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# HOW FDA IS CAUSING A TECHNOLOGICAL EXODUS:

*A Comparative Analysis of Medical Device Regulation — United States, Europe, Canada, and Japan*

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## Abstract

Since World War II, medical devices have become increasingly important in the practice of medicine for diagnosis, monitoring, and therapy. Devices such as pacemakers, cardiac replacement valves, artificial joints, CAT scanners, defibrillators, and thousands of others have revolutionized medical practice.

Despite the diversity of regulatory regimes in the United States, Europe, Canada, and Japan, it is clear that no country has regulated medical devices as extensively or as rigidly as the United States. It is also clear that despite the less stringent regulation of medical devices in Europe, Canada, and Japan, the people of those countries in general have not suffered because of unsafe or ineffective products. In the words of Jim Phillips, vice president at Clarus Medical Systems, "It's not that [these countries] don't have standards. They do. They have specs and you can design by them. The FDA has no specs. It's a black hole."

Medical device regulators elsewhere wield authority over manufacturers that is far less discretionary than the authority wielded by FDA. Respected independent testing organizations in Europe, known as "Notified Bodies," perform the assessments of conformity with standards. Additionally, manufacturers abroad know that certain established standards must govern their operations.

In contrast, the process in the United States is arbitrary and capricious; individual reviewers can and routinely do alter the requirements for product approval as the process unfolds. No matter what the company does, FDA may still withhold approval for any reason, or without a reason. Given FDA's unpredictability and its capacity for destruction, the agency can aptly be described as a "loose cannon".

During the past three to four years, FDA has accepted fewer premarket approval (PMA) and 501(k) (for devices "substantially similar" to some on the market) applications. In the same time period, the average review time for PMAs and 501(k)s increased from 150 days in the late 1980's to 900 days in 1994, in spite of the fact that the FDA is required to rule on them within 90 days. The buildup of a huge backlog of 501(k) applications in 1992 and 1993 led bewildered applicants to speak of a "black hole" and an "eternal limbo."

No corresponding retardation of approvals has occurred elsewhere. Therefore, U.S. device manufacturers have been placed at a substantial disadvantage relative to competitors in other countries. The U.S. approval slowdown has added great costs, delays, and unpredictability to what was already a relatively cumbersome approval process.

Without doubt thousands of Americans have suffered and died because of this "device lag." However, foreigners have definitely benefitted from their early access to the latest,

most innovative devices. Dr. Michael Werner, an American surgeon, observed, "I don't know who [FDA officials] are protecting. Sometimes you wonder."

FDA enforcement authorities, who have long fancied themselves "cops," have become much more hostile, uncommunicative, and punitive during the past four years, as Commissioner Kessler has given the highest priority to aggressive enforcement. Compliance officials promoted a philosophy of "act now, talk later."

FDA has failed to clarify for companies precisely what actions constitute compliance. In contrast, in Europe the companies work with the Notified Bodies, who must deal with them fairly and cooperatively or risk losing business. By making itself the sworn enemy of the device industry, FDA has necessarily made itself the enemy of public health.

Because of the more hostile regulatory environment, U.S. firms have reacted by abandoning product lines or R&D projects, or by transferring work to Europe. Grant Heidrich of the Mayfield Fund says, "We counsel our companies, 'don't screw around with the FDA; let's move these trials to Europe where there's a reasonable process.'" Said Rob Michiels, president of Interventional Technologies, "By the time we're approved in the U.S., that product will have been available in Europe on the free market for three to four years." Numerous surveys have also indicated the growing trend toward relocating research, development, and clinical trials abroad.

In sum, as Dr. Keith Lurie of the University of Minnesota noted, "We're a year and a half behind the rest of the world, thanks to the FDA. We don't get the ... equipment we need to save lives." FDA's policies are, for Americans, a public health problem.

# A Comparative Analysis of Medical Device Regulation: United States, Europe, Canada, and Japan

Robert Higgs[1]

Since World War II, medical devices have become increasingly important in the practice of medicine for diagnosis, monitoring, and therapy. Devices such as cardiac pacemakers, replacement valves for the heart, artificial joints, CAT scanners, defibrillators, and thousands of others have revolutionized medical practice. As the medical device industry grew, it was subjected to government regulation ostensibly intended to assure the safety and efficacy of the products. The type and degree of regulation varied from country to country. Indeed, some countries scarcely regulated devices at all. This diversity complicates a survey, but at the same time it makes possible an inquiry into whether more stringent regulation has affected the cost or quality of products, the rate of innovation, and therefore the well-being of consumers.

An additional complication arises because the regulatory regimes of the European Union, Canada, and Japan are currently in transition to new arrangements more similar, though not identical, to that of the United States. These changes are part of an ongoing effort to harmonize national regulatory requirements for medical devices around the world. Some countries have made the transition quicker than others, and the specific organizations authorized to implement the new system vary from country to country.

Despite the past and present diversity of conditions, it is clear that no country has regulated medical devices as extensively or as rigidly as the

United States; nor does any country intend to adopt a system identical to the U.S. system. The architects of the new systems abroad all recognize that the U.S. system imposes unnecessary costs, impedes the capacity of device firms and consumers to act quickly and flexibly, and discourages the rapid innovation firms require to compete in today's world by offering consumers the best, most up-to-date equipment at affordable prices.

The following analysis begins with a description of medical device regulation in the United States, including the serious problems that have become more prominent during the past few years; then describes the regulatory histories of the major European countries and the present regulatory systems of the European Union and, more briefly, those of Canada and Japan; and finally reaches some conclusions based on the preceding comparisons. The major conclusion is that Americans would be better off with drastic curtailment--ideally the complete abolition--of the current regulatory regime, which imposes major costs while providing little if any genuine protection of the public health.

## Medical Device Regulation in the United States

In the United States, medical devices are regulated by the U.S. Food and Drug Administration (FDA), which began this type of regulation under authority of the Food, Drug, and Cosmetic Act (FDC Act) of 1938. The act defined devices as "instruments, apparatus, and contrivances, including their components, parts, and accessories, intended (1) for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; or (2) to affect the structure or any function of the body of man or other animals."[2] It prohibited all interstate dealings in "adulterated" or "misbranded" devices and authorized FDA to seize such devices by proceeding against them in federal courts.[3] "Adulterated"

meant contaminated by filth, and "misbranded" meant that the labeling was "false or misleading in any particular."[4]

Although the 1938 statute required premarket approval of new drugs, it imposed no such requirement on devices. Therefore FDA could not prevent a device from coming onto the market; it could only ask a court to stop the continued sale or enjoin the production of a device already introduced into interstate commerce. Under this authority, FDA removed from the market scores of fraudulent or "quack" devices in the 1940s and 1950s.[5]

In the 1960s, as the legitimate device industry brought forth a profusion of technologically sophisticated products, FDA officials wanted the power to require premarket testing for safety and effectiveness, the same power they had acquired over new drugs under the 1962 amendments to the FDC Act. Increasingly, device manufacturers were contesting FDA's actions in the courts, and the regulators bridled at the need "to develop extensive evidence that would hold up during long legal proceedings to remove an unsafe device from the market."[6] Pushing their powers beyond the congressionally authorized limit, they resorted to the "regulatory fiction" that devices are drugs for purposes of regulation.[7] They regulated intraocular lenses, soft contact lenses, weight-reducing kits, certain intrauterine contraceptive devices (IUDs), and some *in vitro* diagnostic products as if they were drugs, requiring the manufacturers to provide satisfactory evidence of safety and effectiveness *before* placing the products on the market.[8] Although this legal legerdemain survived two important court challenges in 1968 and 1969, FDA officials recognized that it could be only a stopgap and sought congressional authorization for expanded regulation of devices.[9]

Several years elapsed before FDA received the authority it sought. The movement toward new legislation gained momentum from widespread publicity about faulty cardiac valves, pacemakers, and IUDs, especially the Dalkon Shield. Members of Congress held hearings to showcase the need for more stringent device regulation. FDA officials and interest group representatives, including feminists and so-called consumer advocates, maneuvered in the background. All these efforts culminated in the passage of a major regulatory statute on May 28, 1976.[10]

The Medical Device Amendments (to the FDC Act) of 1976 conferred gatekeeping powers on FDA.[11] The act refined the old definitions, distinguishing a device from a drug by the condition that the former "does not achieve any of its principal intended purposes through chemical action within or on the body of man or other animals and ... is not dependent upon being metabolized for the achievement of any of its principal intended purposes."[12] FDA was required to classify devices into three groups. Class I devices, the least risky, were made subject to general controls, including requirements that manufacturers keep certain records, file certain reports, and follow "good manufacturing practices" (GMP). Class II devices were made subject to the general controls and product-specific performance standards to be developed by FDA in cooperation with panels of experts. Class III devices, the riskiest, were made subject to general controls and premarket approval (PMA). The statutory powers were to be exercised to "provide reasonable assurance of the safety and effectiveness of the device" while "weighing any probable benefit to health from the use of the device against any probable risk of injury or illness from such use."[13] But neither the statute nor its legislative history gave substantive guidance as to how FDA should make the required classifications or weigh

the risks against the benefits. Hence the law gave the regulators enormous discretion over life-and-death matters.[14]

Unless it were "substantially equivalent" to a "preamendment device"--a product already on the market before passage of the Medical Device Amendments--any new device was automatically placed in Class III and thereby made subject to premarket approval. Obtaining premarket approval required presentation of extensive test data, including the results of clinical trials, to satisfy FDA that the product was safe and effective. FDA could also require submission of PMA data from manufacturers of "old," or preamendment, Class III devices, but meanwhile such devices could remain on the market.

During the first 15 years after passage of the 1976 amendments, the makers of only 9 percent of the "old" Class III devices were required to submit PMA applications.[15] Moreover, claiming a lack of resources, FDA never created the performance standards for Class II devices required by the 1976 law.[16] Therefore, in practice FDA's closest control over the manufacture of Class II and most Class III devices occurred through its GMP requirements and its regulation of new versions of "old" devices.[17]

To sell a new version of a preamendment device, the manufacturer had only to file a premarket notification Form 510(k). It would turn out that the great majority--about 98 percent--of products being introduced to the market arrived via the 510(k) route, so how FDA dealt with these notifications would prove critical to the operation of the device industry.[18] A successful 510(k) had to show that the product had the same intended use as well as the same technological and descriptive characteristics as a "predicate device." In deciding whether the similarities were sufficient to establish "substantial equivalence," FDA exercised great discretion and, as

documented below, eventually made increasing and increasingly arbitrary demands for additional information, so that the 510(k) evolved from a simple premarket *notification* to become in many cases an *application for premarket approval.* According to Peter Barton Hutt, former chief counsel at FDA, the reviewers "sent back 510Ks with so many trivial, unimportant questions that they eventually became the same as a PMA."[19]

FDA gained a variety of new enforcement powers from the 1976 amendments. It could ban a device. It could require manufacturers to notify users of risks, to repair or replace products, or to give refunds.[20] Aggrieved manufacturers could seek judicial review of FDA actions, but the tables had been turned. Before, FDA had been required to proceed through the courts before it could exercise its enforcement powers. Now, it could exercise its powers at will, and the offended party bore the burden of contesting the action in court.

FDA's device regulation became the object of intense congressional scrutiny, especially by Congressman John Dingell's Subcommittee on Oversight and Investigations, whose staff made monitoring and hectoring FDA a substantial part of their activities. Dingell enjoyed the publicity that came from publicly haranguing FDA officials about their failings--"cavalier disregard for potential consequences" and "bureaucratic neglect for public health and safety that shocks the conscience."[21] The agency's answer was always the same: not enough personnel, not enough money.[22] The staff of Dingell's subcommittee did not accept this excuse, observing that "the FDA's inability to manage its resources effectively is well known to those who have monitored the Agency for any length of time."[23] FDA also received regular attention from Dingell's committee colleague Henry A. Waxman, who chaired the Subcommittee on Health and Environment, and

from Ted Kennedy, who chaired the Senate's Labor and Human Resources Committee.

Congressional control of the agency's budget and congressional oversight have played a major role in determining how FDA has wielded its regulatory authority and how its powers have expanded over time. Members of Congress, like the so-called consumer advocates and the news media, benefit by drawing attention to allegedly dangerous products and demanding that FDA crack down on the purveyors. Thus, while the agency bears the brunt of chronic accusations of failing to protect the public health, the thrust of political and media efforts is inexorably toward expanding FDA power, a goal heartily endorsed by FDA's leadership. None of these groups, as such, stands to suffer if more stringent regulation slows access to new or improved products or makes existing products more expensive, because the consumers who will suffer from retarded access or increased costs are politically unorganized and therefore largely ignored by the media and politicians alike. Hence, in the political arena, those who espouse more regulation routinely defeat those who desire less, especially when some purported crisis or scandal erupts, such as the recent furor over silicone breast implants. U.S. device regulation has long been highly politicized, and the major political players have incentives to support ever more stringent regulation regardless of the actual benefits and costs to the general public. Although experts have emphasized that the safety of medical devices has more to do with the training, skill, and attentiveness of device users, the regulation has focused heavily on the firms that design, manufacture, and sell the products.[24]

In 1990 a long series of political efforts culminated in passage of important legislation, the Safe Medical Devices Act (SMDA).[25] This

broadened FDA authority in several ways. It requires every "device user facility" to report "information that reasonably suggests that there is a probability that a device has caused or contributed to the death of a patient ... [or] to the serious illness of, or serious injury to, a patient ... not later than 10 working days after becoming aware of the information." (Manufacturers had been required by regulation since 1984 to make similar reports to FDA, by telephone not later than 5 calendar days and in writing not later than 15 working days after becoming aware of the information.)[26] Device user facilities include hospitals, ambulance services, surgical facilities, nursing homes, and outpatient treatment facilities. Death reports go directly to FDA, illness or injury reports to the manufacturer of the suspect device. Failure to report is punishable by a civil penalty assessed by FDA with a maximum of $15,000 per violation and $1,000,000 for all violations adjudicated in a single proceeding.[27]

Failing to provide a clear definition of a reportable event, FDA put the burden of making the proper distinctions on the users themselves. Said FDA official Kay Chesemore, "facilities have to decide for themselves what constitutes a reportable event and what device or devices are implicated in the death or serious injury."[28] As late as May 1994 FDA still had not clarified the requirement of the 1990 law. Bryan H. Benesch, an agency enforcement official, confessed that "the lack of a final regulation has caused a great deal of confusion. Many people just don't know what they're supposed to do."[29] So FDA had the power to punish people, but people didn't know what to do to avoid the punishment--a perfect example of arbitrary government power.

The number of medical device reports (MDRs) increased from 27,883 in 1990 to 88,265 in 1993,[30] but it is doubtful that any benefits accrued

as firms and institutions incurred the substantial costs of piling up these papers. ECRI, the respected independent testing organization whose publications are known as the Consumer Reports of medical technology, wondered "whether such massive amounts of data will add much in the way of meaningful information."[31] Annual costs of the MDR system were estimated at more than $42 million, but in responding to questions in a three-state investigation between November 1992 and June 1993 most user-facility risk managers indicated that "SMSA [which requires the reporting] does not save lives."[32] Of the MDRs received in fiscal 1993, FDA reviewed only 51.5 percent, so nearly half of them just lay in storage, making no contribution to anyone's knowledge. In November 1994, FDA reported a growing backlog of 15,000-20,000 MDRs not even entered into its database. With the number of reports projected to reach 246,000 in 1995, the prospect looms of more wasted effort by the involuntary reporters.[33] Dr. Joel Nobel, president of ECRI, describes the user reporting scheme as "a horribly flawed concept" and presents it as a "bizarre example" of how "Congress passes legislation that demands safe devices and micromanages the process by prescribing in great detail unworkable, inefficient methods."[34]

Because many illnesses, injuries, or deaths to which a device *may* have contributed actually result from operator error or improper maintenance rather than defects in the design or manufacture of the device, the reporting requirements in effect call for users who have made mistakes to report themselves to the feds.[35] Even though the statute forbids admission of the reports into evidence in civil actions,[36] device users understandably have feared that lawyers would use the Freedom of Information Act to secure the reports and "have a field day with medical

device litigation."[37] According to Dr. Nobel, the reporting requirements create a "nightmare for health professionals. It's like throwing them in a tank of sharks."[38] A reporting system with such inherent disincentives for compliance seems destined to fail.

MDRs also invite abuse by incompetent, irresponsible, sensationalistic reporters or opportunistic publicity seekers who call themselves consumer advocates, whose scurrilous pronouncements can cause irreparable harm. Grossly misleading journalistic exploitation of device reports has played an important part in leading FDA to shut down entire companies, including the pioneering defibrillator manufacturer Physio-Control, depriving patients of life-saving products.

The Physio-Control episode perfectly illustrates what is dreadfully wrong with the highly politicized U.S. system for regulating medical devices. A sensationalistic, erroneous report by an investigative reporter for NBC, aired first in Washington, D.C., and later on the nationally broadcast Today Show, aroused Congressman Dingell and his staff, who immediately aroused FDA. The regulators proceeded to make a harsh example of Physio-Control by forcing it to stop producing, first all of its defibrillators and later certain models, during the two years from mid-1992 to mid-1994.[39] Because of the closure, the company lost more than $70 million out of pocket and $100 million in sales. After finally being allowed to resume production, it found that it had lost market share to competitors whose R&D had not been put on hold for two years in order to concentrate on regulatory compliance. More importantly, in the estimation of Dr. Richard Cummins, a leading authority on emergency medicine, perhaps a thousand people lost their lives when defibrillator orders went unfilled because of the shutdown of Physio-Control.[40]

The SMDA also requires creation of a tracking system for implantable and life supporting devices, augments the data requirements for 510(k) applications, and repeals the 1976 law's requirement that performance standards be developed for all Class II products.[41] It imposes new reporting requirements on manufacturers, importers, and distributors, who must now inform FDA of any removal or correction of a product undertaken to reduce a health risk or remedy a violation of regulations.[42] The new law gives FDA authority to require product recalls and, for certain devices, postmarket surveillance.[43] All the additional paperwork has added substantially to the costs of producing and distributing products.

Importantly, the SMDA changes the character of the 510(k) procedure through which the great majority of new products have entered the market since passage of the 1976 law.

> The 510(k) process is no longer simply a notification, but an approval process. SMDA defines the terms "substantially equivalent" and "substantial equivalence," and further stipulates that manufacturers submitting a 510(k) must wait to market a device until notified by FDA that their premarket notification has been found substantially equivalent.[44]

As documented below, this change in the 510(k) procedure led almost immediately to longer waiting times for manufacturers trying to place improved versions of their devices on the market. Changes in the product or the manufacturing process, no matter how small, might cause the product to be consigned to an indefinite stay in preapproval purgatory. FDA failed to differentiate between new devices and manufacturing changes for existing devices. Manufacturers therefore had a reduced incentive to make the minor improvements that, cumulating over time,

could greatly improve the performance of their products and the efficiency of their manufacturing operations.[45]

Also, as FDA began to require more and more 510(k) applications to be supported by clinical trials, the distinction between a 510(k) application and a PMA application became progressively blurred. Increasingly FDA required both types of applicants to employ test protocols like those used in drug trials--not an easy requirement to satisfy, as some elements of a drug test (e.g., the placebo in the double-blind setup for drug testing) rarely have an equivalent in a device trial.[46]

Finally, the SMDA gave FDA authority to impose civil penalties for all violations of the act up to $15,000 per violation and $1,000,000 for all violations adjudicated in a single proceeding.[47] While imposing such fines, the agency shall "take into account the nature, circumstances, extent, and gravity of the violation or violations and, with respect to the violator, ability to pay, effect on ability to continue to do business, any history of prior such violations, the degree of culpability, and such other matters as justice may require," but it "may compromise, modify, or remit, with or without conditions, any civil penalty which may be assessed"[48]--in other words, FDA may do whatever it pleases. This unrestricted ability to impose civil penalties virtually guarantees that FDA will act arbitrarily and capriciously, and experience so far confirms one's expectations in this regard.[49] In view of this practically unlimited discretion, industry representatives must have been dismayed when Ronald Johnson, director of compliance at FDA's Center for Devices and Radiological Health (CDRH), told them at a trade association meeting early in 1994 that imposition of civil penalties would become a "mainstay" of the agency's enforcement activities.[50]

The years 1991 and 1992 ranked among the worst for the FDA. Largely because of the scandal that captured the headlines in 1989 involving the bribery of several FDA officials by companies seeking expedited approval to market generic drugs, the agency was in crisis.[51] Stung by pervasive criticism in Congress and the news media, FDA personnel were hunkering down, trying to protect themselves by avoiding anything, including product approvals, that might expose them to further censure. As a staff report of Dingell's subcommittee observed, "Reluctant to make a decision that may result in criticism from FDA management or from the outside, some reviewers make endless requests for information from applicants to avoid doing so."[52] In addition, David Kessler had become Commissioner in November 1990, his appointment itself being prompted by the scandal, and he was shaking up the organization with new appointments and reassignments of personnel and new agency priorities featuring unprecedented emphasis on aggressive enforcement and more stringent regulation.[53] The unsettled situation in 1991 and 1992, which produced a "devastating slowdown in device clearances," was aptly described as "chaos in US medical device regulation."[54] In the midst of this turmoil, late in 1991, a new storm struck--the furor over silicone breast implants--and the agency's performance deteriorated even further.

## The Great Slowdown in the U.S. Approval Process

From 1983 through 1990, on average, FDA received about 80 PMA applications per year and approved about 45.[55] In 1991 it approved only 27, which was fewer than in any year since 1979, when the approval process was just getting started. In 1992 only 12 PMAs were approved, as the process nearly ground to a halt. The following two years witnessed a rebound to 24 approvals in 1993 and 27 (according to preliminary data) in

1994, but these totals were still only a little more than half the average for the period 1981-1990.[56]

In the late 1980s the average review time for FDA to approve a PMA application was about 150 days. In 1991 it was 285 days, in 1992 it was 186 days (this average being misleading because six of the 12 approvals were licensing agreements with no data review), and in 1993 it was 437 days and still rising. Preliminary data for 1994 showed an average approval time of 604 days. The total time elapsing from the applicant's filing until the approval of the application was substantially longer, nearly 800 days in 1993 and nearly 900 days in 1994. In extreme cases the process could eat up several years. C. R. Bard and Collagen filed a PMA application for their Contigen incontinence device in March 1989. FDA did not approve the application until four and a half years later. Jonathan Kahan, an attorney specializing in device law and regulation, attests that "there are numerous other examples of years of delay for devices which could have an important medical impact."[57]

The 510(k) process for "substantially equivalent" devices, where vastly more applications for marketing approval are processed, experienced a similar slowdown. In the 1980s the number of applications tended upward. By the early 1990s, manufacturers were submitting about 6,000 form 510(k)s per year. In 1993 there were 6,288 submitted and in 1994 there were 6,247 (according to preliminary data). FDA *decisions* on these applications also tended upward in the 1980s, reaching more than 6,000 per year in 1989 and 1990, then dropped to 5,367 in 1991 and further to 4,862 in 1992 and 5,073 in 1993. The number of 510(k)s *approved* fell every year from 1989 to 1992 before rebounding slightly in 1993, as shown by the following table:

| fiscal year | 510(k) approvals |
|---|---|
| 1989 | 4,867 |
| 1990 | 4,748 |
| 1991 | 4,294 |
| 1992 | 3,776 |
| 1993 | 4,007 |

In 1994 (according to preliminary data) FDA, under intense criticism for the slowdown, made 7,101 decisions, including 5,463 approvals, but this rebound hardly indicated a reversal of trend. Even CDRH chief Bruce Burlington admitted that much of the 1994 resurgence had been achieved by what industry critics called "cherry picking," or attending to the easiest cases first, and by temporarily diverting personnel from other tasks.[58]

As the approval rate dropped in the early 1990s, the 510(k) backlog at FDA grew much larger. At the end of fiscal year 1991 there were 2,291 applications awaiting disposition; in 1992 there were 3,951; in 1993 there were 5,157; and in 1994 (according to preliminary data) there were still 4,303. The average active review time increased from less than 90 days in the 1980s to 102 days in 1992 and 182 days in 1994. Counting the time the average application spent "on hold," awaiting the arrival of additional information requested by an FDA reviewer, the total time spent waiting for clearance of a 510(k) reached 214 days in fiscal 1994--up more than 100 percent in the past three years.

Early in 1993 someone leaked to the *Wall Street Journal* the FDA's internal record of 510(k)s pending more than 90 days, and the newspaper published a striking graph of the monthly figures on its editorial page. In November 1991 only two 510(k)s were pending more than 90 days. The number then grew exponentially, reaching 713 a year later. The *Journal's*

editorialists linked the growing backlog to "the aftermath of the Kessler-Congress jihad against breast implants."[59] Six months later the number of overdue 510(k)s had reached about 1,400 and late in (calendar) 1993 peaked at some 2,000 before its reduction by the agency's "cherry picking" in 1994.[60] The buildup of the huge backlog in 1992 and 1993 was the development that led bewildered applicants to speak of a "black hole" and an "eternal limbo."

In August 1994 at the International Medical Device Congress in Salt Lake City, FDA's Susan Alpert, director of the Office of Device Evaluation, presented a graph showing "a steady decline since fiscal year 1988 in the percentage of 510(k)s acted on within 90 days. While approximately 80% met the deadline in 1988, only about 60% did so in 1991 and 40% in 1993."[61] A study by the Health Care Technology Institute, based on a sample of applications classified by the year of their submission rather than (as usual) the year of their disposition, showed even greater deterioration--only 23 percent of the 510(k)s submitted in 1993 received a decision within 90 days--before a turnaround in 1994 that left the agency's 90-day-decision rate for reviews still far below its pre-1992 level.[62]

## More Aggressive FDA Enforcement

Before Kessler took command, FDA tended to use its powers with some sense of restraint and some appreciation of the value of expediting the marketing of innovative products of great benefit to the public, but after Kessler's appointment aggressive enforcement moved to the top of the agency's agenda. District Offices were delegated more enforcement authority and encouraged to use it. Compliance officials promoted a philosophy of "act now, talk later."[63] District Offices responded by finding

more GMP violations, issuing more warning letters, and taking a variety of other enforcement actions at an increased rate. Says former FDA chief counsel Hutt, "The more enforcement actions, the more FDA employees showed they were protecting the public health."[64]

The correlation was spurious: there was no evidence that products became any safer or more effective as a result of the agency's stepped-up compliance program.[65]

FDA inspectors proceed on the assumption that the company being inspected is violating the law; their attitude "resembles that of a police detective's toward suspected felons."[66] Said an official of the Office of Compliance, "We're cops and that's part of the cop psychology."[67] This attitude predisposes the inspectors to be unreasonable--there is, after all, not much similarity between a murderer or a rapist and the producers of life-saving and life-enhancing equipment--and during the past three years, under increased goading by their superiors, they have become more unreasonable. "Companies report an increasing and often inexplicable change in regulatory attitude by device inspectors. The new attitude is characterized by greater hostility and less communication."[68]

Moreover, many of the inspectors are ill-trained or wholly unqualified to deal with the technologies they scrutinize. "Beyond incompetent," says Dr. Nobel, "they are stubborn."[69] According to a 1993 report of Dingell's subcommittee, "FDA now takes aggressive enforcement action, yet lacks the controls and training to avoid inconsistent or arbitrary decisions." The report referred to "untrained inspectors who can not, or will not, distinguish between 'significant' and 'nonsignificant' GMP violations."[70] In general, FDA has failed to clarify for companies precisely what actions constitute compliance. The result has been "an enforcement

program that is perceived by industry as disorganized, inconsistent, and often inappropriately harsh" and "a confused, demoralized industry no better able to comply with the law."[71]

There is no way to measure exactly how much FDA has increased its enforcement activity during the past few years. The agency's own reports give conflicting figures on the number of various kinds of enforcement actions, and even with consistent data no single index tells the whole story. Issuance of regulatory/warning letters more than doubled, increasing from 235 in fiscal 1991 to 548 in 1992, 543 in 1993, and (according to preliminary data) 549 in 1994--a reflection of the unleashing of the District Offices.[72]

Nearly 70 percent of the warning letters pertain to GMP violations, which are often the sort of transgression visible only to an inspector who wants to see it.[73] Despite the name, "good manufacturing practice" violations usually have nothing to do with actual manufacturing or with the quality of the product that reaches the customer; they almost always consist of failures to fill out countless forms in the minute detail that only a bureaucrat could care about.[74] According to Dr. Nobel, whose opinion in this regard deserves more weight than anyone else's, "there is no known relationship between GMP paperwork and actual product performance in the field."[75]

The period 1992-1994 also witnessed an average of 34 device seizure actions annually. In addition, in the three fiscal years combined, FDA's general counsel sought 21 injunctions, brought seven criminal prosecutions, and assessed five civil penalties against device manufacturers. Virtually all industry sources agree that FDA not only has stepped up enforcement activities markedly but has taken these actions in

a way that seems more focused on punishing the industry than working with it to ensure the rapid delivery of safe and effective products to the market. The 1993 report of Dingell's oversight subcommittee properly concluded, "FDA enforcement practices have demoralized and perplexed the medical device industry."[76]

Regulatory Consequences and Industry Responses

Recent changes of FDA policies and conduct have increased the device firms' costs of research and development, product approval, manufacturing, and postmarketing surveillance of product performance. Unfortunately, industry managers perceive no "commensurate increase in safety and efficacy," that is, no substantial additional benefit for consumers of their products and hence no basis for raising product prices enough to offset the increased costs. In the estimation of venture capitalist Robert Daly, "The new regulations and delays mean adding $10 million to $20 million to a company's budget, and several years until the device gets to market. At that rate, most [venture capital] deals don't make sense."[77] Increased costs mean that some investments are no longer expected to generate a satisfactory return, some innovations are no longer worthwhile to develop, and ultimately some patients will suffer and die as a result.

FDA now requires many more device firms to conduct clinical trials similar to those required of drug firms. Before beginning a trial, a company must gain an FDA approval, known as an Investigational Device Exemption (IDE), for its plan to conduct the tests. Like PMAs and 510(k)s, these applications lately have become subject to extended and often inexplicable delays. A consultant who wrote to Dingell's oversight subcommittee in 1993 asked the legislators to "imagine the frustration a clinician/researcher feels when a faceless bureaucrat, often without

medical training or any familiarity with the clinical environment, produces an endless stream of unrealistic questions effectively casting a 'no' vote on a research application."[78]

Venture capitalists increasingly have responded to this situation as did Grant Heidrich of the Mayfield Fund: "We counsel our companies, 'Don't screw around with the F.D.A.; let's move these trials to Europe where there's a reasonable process.'"[79] Likewise, device lawyer and former FDA chief counsel Hutt "has long been advising American companies, if they are only going to build one manufacturing plant, to build it in a foreign country."[80] Indeed, U.S. device firms increasingly are shifting their trials to Europe, even though they must still meet all FDA requirements to get approval to sell their products in the United States. Said Rob Michiels, president of Interventional Technologies, which makes an innovative catheter used to clear arteries, "By the time we're approved in the U.S., that product will have been available in Europe on the free market for three to four years."[81] David Summers, chairman of American Biomed, a small company that also manufactures catheters, echoes Michiels: "We're having to move out of the United States. We just can't take it anymore."[82] One device executive describes the optimal strategy as "working in parallel with the FDA"--"parallel, as in not intersecting until products are established in international markets. At that point, compliance with FDA requirements remains cumbersome but no longer jeopardizes the product's or company's future."[83]

Few firms challenge FDA in court. Doing so makes sense only for those who are desperate and will not survive unless they receive judicial protection. Because FDA controls every aspect of a device firm's activities, even the (very few) firms that win in court cannot expect to survive the

agency's subsequent retribution; a court victory can only buy time for the firm to minimize its losses. The only effective escape is to flee the country, which more and more device firms reluctantly are choosing to do. According to analyst Daniel Lemaitre, "There isn't a company that isn't thinking of moving its research and development, and its manufacturing, overseas."[84]

Several recent surveys confirm that increasing numbers of device firms are leaving or considering leaving the United States. In a 1992 survey by attorney Jeffrey Gibbs of representatives of 168 firms attending regulatory affairs seminars, almost 60 percent of the respondents indicated that in the future they would introduce new products outside the United States first, and almost 75 percent were planning to manufacture at least some of their products abroad. They gave the difficulty of U.S. product approval as the reason for shifting their production overseas.[85]

Early in 1994 the Health Industry Manufacturers Association (HIMA), the largest trade association in the medical device industry, reported the findings to date of three of its own surveys, which indicated an increasing movement offshore. In a survey encompassing 98 companies, the regulatory environment ranked highest as a "decision factor in expected international expansions and new operations"; 40 percent of the respondents gave FDA regulation as the most important reason for moving abroad.[86] In a Strategic Business Decisions Survey, HIMA found that companies "cited the regulatory climate here as their top reason for planning to shift to overseas operations in the next four years--double the number that cited it for the earlier period [1991-1993]."[87] In December 1994 a HIMA official confirmed that the shift of operations to Europe was occurring at an increasing rate.[88]

In April and May 1994 the *Minneapolis Star Tribune* conducted a survey of medical device firms in Minnesota, where many such firms do business. The newspaper secured responses to its questionnaire from 148 firms in device manufacturing or research and development. The survey showed that firms selling Class III devices--the most heavily regulated ones--had 7 percent of their personnel employed overseas five years ago and 12 percent currently, but expected to have 16 percent in 1999. Respondents complained of "costly and cumbersome regulation" in the United States, citing this as a "leading reason for the investing abroad before investing at home."[89]

In November 1994 Medtronic, a Minnesota firm that describes itself as "the world's leading therapeutic medical device company," announced plans to move the headquarters of its Corporate Ventures organization to Europe, explaining that the relocation was being made "because of pressures related to the current unpredictability of regulatory and reimbursement processes in the United States."[90] Only a few months earlier it had been reported that "so much investment is taking place in Europe now that one startup has been formed exclusively to handle the European launch and distribution of novel devices designed in America."[91]

In June 1994 the American Electronics Association (AEA) announced the results of a survey, conducted by the Gallop Organization, of 58 U.S. medical device companies. Of the firms surveyed, 40 percent said they had reduced the number of U.S. employees because of FDA delays; 29 percent said they had shifted investment spending offshore; and 22 percent said they had relocated jobs to overseas facilities. Bob DeHaven, vice chairman of AEA, warned that the U.S. medical device industry faces decline "unless the FDA regulatory process is re-engineered."[92]

Data on capital outflows confirm the survey findings and related reports. From 1989 to 1991, U.S. medical technology firms invested almost the same amount abroad each year, in the range of $321-333 million. Then in 1992, when FDA abruptly made its enforcement and approval policies more onerous, capital outflow jumped more than 200 percent to $993 million. HIMA interprets the increase as a verification that "as the FDA approval process has become more burdensome and slowed, U.S. companies have moved to establish overseas facilities at a much faster rate."[93] Given that during 1991-1993 Europe was wallowing in its worst recession since the 1930s and that labor and other variable costs there may exceed U.S. levels, it does appear that the recent movement offshore represents a regulatory push out of the United States rather than an economic pull toward Europe.

## Medical Device Regulation in Europe

Until recently, European countries imposed relatively little regulation on the producers of medical devices. The Europeans relied more on the formulation of technical standards by professional organizations, leaving manufacturers free in most cases to comply or not comply with the existing standards. Purchasers, of course, could insist that products meet certain standards, and in some countries major purchasing agencies such as the national health authorities were either required or urged to do so. Starting in the 1970s, Europe began to develop a more restrictive system of regulation, but the adoption of the new system proceeded slowly. Now in the process of adoption by the member states of the European Union (EU), the new system will not be in place fully until the end of the century.

When the United States adopted the full-fledged regulatory system required by the Medical Device Amendments of 1976, device regulation in

Europe was relatively limited even in the few countries where it existed at all. In a 1977 survey, Gaikhorst and Koivisto noted that "some legislative requirements governing the production and use of some categories of medical electrical equipment have been in force in several countries in Western Europe for many years."[94] The earliest laws pertained to devices emitting x-rays. After World War II several countries enacted laws to protect patients and users of the more complex electrical devices then coming into use. Gaikhorst and Koivisto noted that "in several countries the legislation refers to recognised technical safety standards which are therefore compulsory. The technical safety standards can, however, be modified by technical committees of experts."[95]

At that time conditions varied greatly from country to country. France had adopted a system known as "homologation," which combined premarket approval of devices with certification of eligibility for reimbursement by the national health system. Under a law passed in 1968, Germany required that all electrical equipment meet standards established by the Association of German Electrical Engineers (VDE). To satisfy the requirement, companies could have their products tested by the VDE laboratory, but VDE testing was voluntary, and companies could simply declare that their products met the standards. Also, standards for measuring instruments such as thermometers and blood pressure monitors were established by a 1969 law on weights and measures. A 1971 law governed conformity with technical standards related to high frequency interference, regarding which the manufacturer's own laboratory might be authorized to perform the required tests. Belgium, Italy, and the Netherlands had no specific law regarding medical electrical equipment, but some regulations existed under a general law. The United Kingdom

had no legal requirements except those pertaining to equipment emitting ionizing radiation, but the National Health Service, which dominated the national market, could set any contractual conditions regarded as necessary to assure the safety and effectiveness of products. Denmark required testing for electrical safety by an independent laboratory but had no official technical standards.[96]

By 1980 the Europeans were considering how to harmonize their regulations for certain high-risk medical electrical equipment and had drafted a Directive of the European Economic Community for that purpose, drawing on existing standards of the International Electrotechnical Commission (IEC), an organization that dates from 1906.[97] It is important to note that these efforts sprang not from any perceived fault of the existing national regulations (or the lack thereof) or any public health calamity. Rather, they "aimed at eliminating technical barriers to trade."[98] *Commercial* objectives have continued, right up to the present, to drive the European harmonization process and, increasingly, the global harmonization process as well.

Writing in 1980, R. T. Rogers correctly foresaw the course that European regulation would take: "further Directives are likely to require more formal methods of demonstrating conformity than a manufacturer's declaration or self-certification. One method employed on other Directives requires a manufacturer to submit an equipment sample to a Test House which has been authorised by a Member State to grant a type-approval certificate."[99] It turned out that this procedure eventually would be adopted by the European Union for the highest-risk types of medical devices.

Presenting a paper to an international conference in 1987, Dr. David Banta observed that "no country regulates medical devices as consistently and thoroughly as the United States. However, there is a trend toward regulation in other industrialized countries, especially in Europe." Summarizing conditions in the largest European countries, he noted: "France requires registration and evaluation of medical devices for public hospitals. Germany passed a law about 3 years ago that requires the registration of all medical devices linked to approval by defined testing organizations. England's Department of Health and Social Security is active in evaluating selected devices. And Italy also has a law, passed in 1986, that requires registration of all medical devices marketed in the country." In addition, the European Commission was continuing to develop its directives related to medical devices.[100]

Banta asserted that "there are problems, and industry does not always behave well," illustrating his point by discussing the Dalkon Shield, but he admitted that "no systematic information is available on the extent to which problems of efficacy and safety occur with devices." Nonetheless, he regarded it as more reasonable to "develop programs aimed at preventing" problems than to wait until evidence of their seriousness emerged.[101] He observed that "because there is no other long-standing program of the size of FDA, approval by FDA for marketing in the United States is often taken by buyers to mean that the device is safe and efficacious."[102] While this practice permitted Europeans to "free ride" on FDA certifications, they could disregard FDA's judgments when they preferred to do so.

In a 1992 survey, G. R. Higson stated that "most of the countries of Europe have some legislation affecting medical devices and these differ

both in scope and details." He presented a table showing for each of 18 European countries whether there existed regulatory requirements, no regulation, or a quasi-regulatory regime or strong code of practice related to five categories: sterile product, electromedical, clinical trials, distributors, and labeling and packaging. Only two countries, Ireland and Luxembourg, had neither regulation nor quasi-regulation across all categories. Austria had a quasi-regulatory regime regarding labeling and packaging but nothing more. The United Kingdom had a quasi-regulatory regime for the sterile product and electromedical categories but nothing more. A majority of the countries imposed regulation on electromedical products and labeling and packaging, but only Germany and Spain had regulation in all five categories. Switzerland, Denmark, and Iceland had regulation for electromedical products but nothing more.[103]

About three years ago the Health Industry Manufacturers Association constructed an elaborate tabular "Comparison of Product Approval Process" for the United Kingdom, Germany, France, Canada, Japan, and the United States.[104] According to this information, the United Kingdom had no premarket approval process. Companies had only to register and pass periodic inspection for GMP compliance. The government would subcontract with private organizations such as the British Standards Institution to perform some of the inspections. A user reporting system for adverse incidents received about 3,000 reports a year from hospitals and manufacturers, who were encouraged to report problems.

In Germany most devices required no premarket approval. The riskiest devices had to show conformity with established standards through type-testing conducted by a qualified private testing organization. Decisions on premarket approval typically were reached in 3-4 months.

No GMP requirements existed for device manufacturers; nor did manufacturers have to report adverse incidents or track users, though device users were required to report problems.

The French homologation system required extensive type-testing and clinical trials for product approval. Waiting times for approval were "at least 18 months for most products," mainly because only one agency was authorized to conduct the type-tests and it lacked sufficient personnel.

Similar information compiled by HIMA late in 1994 showed that the situation in Europe remained largely unchanged since the earlier inquiry. However, U.S. approval times, in contrast, had reached almost 900 days on average for PMAs and 214 days for 510(k)s--far longer than the times for corresponding types of approval in any European country. Illustrating this difference in a striking way, a manufacturer responding to the *Minneapolis Star Tribune* survey in 1994, wrote that in Germany the regulatory approval time was four months and the cost of gaining approval $10,000, whereas in the United States the corresponding figures were four years and $8,000,000. Next to the U.S. numbers, the respondent wrote in capital letters: "THIS IS PROHIBITIVE!"[105]

As another striking example, consider Medtronic's experience in gaining approval for a novel transvenous lead for an implanted defibrillator. In October 1989 the company submitted its bench test results to TUV, a private testing organization in Germany. One month later TUV certified that the product met all applicable standards, and Medtronic began to market it in Germany. In November the company applied to TUV for approval of changes in the product. One month later TUV certified the changes, and the company proceeded to market the altered device in Germany. The company submitted its application to FDA in March 1990

for an IDE--permission to conduct clinical trials. In October FDA approved the IDE, and the company began the trials. In March 1992 Medtronic submitted results of the trials and requested premarket approval. In April FDA granted permission for expanded clinical trials. In December 1993 FDA granted marketing approval, and Medtronic began selling the product in the United States. Total regulatory review time: 3 years and 9 months, for the same product approved in Germany in two months.[106]

From the preceding description of medical device regulation in Europe, one may conclude that (1) the scope, detail, and cost of the regulation have varied widely from country to country but (2) no country has practiced the sort of rigid, elaborate, legislatively defined, centrally directed and enforced regulation that existed in the United States after 1976.

By the end of the 1990s, however, the European situation will have changed drastically, especially in countries that previously had little or no regulation. Notably, no evidence exists that European consumers in general have suffered because of the relatively undemanding regulatory environment, and obviously many European patients have benefited by gaining quicker access to new, more effective devices.[107] The current European changes are being driven by the need to make regulations uniform throughout the European Union in order to preclude their serving as trade barriers. As the uniformity is achieved, the common regulatory system will impose *more* regulation, even in countries such as France and Germany that already had relatively extensive regulation. Still, even when the new EU system is fully in place it will fall far short of FDA-type regulation, leaving European device manufacturers, purchasers, and patients much better off relative to their U.S. counterparts.

To understand the new European system, one must appreciate how the European Union's legal system works. Directives are statutes enacted by the Council of Ministers. Once a directive has been enacted, member states must bring their national laws and regulations into conformity with it within a stipulated period. By this process the European Union creates the single internal market within which goods, people, and capital may move freely.

Three directives affect medical devices. The first applies to "active implantable medical devices," all implantable devices powered by electric current, such as cardiac pacemakers and internal defibrillators. This directive took effect on January 1, 1993. The second applies to medical devices in general, that is, all those not covered by the first and third directives. This took effect on January 1, 1995. The third applies to *in-vitro* diagnostic products. It is still being developed and will not take effect until at least 1997. During a transition period of several years, manufacturers may choose to comply with the requirements established by the directives or to continue to comply with the national requirements previously in force. At the end of the transition period the new requirements become mandatory. The first directive became mandatory on January 1, 1995; the second will become mandatory in June 1998.[108]

To oversee the new arrangements, each country designates a "Competent Authority," usually the ministry of health or one of its subdivisions. The Competent Authorities designate Notified Bodies, which are third parties, most of them private organizations, that perform inspections, audits, and tests to insure that the regulated companies comply with the essential requirements laid out in the directives. *A company is free to deal with any Notified Body in any country.* Further,

companies in every case have a choice of procedures for demonstrating compliance. Once a product has been certified by a Notified Body, the producer may give it the "CE Mark," indicating that it satisfies all regulatory requirements. All products bearing the CE Mark must be admitted to the markets of all member states of the European Union. In addition, five member states of the European Free Trade Area--Finland, Sweden, Norway, Austria, and Iceland--will participate in the EU system on the same terms.

Products will be classified into four categories. Class I contains those presenting the least risk. For them, manufacturers may simply declare that the products meet applicable requirements and proceed to market without the involvement of a Notified Body. Requirements become progressively stiffer as one proceeds up the risk scale from Class IIa to Class IIb to the class containing the highest-risk devices, Class III.[109] Except for Class I products, manufacturers must monitor the use of their products and report adverse incidents to the Competent Authority. All Class III products must have premarket approval, which requires presentation of clinical data to demonstrate an acceptable degree of safety and effectiveness and expected benefit relative to risk.[110] However, the clinical *data* need not come in every case from new clinical *trials*. In some cases the data may be drawn from the relevant scientific literature. The appropriate method for generating the clinical data is to be decided by the company in cooperation with a Notified Body.[111]

Clinical trials will be regulated much more closely than they have been in the past in Europe. Anyone proposing to conduct trials must apply to the Competent Authority, which has 60 days to object. Permission for the trial also must be acquired from a local Ethics Committee--the

counterpart of what are known as Institutional Review Boards in the United States--that looks after the interests of the human subjects in the trials. The necessity of gaining approval from two different holders of veto power is, in the judgment of some observers, "fraught with problems," including long delays in commencing the trials.[112] Despite the increased controls, according to Kahan, "Europe will certainly not be adopting the clinical data and documentation requirements of the US system."[113] If the Europeans do adopt such requirements, it will not be because they lacked warning. At a recent conference in Brussels, Mr. Ernest Carabillo of EXPERTech Associates warned the delegates against following the U.S. example:

> "It has taken the US 18 years to reach the state of chaos of today" where clinical investigations are strictly regulated, he said, and industry lives in fear of civil, administrative and criminal penalties for contravening these laws. ...[Europeans] should work together to avoid the type of policing set-up the US has, where the FDA looks for deviations from the requirements in case there **could** be a risk, rather than reacting to actual problems. ..."Don't make it a requirement in Europe unless it is demonstrably necessary and you have the means to enforce it," he said, "otherwise you'll turn the whole industry into crooks."[114]

The people of Europe will be fortunate if these words of wisdom are heeded.

In comparing the European system of device regulation with its U.S. counterpart, several differences stand out. First, the European system does not impose regulations in the minute detail characteristic of the U.S. system, especially with regard to record-keeping and reporting. Second,

the European system is more predictable, because it relies more on meeting established standards and less on the *ad hoc* judgments of a government reviewer. In the words of Jim Phillips, vice president at Clarus Medical Systems, "It's not that Europe, Japan and Australia don't have standards. They do. They have specs and you can design by them. The FDA has no specs. It's a black hole."[115] Third, in Europe GMP compliance requires satisfying a Notified Body and not a government employee. Fourth--and probably most important--the role of the Notified Bodies in certifying compliance with the Directive's essential requirements provides a large measure of protection to the device manufacturers (and hence to the patients they ultimately serve) that is wholly lacking in the centralized U.S. system.

In the United States, one agency makes the rules, interprets the rules, conducts the inspections, determines what constitutes a violation of the rules, hears objections to rules or agency actions, and imposes punishment, explicitly in the form of FDA law suits or civil penalties and implicitly in the form of delays of product approvals or refusals to approve products. A company has no alternative to dealing with the FDA, which controls every aspect of its operation and can at any moment diminish or destroy its ability to earn income. Making this vast power even more intolerable, the behavior of FDA has become heavily politicized--probably because Congress intended, at least since the 1950s, to make the agency its creature.[116]

The situation is Europe is quite different. A company can choose which Notified Body to patronize; it need not do business with one in its own country; and certification by *any* Notified Body admits its product to *every* country in the European Union. The Notified Bodies, most of which

are private organizations, have excellent incentives to provide helpful service to the companies that patronize them. Consider the statement of Harmut Junker, director of the Medical Department of the Rhineland TUV (Technischer Uberwachungsverein Rheinland), a long-established German testing organization now certified as a Notified Body: "Our philosophy is that if someone comes with a new idea for a medical device, we want them to succeed. We want to be their partner, in a sense."[117] Needless to say, if the Notified Bodies dealt with their clients as FDA deals with U.S. device firms, they would lose all their clients overnight and be forced to go out of business. Still, the Notified Bodies are subject to oversight by the Competent Authorities, which expect them to insure compliance with the essential requirements of the relevant directive. Although the Notified Bodies provide excellent service to clients, they also insist that products meet strict standards. "They pride themselves on efficiency and insist that patients in Germany can expect a high level of safety from their system."[118] Indeed, even before the medical device directives came into force in Europe, TUV Product Services and its affiliated organizations were demonstrating the worth of their services by successfully conducting business in facilities around the world, including several in the United States.[119]

## Medical Device Regulation in Canada

Canada has imposed far less regulation on medical devices than the United States. Except for HIV test kits and devices intended to be implanted in the body for more than 30 days, which require premarket approval, products require only *postmarket* notification within 10 days. Recently some 6,000 such notifications, covering three to four devices each, have been filed annually. Premarket review times have ranged from six to

seven months in the early 1990s--180 days on average in fiscal year 1993--though cardiovascular and orthopedic implants have experienced up to two years of review in some cases. Canada has had no GMP regulations but is developing quality assessment requirements based on the standards established by the International Standards Organization (ISO). There is a voluntary reporting system for device problems, to which both manufacturers and user make reports. The limited nature of the Canadian system is attested by the small size of its staff, which currently has only 25 professionals working on approvals (versus 327 in the United States).[120]

The Canadians are now in the process of adopting a medical device classification system similar to that of the European Union, and new regulatory options are being considered. It seems likely that the Canadian regulations will resemble those of Europe more than those of the United States, if only because a small country would be hard pressed to pay for the resources needed to operate a full-fledged FDA-type regulatory system. Moreover, compatibility with the European system would allow the Canadians to achieve commercial objectives more readily. In any event, a recent forecast is that "it could be two-three years before the system is fully up and running, although some phasing-in of requirements could occur in the meantime."[121]

## Medical Device Regulation in Japan

Japan regulates medical device manufacturers in two ways. First, each business facility must acquire a license (kyoka) and, second, each product must receive marketing approval (shonin). Both are issued by the Medical Device Division (MDD) of the Pharmaceutical Affairs Bureau of the Ministry of Health and Welfare. However, prefectural governors have the

authority to grant kyoka and shonin for certain simple, low-risk products such as needles, syringes, and lenses. In addition, 34 product categories require no shonin, because they are used exclusively by specialists and their safety and effectiveness are well established. Other products are exempt from shonin because they meet an established Japanese Industrial Standard.[122]

Virtually all devices approved for marketing in Japan are treated as "me-too" products, or substantially equivalent to a preexisting device. Review times average about four months, although applicants may need to spend additional time in informal conversations with MDD personnel prior to submitting formal applications for shonin. Here as elsewhere in the Japanese bureaucracy, all parties prefer agreement and accommodation to conflict and possible loss of face. Hence applicants receive much more administrative guidance than they would from FDA. The Japanese government tries to promote the success of its medical device industry, unlike FDA, which now seems determined to destroy the U.S. device industry. Foreign manufacturers who have approval for products in their own country need apply for only a kyoka, not a shonin. U.S. firms have encountered no special obstacles to product approval in Japan. According to Dr. Sachiko Kuno, president of the Tokyo-based consulting firm Kuno & Co., "In comparison with other bureaucratic procedures in Japan, the approval process moves extremely quickly. [MDD] stresses that registration should not be seen as an import barrier."[123] MDD's staff for product approvals amounts to only 20 persons (versus 327 at FDA), reflecting the limited review procedure.

Japanese authorities are currently participating in discussions of global harmonization of device regulations. Japan is adopting a

classification system similar to that adopted in Europe. Products in Class I will be self-certified by manufacturers; most of those in Class II will be assessed by third-party testing organizations similar to the Notified Bodies of Europe; only the highest-risk devices, those in Class III, will require premarket review by the government and tracking of patients. GMP regulations have been brought into conformity with ISO and European standards and will be required for licensing. Exactly how the Japanese system will be revamped remains to be seen, but it seems clear that it will resemble the European system far more than it resembles the U.S. system.[124]

The Japanese system "accommodates the characteristics of device innovation (e.g., incidental changes and the need for rapid approval)."[125] Despite the simplicity of the Japanese regulations and the speed with which new products receive marketing approval, Japan evidently has not suffered any calamities caused by medical devices. However, its simple regulatory system has given "Japanese patients access to state-of-the-art care months or years ahead of Americans." Dr. Michael Werner, an American surgeon suffering from a rare form of brain cancer, recently went to Tokyo for a promising radiation therapy not approved by FDA despite its much higher success rate relative to that of conventional therapy. Attributing his survival to this innovative treatment, Dr. Werner observed, "I don't know who [FDA officials] are protecting. Sometimes you wonder."[126]

## Conclusions

Comparison of the U.S. regulatory system for medical devices with corresponding systems in Europe, Canada, and Japan warrants the following conclusions.

(1) Medical device regulation in the United States during the past 30 years has been driven mainly by political forces, especially by the reaction of members of Congress and FDA officials to shocking or scandalous revelations widely disseminated by the news media. Even without such revelations, however, the same political actors strove relentlessly to increase the scope and detail of the regulations. So-called consumer advocates and investigative reporters have wielded considerable influence, demanding ever more regulation. Events highlighted by the media served mainly to catalyze the outgrowth of incessant iron-triangle politics, by providing apparent justification for new legislation or more aggressive regulatory enforcement.

Outside the United States, medical device regulation has been far less politicized; more nongovernmental input from scientists, engineers, and technicians has been heeded; and commercial incentives to harmonize regulations have been foremost in the minds of the architects of the new regulations. "Consumerism" in the publicizing, lobbying, Naderite form familiar to Americans has played virtually no role.

(2) Medical device regulations in the United States have been formulated mainly by members of Congress, their staffs, and employees of FDA, with limited input from persons knowledgeable about scientific, technical, and economic conditions in the regulated industries. The result has been a form of regulation that apparently seems sensible to lawyers but often seems foolish and counterproductive to well-informed parties.

Outside the United States, the details of medical device regulation have been less the work of lawyers and more the product of persons having some acquaintance with the economics and technology of the regulated sector, especially the specialists in the standards organizations.

(3) Medical device regulators elsewhere wield authority over manufacturers that is far less discretionary than the authority wielded by FDA. In Europe and Japan, many products (Class I) can gain approval on the strength of manufacturers' declarations of compliance with relevant regulations. In Europe, the Notified Bodies--respected independent testing organizations, most in the private sector--perform the assessments of conformity with standards, not the government. Japan will soon operate similarly for nearly all approvals. Abroad, manufacturers know that certain established standards--usually those formulated by ISO, the Comite Europeen de Normalisation (CEN) or the Comite Europeen de Normalisation Electrotechnique (CENELEC)--must govern their operations; they know, therefore, what they must do to gain approval.

In the United States, in contrast, the regulatory requirements are a "moving target," as individual reviewers can and routinely do alter the requirements for product approval as the process unfolds, making repeated requests for additional or different information each time the applicant satisfies a particular demand. No matter what the company does, FDA may still withhold approval for any reason, or without a reason. On some occasions, political motives or bureaucratic desires to retaliate against insufficiently obsequious firms have clearly determined FDA's decisions. To describe FDA as a "loose cannon" would suggest both its unpredictability and its capacity for destruction. Because Congress has enacted statutes delegating open-ended authority to the agency and the courts have tolerated its wide-ranging exercise of discretion, these departments of government bear even more fundamental responsibility than FDA itself for the extent to which the agency acts in an arbitrary and capricious manner.

(4) FDA's medical device reporting system, required by the SMDA, imposes major costs on reporting firms and user facilities and buries FDA under a mountain of data so vast that it cannot be entered into a data base in a timely manner, much less analyzed. This senseless approach to postmarket monitoring of product performance typifies the indifference of Congress and FDA to balancing the benefits of additional information collection against the costs.

In other countries, reporting requirements are much more modest and more often voluntary, yet there is no reason to believe that the patients of Europe, Canada, or Japan have suffered because too little information was available about product performance. Actual users of this equipment are better placed than bureaucrats in a central office to evaluate its performance and to sort out the contributions of user error, improper maintenance, and other factors unrelated to product design or manufacture.

Analysts fishing in oceans of data at FDA headquarters in Rockville are especially susceptible to seizing on correlations that are in fact spurious. Worse, such oceans furnish fertile fishing grounds for scandal-mongering investigative reporters and so-called consumer advocates whose technical understanding is nil and whose ideological bias against the device manufacturers is astronomical.

(5) During the past three to four years, FDA has markedly slowed the rate at which it approves new products. No corresponding retardation of approvals has occurred elsewhere. Therefore, U.S. device manufacturers have been placed at a substantial disadvantage relative to competitors in other countries. The U.S. approval slowdown, clearly produced by political reactions catalyzed by the hysteria about silicone breast implants, has

added great costs, delays, and unpredictability to what was already a relatively cumbersome approval process. Worse, American patients have found themselves increasingly unable to get state-of-the-art treatments unless they are sufficiently wealthy and knowledgeable that they can go abroad. Without doubt thousands of Americans have suffered and died because of this "device lag."

(6) FDA enforcement authorities, who have long fancied themselves "cops," have become much more hostile, uncommunicative, and punitive during the past four years, as Commissioner Kessler has given the highest priority to aggressive enforcement. People who work in the device companies, creating and distributing products of immense benefit to mankind, have been stunned that the authorities would treat them as suspected felons. To say that they have been demoralized would be too weak a statement.

Elsewhere the regulators bear no resemblance to the FDA cops. In Europe the companies work *with* the Notified Bodies, who must deal with them fairly and cooperatively or risk losing business. In Japan the personnel at MDD are concerned that the Japanese medical device industry succeed and that the Japanese public gain access to improved products from foreign as well as domestic sources. Canadian regulators have nothing like the reputation of FDA for hostility and vindictiveness.

By making itself the sworn enemy of the device industry, FDA has necessarily made itself the enemy of the public health. After all, FDA does not invent, refine, produce, and distribute these life-saving and life-enhancing products. When FDA assaults the industry, it assaults the patients served by the industry.

(7) U.S. device firms have reacted to the more hostile regulatory environment of recent years in several ways. In some cases firms have simply abandoned product lines or R&D projects that, in light of the increased costs and uncertainties, no longer promise to be profitable. In other cases the firms have transferred R&D, clinical trials, or manufacturing to Europe. Given that Europe itself was adopting more demanding regulations and that Europe during the early 1990s was enduring its worst recession since the 1930s, the relocation of U.S. device activities to Europe speaks volumes about the effects of FDA regulation on the U.S. device industry. The American economy has suffered lost employment opportunities in a clean, high-tech industry that long enjoyed a strong comparative advantage in the world market. Worse, where projects have been abandoned altogether, future patients will suffer as a result.

(8) Despite the less stringent regulation of medical devices in Europe, Canada, and Japan, the people of those countries in general have not suffered because of unsafe or ineffective products--at least, if they have, no one has reported that fact nor is any of the experts I have interviewed aware of it. Foreigners have definitely benefited, however, from their early access to the latest, most innovative devices.

Dr. Arthur Beall, Jr., a professor at the Baylor College of Medicine, could have been speaking for American physicians in general when he said: "It's not a matter of our losing our edge. We have already lost it." Beall added, "The question is, how many patients have I lost because I don't have this technology [already available in Europe]?"[127] Echoing Beall, Dr. Keith Lurie of the University of Minnesota concluded: "We're a year

and a half behind the rest of the world, thanks to the FDA. We don't get the ... equipment we need to save lives."[128]

In sum, as Dr. Joel Nobel has put it, "This country has a new public health problem--Congress and the FDA."[129]

## Notes

[1] Robert Higgs is research director for the Independent Institute. This paper draws, with permission of the Independent Institute, on his chapter entitled "FDA Regulation of Medical Devices," in *American Health Care: Government, Economic Processes, and the Public Interest*, edited by Simon Rottenberg (forthcoming).

[2] 52 U.S. Stat. 1040 (June 25, 1938), at 1041.

[3] *Ibid.*, at 1042, 1044.

[4] *Ibid.*, at 1049, 1050.

[5] Peter Barton Hutt, "A History of Government Regulation of Adulteration and Misbranding of Medical Devices," *Food Drug Cosmetic Law Journal* 44 (1989): 105; Peter Barton Hutt and Richard A. Merrill, *Food and Drug Law: Cases and Materials*, 2nd ed. (Westbury, N.Y.: Foundation Press, 1991), p. 735.

[6] Hutt and Merrill, *Food and Drug Law*, p. 736; quotation from "Medical Device Regulation," *Congressional Quarterly Almanac 1976*, p. 535.

[7] Hutt, "A History," pp. 102-108.

[8] U.S. Food and Drug Administration, *Regulatory Requirements for Medical Devices*, HHS Pub. FDA 89-4165, May 1989, p. 1.

[9] Susan Bartlett Foote, "Loops and Loopholes: Hazardous Device Regulation Under the 1976 Medical Device Amendments to the Food, Drug and Cosmetic Act," *Ecology Law Quarterly* 7 (1978): 108-110; Richard A. Merrill, "Regulation of Drugs and Devices: An Evolution," *Health Affairs* 13 (Summer 1994): 56-57.

[10] "Legislative History of the Medical Device Amendments of 1976," *United States Code, Congressional & Administrative News*, 94th Cong., 2d Sess., 1976, vol. 3, pp. 1071-1076; Foote, "Loops and Loopholes," pp. 128-131; "Medical Device Regulation," *Congressional Quarterly Almanac 1976*, pp. 535-536; Hutt, "A History," pp. 110-112.

[11] 90 U.S. Stat., 539 (May 28, 1976).

[12] *Ibid.*, at 575.

[13] *Ibid.*, at 541.

[14] Foot, "Loops and Loopholes," pp. 115-116, 121, 123. On FDA's exceptionally wide regulatory latitude, see Hutt and Merrill, *Food and Drug Law*, p. 20.

[15] U.S. House of Representatives, Committee on Energy and Commerce, Subcommittee on Oversight and Investigations, *Less Than the Sum of Its Parts: Reforms Needed in the Organization, Management, and Resources of the Food and Drug Administration's Center for Devices and Radiological Health*, 103d Cong., 1st Sess., Committee Print 103-N, May 1993, p. 8 (cited hereafter as Subcommittee on Oversight, *Less Than the Sum*).

[16] Legal authorities disagree about whether the performance standards for Class II devices were mandatory or discretionary. See Hutt, "A History," pp. 112-113, and Hutt and Merrill, *Food and Drug Law*, p. 772.

[17] Subcommittee on Oversight, *Less Than the Sum*, pp. 7-9.

[18] Merrill, "Regulation of Drugs and Devices," p. 68.

[19] Hutt as quoted in "International Markets Embrace Novel Devices," *In Vitro* (June 1994): 13. See also Subcommittee on Oversight, *Less Than the Sum*, p. 39.

[20] 90 U.S. Stat., at 560-564.

[21] Dingell's 1983 statements as quoted by Susan Bartlett Foote, "Coexistence, Conflict, and Cooperation: Public Policies Toward Medical Devices," *Journal of Health Politics, Policy and Law* 11 (Fall 1986): 517. Dingell used almost identical phrasing while

berating FDA at hearings in May 1987. See *Congressional Quarterly Almanac 1988*, p. 320.

22 Herbert Burkholz, *The FDA Follies* (New York: Basic Books, 1994), pp. 13-14, 47-48; Peter Brimelow and Leslie Spencer, "Food and drugs and politics," *Forbes* 152 (November 22, 1993): 118.

23 Subcommittee on Oversight, *Less Than the Sum*, p. 12.

24 "The Medical Device Amendments: 10 Years After," *FDA Consumer*, May 1986, pp. 30-31; Jim Page, "Can You Trust Your FDA?" *JEMS (Journal of Emergency Medical Services)* 17 (August 1992): 91; Mary Newman, "To Focus on the Forest: Recognizing the Value of Early Defibrillation Despite Isolated Failures," *ibid.* 19 (May 1994): 17 and sources from the medical literature cited therein, p. 20, notes 16-18.

25 104 U.S. Stat., 4511 (November 28, 1990). For background, see "Legislative History of the Safe Medical Devices Act of 1990," *U.S. Code, Congressional and Administrative News*, 101st Cong., 2d Sess., 1990, vol. 8, pp. 6305-6335, and "New Regulations for Medical Devices," *Congressional Quarterly Almanac 1990*, pp. 579-581.

26 49 Fed. Reg. 36,326-36,351 (September 14, 1984), at 36,349.

27 104 U.S. Stat., at 4511, 4527.

28 Chesemore as quoted by Bruce Goldfarb and Doug Wolfberg, "Feds Focus on Medical Devices," *JEMS (Journal of Emergency Medical Services)* 17 (July 1992): 46.

29 Benesch as quoted by Thomas M. Burton, "Law Concerning Medical Devices Is Often Ignored," *Wall Street Journal*, May 2, 1994.

30 *Ibid.*

31 ECRI advisory quoted by Marybeth Burke, "Hospitals wary of interpretation of medical device reporting law," *Hospitals*, October 20, 1991, p. 42.

32 "Device User Facility Civil Penalties Will Go into Effect," *Medical Devices, Diagnostics & Instrumentation*, May 23, 1994, pp. 17-19.

33 *Ibid.*, March 21, 1994, p. 5; "Device Malfunction Report Backlog," *Ibid.*, November 7, 1994, p. I&W-7.

34 Joel Nobel, M.D., Draft of 1993 address to Utah Biomedical Congress, p. 8.

35 Jack Olshansky calls user error "unquestionably the most frequent contributor to MDRs." See "How the Investment Community Views the Food and Drug Administration's Approval Process and Clinical Outcomes," *Food Drug Cosmetic Law Journal* 45 (1990): 506.

36 104 U.S. Stat., at 4512.

37 Goldfarb and Wolfberg, "Feds Focus on Medical Devices," p. 45.

38 *Ibid.* for quotation of Nobel

39 For a more detailed account of this episode, see my "Wrecking Ball: FDA Regulation of Medical Devices," Cato Institute *Policy Analysis* (1995): in press. A brief account appears in Brent Bowers, "Entrepreneurs Find FDA Can Make or Break Them," *Wall Street Journal*, April 12, 1994.

40 Dr. Cummins's statement on ABC's 20/20 television program, August 12, 1994.

41 104 U.S. Stat., at 4514-4519.

42 *Ibid.*, at 4520.

43 *Ibid.*, at 4520-4523.

44 U.S. Food and Drug Administration, Center for Devices and Radiological Health, "FDA Begins Implementing New Device Legislation," *Medical Devices Bulletin 9* (May 1991): 3.

[45] Jonathan Kahan, "The changing 510(k) process," *Clinica* 529 (December 2, 1992): 13; "US rethinking device evaluation priorities," *ibid.* 547/8 (April 21, 1993): 13, 15; "510(k) decision-making process should remain with manufacturer," *Medical Devices, Diagnostics & Instrumentation*, July 4, 1994, pp. 20-21; Subcommittee on Oversight, *Less Than the Sum*, p. 51.

[46] Jonathan Kahan, "1993--A roller coaster ride for US industry," *Clinica* 585 (January 10, 1994): 23-25; *idem*, "Use of clinical data in support of US and EU device clearances," *ibid.* 604 (May 23, 1994): 8-9; Merrill, "Regulation of Drugs and Devices," pp. 48, 62-64.

[47] 104 U.S. Stat., at 4526-4528.

[48] *Ibid.*, at 4527.

[49] See *Medical Devices, Diagnostics & Instrumentation*, February 28, 1994, pp. 3-5 (on FDA fine of Infusaid), and Bowers, "Entrepreneurs Find FDA Can Make or Break Them," (on FDA fine of Lexicor).

[50] *Medical Devices, Diagnostics & Instrumentation*, February 21, 1994, p. 3.

[51] Burkholz, *FDA Follies*, pp. 47-62.

[52] Subcommittee on Oversight, *Less Than the Sum*, p. 45 (see also pp. 46-48); Kahan, "The changing 510(k) process," pp. 13-14; Bruce Ingersoll, "FDA Attacked For Holding Up Medical Devices," *Wall Street Journal*, September 9, 1992 (remarking on the irony that "one of the main reasons for the slowdown [heavily criticized by Dingell in 1992 and 1993] was intense pressure from prominent lawmakers, including Rep. Dingell himself).

[53] Subcommittee on Oversight, *Less Than the Sum*, pp. 65-75; Kathryn Gleason, "US Enforcement Trends in the '90s," *Clinica Supplement* (October 1993): 13-15; Peter Brimelow and Leslie Spencer, "Just call me 'Doc,'" *Forbes* 152 (November 22, 1993): 108-110.

[54] Jonathan Kahan, "US medical device regulation in 1992," *Clinica* 533 (January 6, 1993): 21.

[55] I take these data from compilations graphed in an unpublished paper by Mary Olson, "Regulatory Agency Discretion Among Competing Industries: Inside the FDA," Political Economy Working Paper No. 173, Washington University, April 1993. Years mentioned are federal government fiscal years.

[56] Unless otherwise noted, these data and those that follow are drawn from *Medical Devices, Diagnostics & Instrumentation*, January 3 and July 25, 1994; *Clinica*, March 17, 1993, and March 28, 1994; and data provided to me by the Health Industry Manufacturers Association (courtesy of Gabrielle Williams).

[57] "1993--A roller-coaster ride for US industry," p. 24.

[58] John Schwartz, "FDA Quickly Whittles Down Stack of Applications for Medical Devices," *Washington Post*, November 29, 1994.

[59] "Kessler's Devices," *Wall Street Journal*, February 10, 1993.

[60] "FDA Outlines Steps To Speed Up Reviews Of Medical Devices," *ibid.*, June 25, 1993; Schwartz, "FDA Quickly Whittles."

[61] "FDA-Industry Interaction in Guidance Development Welcomed," *Medical Devices, Diagnostics & Instrumentation*, August 22, 1994, p. 3.

[62] "Understanding FDA Medical Device Review Statistics," *Insight* (A Quarterly Update Prepared by the Health Care Technology Institute), September 1994, p. 8.

[63] "Compliance and Enforcement--Past, Present, and Future: An Interview with William H. Damaska," *Medical Device & Diagnostic Industry* (July 1993): 32.

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64 Hutt as quoted by Elizabeth R. Porter, "David Kessler's High-Wire Act on Enforcement," *Medical Industry Executive* (January 1994): 19.

65 Subcommittee on Oversight, *Less Than the Sum*, p. 82.

66 Porter, "David Kessler's High-Wire Act," p. 19. See also Hutt and Merrill, *Food and Drug Law*, p. 20.

67 Quoted by Burkholz, *FDA Follies*, p. 58.

68 Subcommittee on Oversight, *Less Than the Sum*, p. 83. See also Jonathan Kahan, "Honour lost to tougher device enforcement," *Clinica* 500 (May 13, 1992): 17, and Gleason, "US Enforcement Trends in the '90s," p. 14.

69 Draft of 1993 address, p. 7.

70 Subcommittee on Oversight, *Less Than the Sum*, pp. 66, 88 (see also pp. 69-70, and 73 for additional details).

71 *Ibid.*, p. 66. See also Porter, "David Kessler's High-Wire Act," p. 21, and statements in Appendix 3 below.

72 For 1991 and 1992 my source is "The Enforcement Story," an internal FDA document issued by the Office of Enforcement in the Office of Regulatory Affairs; for 1993 and 1994 it is the Office of Enforcement as reported in data sheets provided to me by the Health Industry Manufacturers Association.

73 "International Markets Embrace Novel Devices," p. 12, quoting Peter Barton Hutt for the 70 percent estimate; Ronald Johnson, director of the Office of Compliance and Surveillance, as quoted in "FDA's regulatory priorities for 1994," *Clinica* 585 (January 10, 1994): 27.

74 Subcommittee on Oversight, *Less Than the Sum*, p. 74 ("FDA simply issued a series of broadly-defined and wide-ranging [GMP] regulations that provided its reviewers and inspectors with maximum flexibility, and largely failed to follow up with detailed guidelines to better advise industry").

75 Draft of 1993 address, p. 22.

76 Subcommittee on Oversight, *Less Than the Sum*, p. 85.

77 Daly as quoted by Laura Jereski, "Block that innovation!" *Forbes*, January 18, 1993, p. 48. See also "Venture Capitalists Still Investing, But Selectively," *Primus* (The Monthly Newsletter of the Health Industry Manufacturers Association) 4 (May 1994): 5; Olshansky, "How the Investment Community Views"; and venture capitalist Mark Knutson, whose congressional testimony is quoted by Tom Hamburger, "Entrepreneur can't imagine starting out in today's climate," *Minnesota Star Tribune*, June 27, 1994.

78 Quoted by Subcommittee on Oversight, *Less Than the Sum*, p. 80.

79 Heidrich as quoted by Lawrence M. Fisher, "Frustration for Medical Innovators," *New York Times*, June 30, 1993.

80 Hutt as quoted by "International Markets Embrace Novel Devices," p. 12.

81 Michiels as quoted by Fisher, "Frustration for Medical Innovators."

82 *Ibid.* for quotation of Summers

83 "International Markets Embrace Novel Devices," p. 11.

84 Lemaitre as quoted by Jereski, "Block that innovation!"

85 "FDA driving device manufacturers out of the US?" *Clinica* 532 (December 23, 1992): 13.

86 "US manufacturers moving out," p. 1; "Preliminary Findings, Strategic Survey," compilation provided to me by HIMA (courtesy of Gabrielle Williams).

[87] "Member Surveys Track Regulatory, Business Actions," *Primus* (The Monthly Newsletter of the Health Industry Manufacturers Association) 4 (May 1994): 4.

[88] Interview with Matthew S. Gallivan, HIMA Associate Vice President for Europe and the Americas, December 9, 1994.

[89] Mike Meyers, "Losing the edge: Survey shows that state's med-tech pioneers are sending money, jobs, products overseas," *Minneapolis Star Tribune*, June 27, 1994.

[90] Medtronic News Release, Minneapolis, November 22, 1994.

[91] "International Markets Embrace Novel Devices," p. 12. See also "Trends in Venture Capital Funding for the Medical Device Industry," *Insight* (A Quarterly Update Prepared by the Health Care Technology Institute), March 1994, p. 5.

[92] American Electronics Association News Release, Washington, D.C., June 23, 1994.

[93] Health Industry Manufacturers Association, *The Global Medical Device Market Update*, 1994 edition, HIMA Publication 94-1, January 1994, pp. 76-77.

[94] G. Gaikhorst and E. Koivisto, "Current problems in the standardisation of medical electrical equipment," *Journal of Medical Engineering and Technology* 1 (July 1977): 203.

[95] *Ibid.* For additional detail on Britain, see David Whelpton, "Will good manufacturing practice produce acceptable equipment? *ibid.* 8 (January/February 1984): 1-2.

[96] Information in this paragraph from Gaikhorst and Koivisto, "Current problems," pp. 204-205.

[97] R. T. Rogers, "Testing of medical electrical and hospital laboratory equipment: DHSS recognition of the BSI Test House, Hemel Hempstead," *Journal of Medical Engineering and Technology* 4 (September 1980): 226. On the IEC, see Gaikhorst and Koivisto, "Current Problems," p. 203.

[98] Rogers, "Testing," p. 226.

[99] *Ibid.*

[100] H. David Banta, "The Regulation of Medical Devices," *Preventive Medicine* 19 (1990): 697.

[101] *Ibid.*, pp. 695-696.

[102] *Ibid.*, p. 698.

[103] G. R. Higson, "Medical device regulations in the New Europe," *Journal of Medical Engineering & Technology* 16 (May/June 1992): 107.

[104] Tables provided to me by HIMA (courtesy Matthew S. Gallivan). See also the description of European device regulation by lawyer Richard Kingham in "International Markets Embrace Novel Devices," pp. 12-13.

[105] Mike Meyers, "Losing the edge: Survey shows that state's med-tech pioneers are sending money, jobs, products overseas," *Minneapolis Star Tribune*, June 27, 1994, p. 7D.

[106] *Minneapolis Star Tribune*, June 26 and 27, 1994, reprint, p. 5H.

[107] For scores of cases, see the *Minneapolis Star Tribune* reports of June 26 and 27, 1994, and the HIMA survey data reproduced in Subcommittee on Oversight, *Less Than the Sum*, pp. 234-243.

[108] In this and the following paragraphs, I draw upon Higson, "Medical device regulations"; Sara Lewis, "Europe: Medical devices and diagnostics," *The Lancet* 341 (January 9, 1993): 106; Susanne M. Ludgate and Don C. Potter, "European directives on medical devices," *British Medical Journal* 307 (21 August 1993): 459-460; Susanne Ludgate and A. John Camm, "New European Regulations on Medical Devices," PACE *(Pacing and Clinical Electrophysiology)* 16 (July 1993): 1427-1428; Gordon Higson,

"The European Medical Device Directives," *Clinica Supplement* (October 1993): 5-7; "Update on EC Medical Device Regulations," *ibid.*, pp. 8-9; and "Third EC Medical Device Directive in the Pipeline," *ibid.*, p. 9.

109 For an introduction to the details of the essential requirements, see Higson, "The European Medical Device Directives," pp. 5-7.

110 "Risk analysis--guided tour of the draft standard," *Clinica* 597/8 (April 11, 1994): 6-9.

111 Kahan, "Use of clinical data," p. 10.

112 Amanda Maxwell, "European clinical investigations between the devil and the deep blue sea," *Clinica* 624 (October 10, 1994): 6.

113 Kahan, "Use of clinical data," p. 10.

114 Maxwell, "European clinical investigations," p. 8. I have been told by an authority who prefers to remain anonymous that Gordon Higson, the leading figure in the development of the new European system, has always been adamant about avoiding an FDA-type arrangement.

115 Phillips as quoted by Meyers, "Minnesota med-tech companies."

116 As argued by, *inter alia*, C. Frederick Beckner, III, "The FDA's War on Drugs," *Georgetown Law Journal* 82 (December 1993): 529-562.

117 Junker as quoted by Tom Hamburger and Mike Meyers, "Losing the edge: Overseas patients reap the benefits of U.S. research while those here wait," *Minneapolis Star Tribune*, June 26, 1994, reprint p. 5H.

118 *Ibid.*

119 Information taken from TUV Product Services brochure, "Zertifikate fur Europa."

120 HIMA, "Comparison of Product Approval Process" and information supplied to me by HIMA on recent product approval times and government approval resources.

121 Dr. Richard Tobin, Director of the [Canadian] Medical Devices Bureau, as quoted by "Canadian classification system moves closer," *Clinica* 630 (November 21, 1994): 8.

122 Sachiko Kuno, "Regulation of Medical Devices in Japan--Current Status & Trends," *Clinica Supplement* (October 1993): 3.

123 *Ibid.* I draw also on HIMA, "Comparison of Product Approval Process" and my interview with Terri L. Ethridge, director of global strategy and analysis at HIMA, December 9, 1994.

124 "Japanese Risk-Based Device Classification System To Be Proposed," *Medical Devices, Diagnostics & Instrumentation*, November 1, 1993, pp. 23-24; Ethridge interview; Kuno, "Regulation of Medical Devices," p. 4.

125 HIMA, "Comparison of Product Approval Process."

126 Werner as quoted by Hamburger and Meyers, "Losing the edge."

127 *Ibid.* for quotation of Beall.

128 *Ibid.* for quotation of Lurie.

129 Nobel, Draft of 1993 address, p. 5.

# Appendix 1

Letter to Reid Stuntz, Staff Director, Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, U.S. House of Representatives, from William W. O'Neill, M.D., Director, Division of Cardiology, William Beaumont Hospital, Royal Oak, Michigan, March 8, 1993.

Source: U.S. House of Representatives, Committee on Energy and Commerce, Subcommittee on Oversight and Investigations, *Less Than the Sum of Its Parts: Reforms Needed in the Organization, Management, and Resources of the Food and Drug Administration's Center for Devices and Radiological Health*, 103d Cong., 1st Sess., Committee Print 103-N, May 1993, pp. 231-233.

Beaumont
William Beaumont Hospital
Royal Oak

March 8, 1993

Reid Stuntz
Staff Director
Subcommittee on Oversight & Investigation
2323 Rayburn House Office Building
Washington, DC 20515-6116

Dear Mr. Stuntz:

I am writing this letter to you today to seek your assistance and that of Representative Dingle in a matter important to the health care of the American public. My name is Dr. William O'Neill. I am the Director of the Division of Cardiovascular Diseases at William Beaumont Hospital. As you know, William Beaumont Hospital is a major community hospital and research institution in southeastern Michigan. We service the needs of southeastern Michigan in general, and have a great number of patients from the downriver area referred to us for treatment of advanced cardiovascular care.

We have had the opportunity to be involved with the investigation of new medical devices to advance the treatment of patients with cardiovascular disease. As a physician caring for hundreds of patients with cardiovascular disease, and as a scientific researcher, I am greatly concerned about the detrimental impact that the Food and Drug Administration's current handling of evaluation and approval of new medical devices has had. Presently, very few patients in the United States have access to new, effective technologies that are commonly used in Europe, Japan and South America for the treatment of heart disease. The medical device industry has been completely paralyzed by the disorganization in the FDA approval process. Tragically, potentially life-saving devices cannot be used early on in the United States. I would like to enumerate some specifics and implore you to assist us in untangling the bureaucratic morass that has been created in the Food and Drug Administration. We at Beaumont Hospital were actively involved with the initial investigation of the Heart Technology Rotablator. We believe that the device is very safe and a very effective method of treating patients non-operatively for removal of obstructions in the coronary blood vessels. The device is especially effective in blockages that cannot be treated by balloon angioplasty. Based on careful scrutiny of the scientific data presented to the physician advisory panel, the device was recommended for approval by the physician advisory panel of the Food and Drug Administration in April of 1992. At the present time, there is no clue as to when final approval for marketing of this device will occur. I have many patients that have been waiting for over a year for this device. One particular patient, Mr. Samuel Sobolavich is a 41 year-old disabled policeman from East Pointe. He has no other

[illegible] 48073-6769 [illegible]

treatment option other than the Rotablator and currently is completely disabled by angina. He has been waiting for over a year to have the device available here in this area for treatment of his intractable angina. This patient and many others can be greatly aided by this device, but we physicians in southeastern Michigan have absolutely no access to it.

A second device, the transluminal extraction (TEC) catheter from Interventional Technologies also was presented to the FDA physician advisory panel in July of 1992. At present, the company has no clue as to when formal approval will be granted for this device. This device is extraordinarily useful for the treatment of diseased saphenous vein bypass grafts. As you know, coronary bypass surgery is commonly performed in the United States. Over 300,000 procedures a year are being performed. Unfortunately, the vein bypass grafts do not last permanently. After about five to seven years, more than half of the grafts begin to wear out. Rather than forcing patients to have a second repeat open heart operation, the TEC catheter has been a very safe and effective method of relieving the underlying obstruction in the diseased vein grafts. This catheter will be a great aid to patients with previous bypass, and will be a great cost savings since the second open heart operation can be avoided. Based on the data presented to the physician advisory panel, unanimous recommendation for approval was granted to the TEC catheter in July of 1992. Again, there is no hint as to when this device will be approved. I have very grave concerns about whether this device will ever be commonly available to the American public. Interventional Technologies is a small start-up company with meager and limited resources. The fact that they cannot market the product now, I believe will have great impact on the viability of the company. I believe it would be a true tragedy if this useful and cost-effective and life-saving technique could not be used by the American public because of bureaucratic delays.

Finally, another very important medical device, the Cook intra-coronary stent has not yet been approved. This device was also given physician recommendation for approval in June of 1992. The device is a metal mesh that is implanted into blood vessels that have been damaged. In hospitals where this device is available, the need for emergency open heart surgery after balloon angioplasty has decreased by almost two-thirds! As you know, balloon angioplasty is commonly performed in the United States. Over 300,000 procedures a year are being performed in the United States. About 2% of the time, (6,000 cases) emergency open heart surgery is required because of the damage to the blood vessels that inadvertently occurs during balloon angioplasty. Intra-coronary stents repair the damage to the blood vessels and eliminate the need for open heart surgery. It is possible that as many as 5,000 open heart surgeries could be eliminated by the approval of this device. This would obviously have enormous consequences, both in terms of patient safety and convenience, as well as economic consequences by decreasing the cost of hospitalization and the need for open heart surgery. The device is extraordinarily effective and is available in Canada, South America, Mexico, Japan and Europe. It is not yet available in the United States.

In my discussions with these medical device companies, it is apparent that the lengthy process and enormous resources required to take a new device from initiation to approval



is going to dramatically limit development of new medical devices in the United States. Heart Technology initiated its clinical trials with the Rotablator in 1985, Interventional Technologies in 1987 and Cook in 1989. Each of these companies have spent between $20-30 million before the devices have been approved. Given the extraordinary amount of time required and the huge sums required for approval of these devices, it is unlikely that small start-up companies will ever have the economic wherewithal to develop new devices. Often times, these small start-up companies are where the most novel, innovative and effective new devices are originated.

There have been dramatic advances made in the treatment of patients with cardiovascular disease over the last two decades. The advent of open-heart surgery, the advent of balloon angioplasty, and most recently, the advent of new non-balloon angioplasty devices will continue to be an enormous aid for patients with cardiovascular disease. As you know, the age-adjusted mortality for cardiovascular disease has dramatically declined over the last two decades. Although in part this is related to changes in life style, a major portion of the credit has to occur because of the advances in cardiovascular care that have occurred. Unfortunately, the citizens of Michigan have the 48th worst cardiovascular mortality of any state in the country. Cardiovascular disease remains in epidemic proportion in Michigan. Because of this, new advances in treatment of cardiovascular disease will have a disproportionately greater impact in Michigan compared to other states. In addition, because of the high incidence of cardiovascular disease, southeastern Michigan itself could serve as a national resource for development of new technologies. This area could blossom as an area for testing of innovative new medical devices for the treatment of cardiovascular disease. This could have great impact in terms of creation of new good jobs in the medical device industry in southeastern Michigan. For all of these reasons, I implore you and Mr. Dingle to assist us in streamlining the enormous bureaucracy that occurs and decreasing the time that it takes to test and approve new safe and effective medical devices. I look forward to discussing this with you in the future. I am fully and totally committed to advancing the treatment of patients with cardiovascular disease. I am at your disposal as a specialist in this area and would be delighted to visit you in the Dearborn offices or in the Washington offices to hopefully discuss this matter with you.

Sincerely yours,

William W. O'Neill

William W. O'Neill, M.D.
Director, Division of Cardiology

WWO/mc

# Appendix 2

Health Industry Manufacturers Association, Executive Summary of "Product Approvals Overseas Project."

Source: U.S. House of Representatives, Committee on Energy and Commerce, Subcommittee on Oversight and Investigations, *Less Than the Sum of Its Parts: Reforms Needed in the Organization, Management, and Resources of the Food and Drug Administration's Center for Devices and Radiological Health*, 103d Cong., 1st Sess., Committee Print 103-N, May 1993, pp. 234-237.

APPENDIX XIV

## Product Approvals Overseas Project

### Executive Summary

In January 1993, the U.S. Department of Commerce reported that the U.S. medical device industry ranked as the fastest growing manufacturing industry in the United States for the period 1988-1993 (projected). U.S. producers of medical technology currently supply 49% of the world's medical device needs. Over the past five years, 37% of the growth in U.S. medical device production has been used to keep up with strong overseas demand for U.S. medical device exports. The solid global demand for U.S. medical devices has helped to boost U.S. medical device production, U.S. industry employment and the U.S. industry trade surplus an average of 8%, 5% and 20% a year, respectively, even throughout the recent U.S. recession.

While the U.S. medical device industry discovers, develops and supplies nearly 50% of the world's medical device needs, U.S. firms are no longer always able to first market their new medical technology in the United States, despite their desire to do so. New U.S. medical technology is increasingly becoming available in Europe, Japan and elsewhere months and sometimes years before it is also available in the United States, if at all. Doctors and patients in the United States face the daunting prospect of either: having to travel to a foreign land to have access to the latest medical technology or having to accept a less effective and/or a higher risk treatment for their illness in the United States.

The following is a summary of a recent informal survey of some leading medical device firms in the United States on the availability of U.S. medical technology in major overseas markets:

- Number of participating companies: Twelve, including 2 divisions from same parent corporation; estimated annual revenues of the companies with medical devices covered in this study are:

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|---|---|
| Greater than $ 500 M | = 6 |
| Less than $ 500 M | = 2 |
| Less than $ 100 M | = 1 |
| Less than $ 20 M | = 3 |

The lack of access to the U.S. medical device market can imperil the very existence of medium to small companies.

- Number of devices: Of the 49 products offered as examples by companies, the majority are Class III devices with 84% of the total.

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| Class III | = 41 |
| Class II | = 7 |
| Class I | = 0 |
| Drug | = 1 |



- Types of devices: The device cited most frequently as being approved overseas first was cardiovascular devices, with 53% of the total; orthopedic devices added another 22%.

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| Cardiovascular devices, e.g. implantable defibrillators, pacemakers, related devices | = 26 (life sustaining) |
| Orthopedic devices | = 11 (life enhancing) |
| Other, e.g. urological devices, infertility aids, ophthalmic devices | = 7 (life enhancing) |
| IVD reagents/diagnostic tests | = 5 |

- Length of time devices have been available in overseas markets: Of the devices available overseas but not in the U.S., 33% have been marketed overseas for longer than 3 years, only 3 devices among this group are now available in the U.S. Another 59% of the devices have been marketed overseas for 6 months up to 2 years, again with only 3 devices available to U.S. patients.

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| Less than 6 months | = 4 |
| 6 mos. - 1 year | = 6, (only 2 devices are now available in the U.S.) |
| 1 - 2 years | = 14, (only 1 device is now available in the U.S.) |
| 2 - 3 years | = 9 |
| Longer than 3 years | = 16, (only 3 devices are now available in the U.S.) |

Of the 16 devices available overseas for longer than 3 years, 11 are cardiovascular devices; 81% of the cardiovascular devices included in this study have been available overseas for at least one year or longer.

- Although the decision to bring a product to a particular geographic market in advance of other geographic markets is based on multiple factors, the facility of meeting local regulatory requirements can be viewed as a pivotal component in that decision. Below are the number of devices that were first made available overseas by country.

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| Netherlands | = 8 | Belgium | = 2 |
| Canada | = 7 | France | = 2 |
| Germany | = 5 | Australia | = 1 |
| United Kingdom | = 3 | No requirements | = 2 |
| | | Not reported | = 19 |

At least 27 of the 49 devices were first marketed in either Europe or Canada.

- Once introduced in a "lead" country, devices achieve credibility within the regional medical community and become widely marketed throughout the region where first introduced as well as elsewhere. As indicated below, most of the devices covered by this survey are available in Europe and Canada.

| | |
|---|---|
| Europe | = 43 |
| Canada | = 12 |
| Asia/Pacific | = 10 |
| Japan | = 7 |
| Rest of World | = 2 |

- Price range of devices available overseas, but not in the U.S.: For the most part, these are not costly devices with 63% available to the end user for less than $ 5 K.

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| Less than $ 500 | = 13 |
| $ 500 - 1 K | = 9 |
| $ 1 - 5 K | = 9 |
| Greater than $ 5 K | = 18 |

- Reasons for delay in receiving FDA clearance: The most pervasive concern voiced by device manufacturers involved the ever changing nature of data required for all types of submissions, IDE, PMA or 510(k), 59% of the devices were affected by this concern.

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| Data requirements, unclear, arbitrary, excessive | = 29 |
| Indecision on classification | = 5 |
| Workload-related delay at FDA | = 4 |
| FDA safety/GMP concerns | = 4 |
| Unknown/other | = 7 |

- Substitute devices or therapies are available for 46 of the 49 devices. Many of these substitutes prove to be less effective and may pose a greater risk to the patient, at an equal or higher cost than for those devices not marketed in the U.S. .

  Fifty-one percent of the devices were deemed to be more effective than the substitute device/therapy. In the remaining 49%, effectiveness was equal. Substitute device or therapy is:

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| Equal in effectiveness | = 21 |
| Less effective | = 25 |
| More effective | = 0 |



- Substitute devices, continued.

  Twenty-two percent of the substitute devices pose a greater risk to the patient, whereas the remaining 78% represent equal risk. Substitute device or therapy poses:

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|---|---|
| Equal risk | = 35 |
| Less risk | = 0 |
| Greater risk | = 11 |

  Contrary to increasing health care costs, 35% of the devices are less expensive than the substitute, and 59% are comparable in cost to the end user. None of the devices are more costly than the substitute. Substitute device or alternative therapy is:

| | |
|---|---|
| Equal in cost | = 29 |
| More expensive | = 17 |
| Less expensive | = 0 |

Note: Numbers in some of the analysis may not add up exactly in all cases due to a lack of data; or in some cases, numbers may exceed total due to multiple citings.

## Conclusion

While the results of the informal survey may have raised some additional questions, a number of observations can be made:

- Foreign patients have access to some of the latest U.S. medical technology before U.S. patients. A number of these devices involve life-saving or life-sustaining medical technology.

- The use of more costly, less effective or higher risk medical technology alternatives in the United States can unnecessarily add to the total cost of health care in the United States.

- Regulatory uncertainty or unclear U.S. submission requirements appears to be a major cause of the delay in U.S. product approval, regardless of whether the medical device is Class II or III (i.e., a 510(k) or PMA device).

- It is unclear why medical devices that have undergone both regulatory scrutiny and actual market use in Europe, Canada and Japan are not also approved in the United States within a similar timeframe, particularly since U.S. medical device firms generally seek to first market their products in the United States. There is no evidence which indicates that products available in these major overseas markets are any less safe than products available in the United States.

- To exacerbate the situation, the circumstances that prompt U.S. device manufacturers to first market overseas also set into motion other strategic business decisions that do not favor the long term interests of the United States. For example, medical device firms typically locate substantial portions of their creative, regulatory, marketing and production capacity in or near the major country where the company first markets its latest medical technology.

In sum, the issues raised by this informal industry survey merit additional study to avoid the further erosion of U.S. patient access to new cost-effective medical technology as well as the competitiveness of one of America's top performing industries.

# Appendix 3

Excerpts from volunteered comments, Health Industry Manufacturers Association, Strategic Business Decisions Survey, 1994.

Source: Health Industry Manufacturers Association (courtesy of Gabrielle Williams).

The final question of HIMA's 1994 Strategic Business Decisions Survey was "Please include any additional information with regard to concerns about the U.S. regulatory environment, present and future." Excerpts from the responses follow. Numbers are those assigned to the firms in the survey.

1. "... we have decided that the costs of remaining in the area of Blood Bank [information] systems are too high. Even though our system has been evaluated as superior by an independent consultant, and is well-received by our users, we do not feel that it is economically feasible for us to comply with the regulatory burden."

2. "There is a lack of consistency in compliance and product approval review."

3. "'Unfriendly' government attitude.... Ever increasing rules/regulations to deal with...."

4. "New CGMP & user fees will cause us to start manufacturing our products in Europe."

6. "Guidance documents, instructions and recommendations are not written in the most easy to understand language. (Reps from FDA have admitted this to me.)"

7. "Today's FDA enforcement and slow review of new products is driving new technology off shore...."

8. "Much easier to bring new product to market outside the U.S. even if you have to assemble outside the U.S."

9. "...ever-increasing demands and authority of the FDA. ...the new regulations and associated financial burdens are being imposed in a non-discerning manner with the end result of eliminating the small manufacturing companies from the health care industry."

11. "Ever increasing ratcheting of regulatory requirements.... Emphasis on 'Form over substance' in facility inspections and lack of uniform guidelines for companies to follow discourages U.S. new product investments...."

13. "The FDA's attitude toward our industry that they are 'enforcers of the law' against a group of unethical businessmen needs to be corrected."

14. "FDA is driving our business overseas!!"

15. "(1) Continued delay and excessive review of 510(k)'s submittals.

(2) Changes to GMP regulation which may have negative impact....

(3) Apparent antagonistic attitude of FDA towards the industry."

16. "It is exceedingly bad and getting worse. Dr. Kessler and his recent appointments to FDA posts clearly believe that the medical device industry is made up of incompetents and criminals. He is out to decimate the industry, company by company. Several ex FDA people have said he has given direct instructions to 1) 'Never believe anyone in industry', and 2) 'Don't ever admit that you (FDA) have made a mistake.'

The implementation of new, onerous regulations has been fraught with ambiguity along with stiff penalties for not being able to decipher the code. Moreover, there is no apparent consideration given to the intrinsic safety and reliability of a product--just the slavish adherence to GMP's that were developed by people with little or no real world industry experience. The paper that we are forced to keep is more important and time consuming than our products.

...the U.S. medical device industry will soon be on the ropes vis a vis its foreign competitors if the current regulatory environment in the U.S. continues."

17. "...regulation is becoming particularly onerous. Worst example--FDA."

18. "The current regulatory environment in the US is stifling a once vibrant medical device industry."

19. "The issue with our firm is ... the uncertainty and unpredictability of the U.S. Regulatory process and time of approvals."

22. "...slow product approval, loss of communication between industry and the FDA...."

23. "Regulatory demands/costs make decisions to expand in this market difficult...."

24. "...almost every device company I have talked to or heard from has implemented a strategy to launch sales in whatever country they can achieve regulatory clearance from first."

25. "...snail's pace of FDA...."

26. "US FDA regulatory conditions/guidelines are so fouled up you cannot plan for the future. The process has no defined playing field or rules. The referee is the FDA and they make them up as the game progresses. Then in some games the referee leaves the agency and the game begins all over again."

27. "Unevenness and unpredictability of enforcement and approval process is making market success too random."

30. "Clinical research outside U.S. accelerates benchmark achievement for start-up companies."

31. "a. Increasingly excessive delays.... [just] talk about reform and improvement....

b. ...congressional oversight of FDA activities which appeared to be politically motivated.

c. ...leaving compliance interpretation to the discretion of the district offices."

32. "The regulatory climate, especially for inspections, is like a police state. ...We plan to put more outside US because the climate from FDA and other mandates is just a lot more business friendly [elsewhere]."

33. "U.S. Regulatory requirements are overly burdensome in many cases.... In addition, delays in receiving feedback from FDA are unreasonably long."

34. "International expansion becomes a necessity as a hedge against an increasingly uncertain domestic regulatory environment, especially the product approval process."

35. "Trends are all in wrong direction."

36. "A more intense regulatory environment will increase our costs and the cost of our products."

37. "Difficult if not impossible environment to work in due to FDA's lack of timely action on product applications."

38. "European produced diagnostics reach the market 2 years faster than the US produced diagnostics due to US regulatory delays vs. no regulatory requirements in Europe."

40. "Major concern obviously increased time and cost of 510(k) process, will reduce innovation and lessen US industry's competitive advantage."

41. "Current regulatory environment, including enforcement and new product approvals time may cause expansion off shore."

42. "Always, as a small company, we are concerned with increasing regulatory costs...."

43. "The U.S. Regulatory environment should attempt to align itself to the international regulatory environment.... A CE Mark should allow the company to distribute their products."

44. FDA "will not return phone calls to answer questions or accept information (whichever is the case)."

46. "At present we are seriously considering all of our business activity being conducted in Europe. This is due to a long, expensive, and uncertain domestic regulatory road. ...We have spent $35 million plus in getting to this point and have essentially been told by FDA that the rules have changed.... Our money will be better spent overseas...."

47. "U.S. regulatory environment ... [is] disproportionately burdensome to the smaller manufacturers. ...ever more onerous regulatory burdens ... many small, innovative companies may be driven out of business."