched in August 1997, in which the agency asserted legal authority to require manufacturers to conduct pediatric studies even if they did not wish to market their drugs for pediatric use.<sup>21</sup>

*Expedited review.* Nearly two decades ago the FDA established a framework for expedited review of drugs that promise a significant advance over existing therapies. Later, by regulation, the agency announced that it would consider early approval of drugs that address unmet medical needs resulting from serious or life-threatening conditions.<sup>22</sup> On more than one occasion it has approved such drugs based on a single Phase III study and, occasionally, after the conclusion of Phase II studies. In evaluating drugs for the treatment of AIDS, it has accepted evidence of effect on “surrogate endpoints” rather than insisting on proof of extended survival.

The Modernization Act essentially codifies the framework that the FDA devised.<sup>23</sup> It ratifies the agency’s authority to require post-approval “Phase IV” studies for such drugs and to review promotional materials prior to their use. It also provides for expedited withdrawal of approval if experience reveals unanticipated safety problems or undermines the agency’s initial finding of effectiveness. The law also allows a manufacturer to request “fast-track” treatment and obligates the agency to respond within thirty days. Finally, the law provides for a “rolling” new drug approval (NDA) for a fast-track drug, permitting the FDA to begin review of portions of an application as they are completed rather than waiting for the complete application to be assembled and filed.

FDAMA includes provisions to publicize the FDA’s fast-track system and the potential availability of drugs for life-threatening disease.<sup>24</sup> The agency is directed to establish, with the NIH, a program for providing information to clinicians and patients about ongoing research into treatments for life-threatening diseases. The prescribed vehicle is a registry of clinical trials, containing information about eligibility criteria, trial sites, and persons to contact. The objective is to facilitate enrollment by eligible patients or applica-

tion by a patient (or his or her physician) for access under one of the FDA's various "compassionate" or "parallel-track" programs.

*Use of expert advisers.* New FDCA section 505(n) directs the FDA to consult scientific advisory committees for advice and recommendations on the clinical study and, later, marketing approval of new drugs. This provision is genuinely old news. The FDA's Drug Center has used expert advisory committees since the early 1970s. The committees' role was at first controversial among members of Congress, who believed that the committees would weaken the agency's protective posture, and among staff reviewers, who saw their influence threatened. Manufacturers generally have supported the agency's use of these committees, although they often have complained about a lack of consistency in their functions and procedures.<sup>25</sup>

The debate over the FDA's role has advanced to the point that Congress has now mandated, rather than reluctantly tolerated, a role for advisory committees. The 1997 act does not, however, leave the establishment or roles of advisory committees to agency discretion. Moreover, it attempts to limit staff influence by stipulating that committees shall be appointed and overseen by the director of the FDA's Drug Center, not the heads of reviewing divisions.

Finally, the advisory committees are empowered to adjudicate disputes between agency reviewers and drug sponsors.<sup>26</sup> The lack of any formal mechanism for resolving such disputes has been a recurrent complaint among manufacturers. The Modernization Act also requires the FDA to establish channels by which a frustrated sponsor can get prompt higher review of an adverse staff determination.<sup>27</sup>

*Approval criteria.* Product sponsors have often charged that the FDA's approval criteria—that is, how a drug should be studied and what study results must show—are elusive targets. In recent years the FDA managers have encouraged meetings between sponsors and agency reviewers before clinical trials commence.<sup>28</sup> This so-called pre-clinical trials conference often was followed by a later meeting prior to the submission of the completed NDA. Observers have attributed part of the FDA's success in meeting PDUFA's performance goals to increased reliance on these sessions.

The amended statute makes such meetings obligatory.<sup>29</sup> The FDA is required, on written request, to meet with a sponsor to reach agreement on the design of "pivotal" trials for a drug or Class III medical device. The agency may decline such a meeting only if the sponsor fails to provide requested information or if agency officials conclude that, and explain why, such a meeting would be premature. The agency is to share minutes of any meeting with the sponsor. If an agreement on study design is reached, it must be put in writing. Thereafter, the FDA cannot change the regime unless the

division director determines, in writing, that “a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.”

■ **Changes in drug promotion and labeling rules.** In many areas, as I have noted, the Modernization Act essentially codifies measures that the FDA had already undertaken. However, in one area (dissemination of information about drugs and devices) FDAMA is more ambitious. It addresses for the first time the conditions that a manufacturer must satisfy before it may promote the economic benefits of a product. It also allows manufacturers, under defined circumstances, to disseminate information about uses that the FDA has not yet approved.

*Economic information.* Section 114(a) of the Modernization Act adds to the misbranding section of the FDCA a new paragraph addressing so-called health care economic information. There is a growing demand for such information from managed care plans, other providers, and insurers. Historically, the FDA has insisted that claims about a drug’s cost-effectiveness meet the act’s “substantial evidence” standard.<sup>30</sup> This demand has been a significant barrier to the study and reporting of the economic impact of drug usage.

The Modernization Act defines *health care economic information* as “any analysis that identifies, measures, or compares the economic consequences . . . of the use of a drug to the use of another drug, to another health care intervention, or to no intervention.” It then relaxes the FDA’s traditional standard permitting claims that are based on “competent and reliable scientific evidence.” The latter phrase is elaborated in the House Report as evidence meeting standards that are “widely accepted by experts” in the field.<sup>31</sup> The act goes on to state that a drug whose manufacturer provides health care economic information meeting the “competent and reliable evidence” standard will not be considered misbranded. However, the act stipulates, such information must “directly” relate to specific indications that the FDA has approved.

FDAMA’s authorization of cost-effectiveness claims for approved drugs thus is couched in vague language whose meaning will become clear only with experience.<sup>32</sup> Congress apparently wanted to proceed with caution, for it directed the comptroller general to study the impact of its amendments. Furthermore, the accompanying House Report says that the FDA may require a manufacturer that plans to disseminate health care economic information to submit it to the agency when it is first disseminated.<sup>33</sup>

*Off-label indications.* Without question, the most controversial “reform” made by the Modernization Act is reflected in new subchapter D of the FDCA. These sections authorize manufacturers of ap-

proved drugs, biologics, and medical devices, under prescribed circumstances, to disseminate information about uses of their products that the FDA has not yet approved—so-called off-label indications. The FDA has long taken the position that any promotion of the off-label use of an approved product is a violation of the law.<sup>34</sup> The FDA's position had been questioned, on both policy and legal grounds, and its application was recently successfully challenged in court as a violation of the First Amendment.<sup>35</sup>

The 1997 act represents a modest victory for manufacturers and sellers of medical products. The key features of subchapter D can be summarized as follows: (1) The drug, biologic, or device for which information is distributed must have been approved by the FDA (Sec. 551[6][1]). (2) The information disseminated must be either an unabridged reprint of a peer-reviewed journal article about a clinical investigation that would be considered “scientifically sound” or a reference publication containing similar information (Sec. 552). (3) The manufacturer must submit the information to the FDA no less than sixty days before beginning distribution (Sec. 551[6][4]). (4) The manufacturer must include with the information to be disseminated a prominent statement that the use discussed has not been approved, a copy of the FDA-approved labeling (listing approved uses), and disclosures relating to authorship and funding of the studies discussed (Sec. 551[6][6][A]).

In addition, to be eligible to disseminate permitted information about an off-label use, the manufacturer must either have submitted or certify that it will submit a supplemental application seeking approval for the use. If no supplemental application has yet been submitted, the manufacturer must submit to the agency a proposed protocol and schedule for completing the necessary studies for submission within thirty-six months.<sup>36</sup>

If these conditions are met, qualifying information may be disseminated to medical practitioners, pharmacy benefit managers, insurers, group health plans, and governmental agencies, but not directly to patients.<sup>37</sup> This means that off-label uses, regardless of how well supported they are scientifically, may not be mentioned in advertisements for prescription drugs directed at consumers.

The amendments go further and define the “scientific or medical journal[s]” whose articles on off-label uses may be eligible for dissemination.<sup>38</sup> The amended law also gives the FDA special authority to take summary corrective action—halting dissemination or requiring corrective disclosure—if a manufacturer fails to comply with any of the foregoing requirements or to fulfill its commitment to complete an application for approval of the new indication.<sup>39</sup>

## Changes In Medical-Device Regulation

The Modernization Act made several changes in the FDCA provisions applicable to medical devices, which some observers consider or hope will prove more significant than the reforms made for drugs.

Prior to 1976 medical devices were subject to very modest regulatory controls.<sup>40</sup> No device was required to have FDA approval before it could be commercialized. Public reaction to a few well-publicized examples of regulatory inadequacy—most notably perhaps the Dalkon Shield contraceptive device—precipitated passage of the 1976 Medical Device Amendments to the FDCA. These amendments replaced the existing simple regime with a scheme far more complicated than the one applicable to prescription drugs. The statute grew in length by more than one-third. The amendments provided for three different levels, or “classes,” of regulatory control, calibrated to the risk posed by a device, and established a mechanism for assigning individual devices to the appropriate class. Only devices that posed significant risks—about 10 percent—were to require individual clinical proof of safety and effectiveness. However, the amended law mandated that the FDA be notified prior to the marketing of any post-1976 device. Over time this requirement evolved into a mini-premarket review system for new products.

The FDCA device provisions were amended twice earlier this decade. In each instance, Congress (characteristically) attempted both to facilitate the introduction of new devices and to expand the FDA’s authority to control the marketing and use of unsafe devices. Thus, by 1997 the regime established a generation earlier had become even more cumbersome, and device manufacturers had become some of the FDA’s sharpest critics.

■ **Reforms in device regulation.** The complexity of the regulatory scheme for devices is an obstacle to any simple summary of the changes Congress made in 1997. Among the more important are an instruction to the FDA to exempt more low-risk devices from the 1976 law’s premarket notification requirement; a provision permitting makers of novel but low-risk devices to escape the law’s default requirement of premarket notification; permission for manufacturers of devices in clinical trial to implement and report, rather than waiting for the FDA approval of, modifications of the device or the trial protocol; and a provision barring the FDA from holding approval of a device hostage to the sponsor’s compliance with other unrelated regulatory requirements.<sup>41</sup> The 1997 act also relaxed the law’s reporting and record-keeping obligations for health care providers who use medical devices.<sup>42</sup>

■ **Third-party review.** The most controversial amendment made

by the Modernization Act to the FDCA device provisions provides for “third-party review” of new devices.<sup>43</sup> Impatient with the FDA’s tardy processing of premarket approval applications for Class III devices and even more frustrated by the agency’s failure to meet the statutory ninety-day deadline for action on premarket notifications for all post-1976 devices, manufacturers advocated privatizing the review process. They argued that a device sponsor should be able to seek review by one of several nongovernmental “third parties” accredited by the FDA, which in turn would make a recommendation to the agency. They contended that an alternative channel would expedite regulatory approvals and bolster incentives for innovation.

The concept of third-party review never gained the support of drug manufacturers, probably because the user-fee scheme was achieving their goals. The FDA at first opposed the idea unequivocally, but in 1996, under pressure from the White House, the agency initiated its own pilot program.<sup>44</sup> The Modernization Act codifies and enlarges the FDA experiment. It directs the agency, within one year, to “accredit” organizations that will be considered qualified to perform reviews on request by device manufacturers.<sup>45</sup> The scheme applies only to so-called 510k notifications—premarket notifications—for new devices that are claimed to be similar to a device already on the market.<sup>46</sup> The manufacturer of a Class III device may not opt for external review of its premarket approval application. Furthermore, only low-risk devices—devices similar to products already in Class I or Class II—are eligible.<sup>47</sup> Accredited review bodies will not have authority to approve marketing; their assessments are to be submitted to the FDA, which then has thirty days in which to accept or reject the action recommended.<sup>48</sup>

The new provisions set forth criteria that the FDA must apply in evaluating organizations that seek to become accredited review bodies.<sup>49</sup> These include demonstrated technical competence, clear scientific independence, and adherence to a transparent process of review. Accredited organizations may charge for their services but may have no other financial ties to any sponsor of a device.<sup>50</sup>

The experiment that Congress has authorized is precisely that: an experiment. The FDA’s authority to accredit third-party review organizations expires no later than five years from the enactment of the 1997 act, or as soon as the agency has acted on approximately one-third of the 510k notifications submitted.<sup>51</sup> Within the same period the U.S. General Accounting Office (GAO) is to study the impact of the third-party review program.<sup>52</sup>

It is far from clear whether demand for this third-party review will be great enough to show the utility of Congress’s experiment. When it launched its own pilot program, the FDA was conservative

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in approving applicants to perform reviews. The agency turned down several candidates, including at least one university medical department, out of concern about potential conflicts of interest. Device manufacturers themselves proved to be reluctant to allow their own products to become the subjects of the FDA's experiment.

■ **Mutual recognition and international harmonization.** Any overview of the Modernization Act would be incomplete without some reference to the law's attention to the globalization of the market for medical products. The United States is both an exporter and an importer of drugs and devices. There is mounting industry pressure on the regulatory bodies of the major industrialized countries to unify their standards for marketing. For their part, regulatory officials have come to acknowledge their limited ability, through physical inspection, to assure that imported products meet domestic requirements. Hence, in the medical products area, the FDA has entered into information exchange and work-sharing agreements with several of its counterparts throughout the world.<sup>53</sup>

Such international agreements can take a variety of forms, ranging from mere sharing of information to effective delegation of regulatory oversight. Their viability depends on verification of the capabilities and integrity of foreign agencies and requires some confidence in the comparability of regulatory standards. In 1997 the United States entered into an important umbrella agreement with the European Community (EC) that contemplates future specific agreements for reciprocal recognition of pharmaceutical inspections and premarket evaluation of new medical devices.<sup>54</sup>

FDAMA gives these efforts explicit albeit cautious endorsement. It directs the FDA to take steps to assure that the agency's good-manufacturing-practice requirements for devices conform “to the extent practical” with internationally recognized standards.<sup>55</sup> Another provision directs the FDA to support the U.S. Trade Representative's efforts to harmonize regulatory requirements that will “continue consumer protections consistent with the purposes of” the FDCA.<sup>56</sup> A third specifically obligates the FDA to support “mutual recognition agreements” with the EC.<sup>57</sup>

## Conclusions And Policy Recommendations

Passage of the FDA Modernization Act was widely publicized. President Bill Clinton signed the legislation before a bipartisan clus-

ter of proud congressional supporters. The lay press was appropriately impressed.<sup>58</sup> The FDA pointed with pride to the provisions that codified initiatives it had already launched, and trade associations boasted about their legislative victories. But the *Journal of the American Medical Association* devoted only three brief paragraphs to the 100-page law, and the *Lancet's* summary of the legislation, a half page.<sup>59</sup>

■ **Importance.** FDAMA surely will not prove as important as several other legislative revisions of the agency's charter, such as the 1976 Medical Device Amendments, the 1962 Drug Amendments, or even the 1984 Waxman-Hatch Amendments. These laws fundamentally changed the legal standards for the marketing of new products. FDAMA largely accepts the basic framework and seeks to improve the FDA's implementation. With two exceptions, its enactment is a better barometer of congressional attitudes toward executive-branch regulation than it is a blueprint for significant FDA reform.

Without question, implementation of FDAMA will dominate the FDA's agenda for several months, perhaps years. The act requires the FDA to produce a long list of new administrative policies and procedural regulations, and already the agency is being pressed by Congress to defend its interpretation and explain delays. However, Congress has provided no new resources to carry out these tasks. Indeed, the single most pressing dilemma facing the FDA's managers is the growing gap between resources and public—including congressional—expectations.

■ **Innovations.** At the same time, one should not dismiss FDAMA's few genuine innovations. The act inaugurates two notable experiments. One is its authorization for makers of drugs and devices to disseminate information about off-label uses. The FDA opposed this and might have frustrated it by imposing conditions that most manufacturers would not have attempted to satisfy. However, a recent court ruling that partially invalidated, on First Amendment grounds, the agency's historical policy may force it to tolerate more robust communication about off-label uses than even FDAMA permits.<sup>60</sup> The second notable experiment is the directive to the FDA to implement a pilot program for third-party review of device premarket notifications. This could prove to be the first step toward greater regulatory reliance on private assessments of medical products generally.

■ **Continued scrutiny.** The impact of these and a handful of other changes made by FDAMA will be the focus of continuing scrutiny among makers of medical products, providers of medical care, and, most significantly, the members of Congress who crafted the changes. These groups are already anticipating the next opportunity for revision of the FDCA. The most significant effect of

FDAMA is its implicit assurance that the FDA reform will be on Congress's agenda again within five years. FDAMA reauthorized the prescription drug user-fee program, but only for five years. This program is so important, to both the drug industry and the FDA, that neither can afford to allow it to lapse or die.

**H**ISTORICALLY, MAJOR CHANGES in the FDCA have been a response to apparent public health crises. With the enactment of FDAMA, and its inextricable link to reauthorization of prescription drug user fees, amendment of the substantive provisions of the FDCA is destined to become a recurrent topic on the congressional agenda. We thus can expect the statute to continue to grow in both complexity and detail, reflecting Congress's determination to narrow the agency's discretion and flexibility. The FDCA has long since ceased to resemble the "Constitution" that an agency official once proclaimed.<sup>61</sup> The current edition of the law reads more like an insurance policy.

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## NOTES

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