FOOD AND DRUG ENFORCEMENT STANDARDS FOR MEDICAL DEVICES

JOINT HEARING

BEFORE THE

SUBCOMMITTEE ON HUMAN RESOURCES AND INTERGOVERNMENTAL RELATIONS

AND THE

SUBCOMMITTEE ON NATIONAL ECONOMIC GROWTH, NATURAL RESOURCES, AND REGULATORY AFFAIRS

OF THE

COMMITTEE ON GOVERNMENT REFORM AND OVERSIGHT HOUSE OF REPRESENTATIVES

ONE HUNDRED FOURTH CONGRESS

FIRST SESSION

SEPTEMBER 14, 1995

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FOOD AND DRUG ENFORCEMENT STANDARDS FOR MEDICAL DEVICES

THURSDAY, SEPTEMBER 14, 1995

HOUSE OF REPRESENTATIVES, SUBCOMMITTEE ON HUMAN RESOURCES AND INTERGOVERNMENTAL RELATIONS, JOINT WITH THE SUBCOMMITTEE ON NATIONAL ECONOMIC GROWTH, NATURAL RESOURCES, AND REGULATORY AFFAIRS, COMMITTEE ON GOVERNMENT REFORM AND OVERSIGHT,

Washington, DC.

The subcommittees met, pursuant to notice, at 2 p.m., in room 2247, Rayburn House Office Building, Hon. Christopher Shays (chairman of the Subcommittee on Human Resources and Intergovernmental Relations) presiding.

Present from the Subcommittee on Human Resources and Intergovernmental Relations: Representatives Shays, Souder, Towns, Green, and Waxman.

Present from the Subcommittee on National Economic Growth, Natural Resources, and Regulatory Affairs: Representatives McIntosh, Fox, Peterson, Waxman, and Slaughter.

Staff Present: Lawrence J. Halloran, staff director and counsel; Anne Marie Finley and Robert Newman, professional staff members; and Thomas M. Costa, clerk, Subcommittee on Human Resources and Intergovernmental Relations; Jon Praed, chief counsel, Subcommittee on National Economic Growth, Natural Resources, and Regulatory Affairs; Kevin Davis, minority professional staff; and Elisabeth Campbell, minority staff assistant, Committee on Government Reform and Oversight.

Mr. SHAYS. The hearing will come to order.

This joint hearing continues our oversight of the Food and Drug Administration's regulation of medical devices. We began this inquiry with a hearing August 1, focusing on risk assessment standards for breast implants and biomaterials. Today, we focus on FDA enforcement standards, particularly the important issues raised by the Indiana Medical Device Manufacturers in their recent petition.

We have asked our witnesses to address the following questions: How does the FDA establish enforcement standards for medical device regulations? What factors determine the use of informal versus formal procedures to promulgate enforcement standards? How consistently are those standards applied? How does the FDA guard against selective or arbitrary enforcement? And most importantly, what are the effects of current FDA device approval and enforcement policies on patient outcomes and public health?

Underlying all these questions is the need for balance, balance between the medical risks and benefits of new devices; balance between the pace of technological advances and the capacity of regulatory systems; and balance between global market realities, government authority, and the right of patients to make their own health care decisions.

Any loss of equilibrium costs lives. People will die if unsafe and ineffective devices reach the marketplace, just as patients die when lifesaving devices are not available due to primarily bureaucratic roadblocks.

So today we hear from the FDA, device manufacturers, and industry analysts on how to achieve and maintain that essential balance in the face of rapid technological progress, relentless foreign competition, and tight Federal budgets. We look forward to testimony from all our witnesses and to working with all of them in evaluating proposals to reform the regulation of medical devices.

[The prepared statement of Hon. Christopher Shays follows:]

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Statement of Rep. Christopher Shays

September 14, 1995

This joint hearing continues our oversight of the Food and Drug Administration's regulation of medical devices. We began this inquiry with a hearing August 1 focusing on risk assessment standards for breast implants and biomaterials. Today we focus on FDA enforcement standards, particularly the important issues raised by the Indiana Medical Device Manufacturers in their recent petition.

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Underlying all these questions is the need for balance. Balance between the medical risks and benefits of new devices. Balance between the pace of technological advances and the capacity of regulatory systems. And, balance between global market realities, government authority and the right of patients to make their own health care decisions. Any loss of equilibrium costs lives. People will die if unsafe and ineffective devices reach the marketplace. Just as patients die when life-saving devices are not available due only to bureaucratic roadblocks.

So today we hear from the FDA, device manufacturers and industry analysts on how to achieve and maintain that essential balance in the face of rapid technical progress, relentless foreign competition and tight federal budgets. We look forward to your testimony and to working with all of you in evaluating proposals to reform the regulation of medical devices.

Mr. SHAYS. This is a joint hearing between the Subcommittee on Human Resources and Intergovernmental Relations and the Subcommittee on National Economic Growth, Natural Resources, and Regulatory Affairs. Before asking the chairman, Mr. McIntosh, of that subcommittee to speak, I invite my ranking member, Mr. Towns, to make an opening statement.

Mr. TOWNS. Thank you very much, Mr. Chairman, for calling this hearing which continues the Human Resources and National Economic Growth Subcommittees' oversight of the FDA.

The issue of enforcement standards for medical devices has been a source of great concern within the medical device community. The specific concern is that the FDA has abdicated its responsibility under the Administrative Procedures Act to provide for public participation when developing substantive regulations.

These concerns are set forth in the Indiana Medical Device Manufacturers Council citizens' petition filed with the FDA. In the petition, the IMDMC alleges that the FDA has created substantive policy through informal mechanisms such as press releases and speeches and, in so doing, has violated the notice-and-comment requirement of the APA. The IMDMC further contends that such informal policy pronouncements have been the basis for enforcement actions against medical device manufacturers, many of whom have not been given notice of the policies being enforced.

If it is true that the FDA is violating the APA, then some action must be taken to prevent this from occurring in the future. We cannot have Federal agencies issuing substantive policy in speeches and then turning around and basing an enforcement action on the contents of a speech.

However, I do not believe that requiring notice and comments for all rules, including interpretive rules, is a proper solution. My concern is that such a requirement would greatly lengthen the medical device approval process. In addition, let me point out that requiring notice and comment for all rules must be a severe drain on FDA resources, and I understand that, as greater funding would have to be dedicated to the notice-and-comment process.

At a time of belt-tightening within the government, less funding would be available for the review of premarket approval applications and enforcement activities. As a result, this could further lengthen the time it takes to receive FDA approval of not only medical devices but of drugs, biologics, food additives, and the like. Mr. Chairman, as you well know, the FDA cannot afford to enact measures that would lengthen the already protracted premarket approval period.

Today the subcommittee will also examine the human cost of delays in medical device approvals at the FDA. Our consideration of this issue corresponds to the release of a report on the subject by the Hudson Institute. As I indicated earlier, in the interest of coherence, I would appreciate our witnesses tying the issues together, enforcement standards issues. I look forward to hearing witness testimony on the report, in addition to an assessment of the conclusions drawn.

Mr. Chairman, again I thank you for calling this hearing, and I anticipate both an engaging and constructive discussion, because it is needed, and the sooner the better.

Thank you very much. I yield back the balance of my time.

[The prepared statement of Hon. Edolphus Towns follows:]

OPENING STATEMENT OF REP. ED TOWNS
SUBCOMMITTEE ON HUMAN RESOURCES AND INTERGOVERNMENTAL RELATIONS
AND THE SUBCOMMITTEE ON NATIONAL ECONOMIC GROWTH, NATURAL RESOURCES, AND REGULATORY AFFAIRS

SEPTEMBER 14, 1995

MR. CHAIRMAN, THANK YOU FOR CALLING THIS HEARING, WHICH CONTINUES THE HUMAN RESOURCES, AND THE NATIONAL ECONOMIC GROWTH SUBCOMMITTEES' OVERSIGHT OF THE FDA.

IT IS THE MISSION OF THE FDA TO ENSURE THE SAFETY OF OUR NATION'S FOOD SUPPLY, DRUGS, BIOLOGICS, AND MEDICAL DEVICES. IN CARRYING OUT THIS MISSION, THE FDA HAS SAVED COUNTLESS LIVES. HOWEVER, CRITICISM HAS BEEN LODGED THAT THE AGENCY'S DELIBERATE PACE IN PRODUCT APPROVALS HAS COST LIVES. IN ADDITION, MANY HAVE CHARGED THE AGENCY WITH VIOLATING THE LAW IN ITS PROMULGATION OF ENFORCEMENT STANDARDS. THESE ARE VERY SERIOUS CHARGES, DESERVING OF THESE SUBCOMMITTEES' ATTENTION. HOWEVER, MR. CHAIRMAN, THE ISSUES RAISED IN THESE CRITICISMS THAT ARE THE SUBJECT OF TODAY'S HEARING SEEM LARGELY DISCONNECTED. IT IS AS IF WE ARE COMPARING APPLES AND ORANGES. I WOULD HOPE THAT OUR WITNESSES CAN CONNECT THESE ISSUES FOR US SO THAT WE CAN HAVE A COHESIVE HEARING RECORD.

THE ISSUE OF ENFORCEMENT STANDARDS FOR MEDICAL DEVICES HAS BEEN THE SOURCE OF GREAT CONCERN WITHIN THE MEDICAL DEVICE COMMUNITY. THE SPECIFIC CONCERN IS THAT THE FDA HAS ABDICATED ITS RESPONSIBILITY UNDER THE ADMINISTRATIVE PROCEDURE ACT TO PROVIDE FOR PUBLIC PARTICIPATION WHEN DEVELOPING SUBSTANTIVE REGULATIONS.

THESE CONCERNS ARE SET FORTH IN THE INDIANA MEDICAL DEVICE MANUFACTURERS COUNCIL CITIZENS PETITION FILED WITH THE FDA. IN THE PETITION, THE I.M.D.M.C. ALLEGES THAT THE FDA HAS CREATED SUBSTANTIVE POLICY THROUGH INFORMAL MECHANISMS SUCH AS PRESS RELEASES AND SPEECHES, AND IN SO DOING HAS VIOLATED THE "NOTICE AND COMMENT" REQUIREMENT OF THE A.P.A. THE I.M.D.M.C. FURTHER CONTENDS THAT SUCH INFORMAL POLICY PRONOUNCEMENTS HAVE BEEN THE BASIS FOR ENFORCEMENT ACTIONS AGAINST MEDICAL DEVICE MANUFACTURERS, MANY OF WHOM HAVE NOT BEEN GIVEN NOTICE OF THE POLICIES BEING ENFORCED.

IF IT IS TRUE THAT THE FDA IS VIOLATING THE A.P.A., THEN SOME ACTION MUST BE TAKEN TO PREVENT THIS FROM OCCURRING IN THE FUTURE. WE CANNOT HAVE FEDERAL AGENCIES ISSUING SUBSTANTIVE POLICY IN SPEECHES AND THEN TURNING AROUND AND BASING AN ENFORCEMENT ACTION ON THE CONTENTS OF THE SPEECH. HOWEVER, I DO NOT BELIEVE THAT REQUIRING "NOTICE AND COMMENT" FOR ALL RULES, INCLUDING INTERPRETIVE RULES, IS THE PROPER SOLUTION. MY CONCERN IS THAT SUCH A REQUIREMENT WOULD GREATLY LENGTHEN THE MEDICAL DEVICE APPROVAL PROCESS.

IN ADDITION, LET ME POINT OUT THAT REQUIRING "NOTICE AND COMMENT" FOR ALL RULES WOULD BE A SEVERE DRAIN ON FDA RESOURCES, AS GREATER FUNDING WOULD HAVE TO BE DEDICATED TO THE "NOTICE AND COMMENT" PROCESS. IN A TIME OF "BELT TIGHTENING" WITHIN THE GOVERNMENT, LESS FUNDING WOULD BE AVAILABLE FOR THE REVIEW OF PREMARKET APPROVAL APPLICATIONS AND ENFORCEMENT ACTIVITIES. AS A RESULT, THIS COULD FURTHER LENGTHEN THE TIME IT TAKES TO RECEIVE FDA APPROVAL OF NOT ONLY MEDICAL DEVICES, BUT OF DRUGS, BIOLOGICS, FOOD ADDITIVES, AND THE LIKE. MR. CHAIRMAN, AS YOU WELL KNOW, THE FDA CANNOT AFFORD TO ENACT MEASURES THAT WOULD LENGTHEN THE ALREADY PROTRACTED PREMARKET APPROVAL PERIOD.

TODAY, THE SUBCOMMITTEES WILL ALSO EXAMINE THE HUMAN COSTS OF DELAYS IN MEDICAL DEVICE APPROVALS AT THE FDA. OUR CONSIDERATION OF THIS ISSUE CORRESPONDS TO THE RELEASE OF A REPORT ON THIS SUBJECT BY THE HUDSON INSTITUTE. AS I INDICATED EARLIER, IN THE INTEREST OF COHERENCE, I WOULD APPRECIATE OUR WITNESSES TYING THIS ISSUE INTO THE ENFORCEMENT STANDARDS ISSUE. I LOOK FORWARD TO HEARING WITNESS TESTIMONY ON THE REPORT, IN ADDITION TO AN ASSESSMENT OF THE CONCLUSIONS DRAWN.

MR. CHAIRMAN, AGAIN I THANK YOU FOR CALLING THIS HEARING, AND I ANTICIPATE BOTH AN ENGAGING AND CONSTRUCTIVE DISCUSSION.

Mr. SHAYS. I thank the gentleman.

Mr. McIntosh.

Mr. MCINTOSH. Thank you, Mr. Chairman. First, let me say, I appreciate your holding these joint hearings. I think they are tremendously helpful in this area, and I am glad that we can be of assistance in holding them jointly with you.

Past hearings before the subcommittee have focused on a little known fact that every American needs to understand. Put simply, many of the FDA policies are leading to people in America dying as a result. At today's hearing we will take it a step further and expose the fact that FDA has adopted a policymaking process that acts in secret to support those policies.

The evidence to support these facts is compelling. In June, at a field hearing in Vice Chairman Fox's district in Norristown, PA, this subcommittee heard from a number of sick and dying Americans who complained that the FDA was standing between them and lifesaving products. Heroic people like Mariah Gladis, who suffers from ALS, the same disease that killed Lou Gehrig 50 years ago—as you know this month, Cal Ripken broke Lou Gehrig's record for the most consecutive games played, but Mrs. Gladis still suffers from ALS and is still waiting for action.

Shortly after a hearing last June, the FDA did take action on the drug Rilutek, and it significantly broadened the application of that drug to fight that disease. Unfortunately, it took time, and Mrs. Gladis' condition deteriorated. For those of you who weren't there, you can imagine the sadness that I felt watching her raise her arm to swear in, to be able to give her testimony, and having to depend upon her husband in order to take that oath, because of her frailty.

There are also heroic people like Kiyoshi Kuromiya, who is struggling to survive AIDS, and came and asked us that we speed FDA approval of drugs that could save his life. And heroic people like the little girl who came before the joint hearing we had last time, asking that FDA take action on the question of silicone so that she can be assured there will be a replacement shunt when the time comes for her to receive that operation.

Today we will start hearing about new facts, facts developed by the Hudson Institute in the attempt to qualify and quantify the effects of FDA's failure to act expeditiously in approving new medical devices. In just one example, 2,888 Americans have died needlessly because of FDA's lengthy approval procedure for a coronary stent. Today the coronary stent is used as a safe and effective emergency procedure when an artery collapses during angioplasty. Since the FDA approved the stent, tens of thousands of Americans have benefited from this device and are still alive.

We will also hear today from a group of medical device manufacturers in my home State of Indiana, who are here to tell us about a process in which FDA develops policies that are not published for comment. They have taken the action to petition the agency to end this bad habit of developing guidance documents in secret and require them to return to the policy that published those for comment and consensus among the regulated community.

In documents just released by the agency, we have learned that the Administrative Conference of the United States, a nonpartisan Federal agency, warned them back in 1990 that it was flirting with

a dangerous habit and to change its procedures in that area. Unfortunately, the agency did not listen, and the result has been a slowdown in the approval of devices as a result.

In 1992, the FDA announced for the first time that it was keeping a secret list of manufacturers that it was going to deny approvals under the 510(k) process. Although the FDA claims it has stopped using that list, I continue to believe it is important that we revert back to the earlier process of public proceedings in order to develop those types of procedures.

I am anxious to hear from the FDA, to hear their explanations for their policies and their comments on the citizens' petition. Although this citizens' petition focuses on intricate aspects of administrative law that even, frankly, most lawyers don't fully understand, we all must understand the consequence of one thing, it is a plea that the FDA follow the simple rule of law of consulting those who will be affected by their actions. It is not hard to see how their failure to do so has been debilitating in this area.

According to a study by Price Waterhouse, fully 75 percent of the manufacturers recently surveyed believe that FDA's policy on guidelines had either no positive impact or actually hindered the approval of new, lifesaving medical devices.

If this hearing accomplishes one thing, Mr. Chairman, I hope it sends a clear signal to FDA and to the commissioner and to the employees who are serving in that agency that we must change the direction in this country. We must realize that there is a cultural problem that leads to bureaucratic inaction in cases where lives are at stake. Second, we must understand that failure to act to approve devices and other medical products will take lives and that there is a cost to agency inaction.

So I would call upon FDA to speed up its initiatives, to simplify the regulatory approval process of medical devices and adopt changes requested by the citizens' petition regarding the use of guidance documents.

As preliminary steps toward that end, I would urge them to publish in the Federal Register a notice regarding the citizens' petition, schedule a conference on the petition so that public comments can be formally received and considered by the agency before it acts, obey the law that requires it to act on petitions within 180 days of filing—in this case, the deadline is October 28, and it is fast approaching—and, finally, drop secret policies or those that have been developed without a full public notice-and-comment proceeding, to ensure that the agency is not acting in a way that unnecessarily threatens the health and safety of the American public.

In closing, I hold much hope that the serious problems identified in this and earlier hearings will be solved by the many good people inside FDA. However, they cannot solve their problems on their own. They do need the advice and the input from those who are working in these fields, from patients who will benefit from the products that they are considering, from the experts at places like the Hudson Institute and the Progress & Freedom Foundation, and from people here in Congress who have a great interest in making sure that the right thing is done.

I have no doubt that, if that happens, we can solve these problems and break out of the command and control mind-set, stop set-

ting policies in secret, and work together to put these new technologies to work to save American lives.

Thank you, Mr. Chairman.

[The prepared statement of Hon. David M. McIntosh follows:]

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Opening Statement

The Honorable David M. McIntosh

Joint Hearing: FDA Medical Device Regulation

September 14, 1995

Past hearings before this Subcommittee have focused on a little known fact that every American needs to understand -- put simply -- the FDA is killing people.

At today's hearing, we will go a step further and expose the fact that the FDA is not only killing people, but is doing so while secretly breaking the law. The evidence to support these facts is compelling.

In June, at a hearing held in Vice-Chairman Fox's district in Norristown Pennsylvania, this Subcommittee heard from a number of sick and dying Americans who all complained that the FDA was standing between them and live-saving medical products. Heroic people like Mariah Gladis who suffers from ALS -- the same disease that killed Lou Gehrig 50 years ago. This month, Cal Ripken broke Lou Gehrig's record for most consecutive games played, but Ms. Gladis still suffers from ALS.

Shortly after our hearing last June, the FDA finally approved a drug that could significantly improve or extend Ms. Gladis' life. Unfortunately, in the time it took to approve, her health significantly declined. For those of you who weren't at that hearing, you can't imagine the sadness I felt for Ms. Gladis and the thousands of ALS sufferers like her when she slowly stood to take the oath and her husband had to carefully raise her limp right arm because ALS had crippled it.

Heroic people like Kiyoshi Kuromiya who is struggling to survive AIDS long enough for the FDA to approve drugs that could save his life. And heroic people like the little girl I met months ago who has a silicon shunt implanted in her brain to drain off deadly fluid build up.

Today we will hear startling new facts from a major American think tank -- the Hudson Institute -- that quantify the number of dead and dying as a result of the FDA's failure to quickly approve only four medical devices. As just one example, 2888 Americans have died needlessly because the FDA took too long to approve the coronary stent.

How did they die? Horribly -- with their chests split open and a doctor's hands frantically trying to perform an emergency heart by-pass operation -- an operation that could have been avoided had the FDA acted faster. Today, the coronary stent is used as a safe and effective emergency procedure when an artery collapses during angioplasty. Since the FDA approved the stent, tens of thousands of Americans have benefited from the device and are still alive.

We will also hear today from a group of medical device manufacturers in my home state of Indiana who know that the FDA is killing people. Despite real fears of retribution, they have filed with the FDA a citizens' petition that asks the FDA to stop breaking the law. They are to be

commended today for their decision to question the FDA's lawlessness.

Their petition focuses on the FDA's bad habit of using guidance documents as a substitute for formal, legal rulemaking.

The FDA adopted this illegal policy in 1991 -- in large part to side step President Bush's efforts to control the federal regulatory monster. In documents just released by the FDA to my Subcommittee, we have learned that the Administrative Conference of the United States -- a non-partisan federal agency -- warned the FDA back in 1990 that it was flirting with a dangerous habit. The FDA did not listen, and thousands of Americans have died as a result.

The Citizens' Petition contains dozens of examples of FDA lawlessness. In 1992, for example, the FDA announced for the first time that it kept a secret list of manufacturers that it was using to illegally delay 510(k) approvals. Although the FDA claims it has stopped using the list, I continue to believe the FDA is breaking the law.

I am anxious to hear the FDA defend its policy on the reference list and the other examples raised in the Citizens' Petition. Although their citizens' petition focuses on intricate aspects of administrative law that even most lawyers don't fully understand, we must all understand one thing -- this petition is really a plea to the FDA -- a plea for it to follow the rule of law, to submit its regulatory enforcement actions to public scrutiny, and to stop killing people.

It is not hard to see how the FDA's failure to follow the Administrative Procedures Act has cost lives. According to the accounting firm of Price Waterhouse, fully 75% of all device manufacturers recently surveyed believe that the FDA's policy on guidelines had either no positive

impact or actually hindered the approval of new life-saving medical devices.
If this hearing accomplishes anything, I hope that it sends a clear signal to the FDA and to its Commissioner, Dr. David Kessler, that it must immediately begin to serve the interests of Americans.

First, the FDA must recognize that a cultural problem exists within the agency that leads to bureaucratic arrogance, secrecy and lawlessness. Second, the FDA must understand that its failure to quickly approve devices and other medical products kills Americans just as surely as its failure to keep dangerous devices off the market.

I call on the FDA to: Speed up major initiatives to simplify the regulation and approval of medical devices; Adopt the changes requested by the Citizens' Petition regarding the use of guidance documents.

As preliminary steps toward that end, the FDA must (1) publish in the Federal Register a notice regarding the Citizens' Petition; (2) schedule a conference on the Petition so that public comments can be formally received and considered by the agency before it acts on the Petition; (3) obey the law that requires it to act on all petitions within 180 days of filing -- in this case that deadline is October 28 and it is fast approaching; and (4) drop all secret policies or those that have been the focus of public severe criticism until it can publicly vet these policies to ensure that they are not needlessly killing Americans.

In closing, I hold much hope that the serious problems identified in this and earlier hearings will be solved by the many good people inside the FDA. They cannot solve these problems on their own. They need the advice and help of the American people -- including brave patients like

Mariah Gladis; smart and honest inventors and manufacturers like those in Indiana and throughout this country, and brilliant members of think tanks like The Progress and Freedom Foundation and The Hudson Institute. As long as brave people like those who are about to testify today are willing to come forward to challenge the FDA when it is wrong, I have no doubt that the problems can be solved if we break outof the command and control mind set, stop setting secret policies and work together to get new technology to patients who so desperately need it.

Mr. SHAYS. I thank the gentleman.

Mr. Peterson.

Mr. PETERSON. Thank you, Chairman Shays. I want to commend you and Chairman McIntosh for your tenacity in continuing to hold these hearings.

I frankly have to tell you that we keep holding hearings, especially in our committee on regulatory reform, and we have had a couple of hearings on the FDA, field hearings and others, and the more I get into this—I hate to say this—but I actually some days get more skeptical about whether we are ever going to make any progress changing this psychology that you talked about within these regulatory agencies. But maybe the way to deal with it is to keep having hearings and keep the pressure on, so I commend you for doing that.

I have an opening statement that I would like to submit for the record. I'm not going to read the whole thing.

Mr. SHAYS. I might just take the opportunity, then, to ask unanimous consent that all members of the subcommittee be permitted to place an opening statement in the record and that the record remain open for 3 days for that purpose. Without objection, so ordered.

The gentleman may continue.

Mr. PETERSON. I hope we can do some good with these hearings. The problem is not just with the FDA. We have problems with other agencies that are similar in nature. My staff, when we are out in my district working on economic development, tells me the biggest problem we run into is not the adverse decisions from these agencies, it's that you can't get a decision from them at all.

And it seems to me that the very agencies we have set up to solve some of these problems, in effect, cause more problems than we had to start with. So, somehow or another, we've got to get this regulatory process changed. I am committed to doing whatever we can to make that happen.

I again commend you for holding these hearings and apologize, I'm going to have to leave. We've got farm bill stuff going on. As is typical around this place, there are too many things happening. But I commend you for your leadership and hope we have some positive outcome.

[The prepared statement of Hon. Collin Peterson follows:]

TALKING POINTS FOR REP. COLLIN PETERSON SUBCOMMITTEE ON NATIONAL ECONOMIC GROWTH, NATURAL RESOURCES, AND REGULATORY AFFAIRS

SEPTEMBER 14, 1995

* I would like to thank both Chairman McIntosh and Chairman Shays for convening this joint oversight hearing on the FDA. I would also like to commend them for their efforts to promote regulatory reform throughout the various centers within the agency.

* Today's hearing will focus on the regulatory activities of the Center for Device and Radiological Health within the FDA, and will address two primary issues:
  1) how the FDA establishes regulatory requirements for medical devices and how those requirements are enforced, and

2) whether the time necessary to receive FDA approval for medical devices in the U.S. relative to Europe has led to the loss of American lives.

* This hearing has been called following the submission of a Citizens Petition to the FDA by the Indiana Medical Device Manufacturers Council. In the petition, the I.M.D.M.C. alleges that the FDA has violated the Administrative Procedure Act by promulgating regulations without public participation. This is a very serious allegation, and one that I fully expect to get to the bottom of by the conclusion of this hearing.

* In addition, we will also review the conclusions of a report being released by the Hudson Institute that attempts to measure the cost in human lives of delays in the approval of medical devices. I look forward to hearing from our witnesses on this issue.

* Again, I would like to commend both Chairmen for calling this hearing and I look forward to witness testimony.

Mr. SHAYS. I thank the gentleman. I might take the opportunity to say that my two colleagues to the right were chairmen of the two basic subcommittees that are now hearing this issue and really started that process. So this is really a continuation of what Mr. Towns has done, and Mr. Peterson, in other areas as well, when you were chairing the committee that I now chair.

Mr. Souder, you have been very patient. You were the first here, and I thank you, and welcome any statement you would like to make.

Mr. SOUDER. I don't have a statement. I want to commend our subcommittee chairman for his persistence, too, in oversight, and patience that he goes through. We make sure we hear all sides. I am particularly excited today that we have Hoosiers representing the legal profession, representing the business profession, and a think tank. I'm proud of our home State today, too.

Mr. SHAYS. OK.

I would like to welcome our first panel. Our first panel is testimony from William Schultz, the deputy commissioner for policy at the FDA, accompanied by Dr. Bruce Burlington, Mr. Ronald Chesemore, and Ms. Ann Wion. If you would come forward—did I leave anyone out? Is there anyone else coming forward?

We are going to swear in all the witnesses, that's our practice, whoever they are. They are welcome to come forward, and if they would remain standing, I will swear in our witnesses. This is the practice in our investigative committee.

[Witnesses sworn.]

Mr. SHAYS. Thank you very much. May I note for the record that the witnesses all answered in the affirmative. I welcome you to sit down.

If I also, at this point, could ask unanimous consent that our witnesses be permitted to include a written statement in the record. Without objection, so ordered.

We really have one witness accompanied by others who may help you respond, Mr. Schultz.

What I would like to just say for the record is that we invited the FDA to stay and respond after panel two had spoken, and they have declined. I, candidly, just learned about that decision not to stay. I am going to respect that today, but I do want to say for the record that this committee reserves the right to have an agency come either in the beginning, the middle, or the end.

Today you are coming first, but sometimes it's very helpful for an agency to respond after others have made comments. And where an agency isn't prepared to answer because they don't have the answer, given it might be new information, and so on, we would always respect the agency not responding.

I just want to put on the record that the FDA was invited to stay and has declined, and we will respect that today but will reserve, in the future, our right to have them come at any time.

I would like to welcome—before, Mr. Schultz, you make your statement—our colleague from Pennsylvania and ask if he has any comments or statement for the record.

Mr. FOX. Thank you, Mr. Chairman. I am pleased that you have organized today's hearing on the important issues regarding FDA's

medical device regulation, and to recognize your leadership in the Congress and this committee in that regard.

Since its inception in 1938, regulation of the medical devices industry by the FDA has increased in scope, detail, and cost to the American people. Historically, legislative authority and regulatory stringency have made discreet leaps, each prompted by shocking revelations widely disseminated by the news media. To demonstrate their devotion to protecting the public health, legislators and regulators have augmented regulations, emphasizing the alleged benefits and disregarding the negative consequences for the industry and the patients it ultimately serves.

In the past 4 years, the FDA has drastically slowed the rate at which it approves lifesaving and life-extending medical devices. It has pursued an aggressive enforcement strategy that treats all regulated firms as suspected felons, restricting its communication and cooperation with them, and substantially increasing the number of punitive actions.

In response, increasing numbers of firms have moved their operations abroad or begun planning to do so. The FDA's regulation of medical devices has produced little, if any, benefit, but imposed large and increasing costs. Those costs are not just economic, they also include deaths and human suffering.

It is important to note that the FDA serves a valuable purpose in maintaining safety and efficacy standards. However, it is also important to recognize that the FDA's actions directly affect the lives of patients and the ability of physicians to provide state-of-the-art care for their patients. That is why many of my colleagues have joined with me to introduce H.R. 2290, which would provide positive changes to the present system without adversely affecting the FDA's high safety and efficacy standards.

Finally, I share Chairman McIntosh's concern regarding the IMDMC's citizens' petition, and I equally hope that today's hearing focuses on solutions and not just problems. I am confident that, with the help of the many good people inside the FDA, we can develop effective and efficient ways to involve the public better in its development of guidance documents.

I welcome today's witnesses and look forward to the testimony. And I thank you, Mr. Chairman and Congressman Shays, for your leadership and assistance.

Mr. SHAYS. Thank you, Mr. Fox.

My staff goes crazy when I say a name incorrectly sometimes. Mr. Chesemore, not Mr. Chesemore. My apologies.

Mr. CHESEMORE. That's quite all right.

Mr. SHAYS. In spite of the strong statements made, you are very welcome guests, and we know your task is not an easy one. We know there's a lot that you recognize can be improved in the agency. In that spirit, we look forward to your testimony.

Mr. Schultz.

STATEMENTS OF WILLIAM B. SCHULTZ, DEPUTY COMMISSIONER FOR POLICY, FOOD AND DRUG ADMINISTRATION, ACCOMPANIED BY DR. BRUCE BURLINGTON, DIRECTOR, CENTER FOR DEVICES AND RADIOLOGICAL HEALTH; RONALD CHESEMORE, ASSOCIATE COMMISSIONER FOR REGULATORY AFFAIRS; AND ANN WION, DEPUTY CHIEF COUNSEL FOR PROGRAM REVIEW

Mr. SCHULTZ. Thank you very much, Mr. Chairman. As you indicated, I am accompanied by Dr. Bruce Burlington.

Mr. SHAYS. Just turn the mike a little bit more so it's under your voice. That's good, if that's all right. Thank you.

Mr. SCHULTZ. Dr. Bruce Burlington is director of our Center for Devices and Radiological Health. Mr. Ronald Chesemore is our associate director for regulatory affairs, and Ms. Ann Wion is our deputy chief counsel for program review.

I think, given that Indiana is so well represented here, I should disclose that I am also from Indiana. I was born there and spent the early years of my life there.

Mr. SHAYS. That's nice to know.

Mr. SCHULTZ. And look back on it fondly, I should say.

Mr. SHAYS. And it has probably shaped your life in very positive ways, as well.

Mr. SCHULTZ. I hope it did.

I appreciate the opportunity to testify about the relationship between regulations and informal guidance at the Food and Drug Administration. It's an issue that I have been interested in for a number of years. I think I should start by saying that, on one level, the difference between a regulation and a guidance document is simple to explain.

A regulation is binding as law. In fact, a regulation is law. A violation of a regulation is a violation of law. Because a regulation has such a significant status, the Administrative Procedures Act requires an agency such as the FDA to go through a very formal process of notice-and-comment rulemaking to issue a regulation. An example would be the nutrition label on food that we see so often. The agency specified exactly what must be on that label, in what order and what format, and a violation of that regulation would be treated as a violation of law.

A guidance document, on the other hand, sets out the agency's current thinking but is not binding on the agency or on the regulated industry. Instead, it is used to inform our employees as to how we interpret the statute or regulations. It is used to promote consistency. For example, guidance could be used to ensure that different medical reviewers, when they are reviewing similar products, apply consistent standards. It could be used to ensure that different inspectors, inspecting different plants, do so in a consistent manner.

Second, guidance is used to inform industry, not as to what is legally required, but as to what the agency's thinking is, so that the agency can get that advantage in complying with legal requirements. But, as I say that, I want to underline that, in contrast to a regulation, industry is not required to comply with guidance.

While those are the basic parameters, it is also true that the FDA has not always been entirely consistent about how it uses

guidance documents, or what it calls them, or how it issues them. That is, in part, due to the fact that they are issued by different centers; it is, in part, due to the fact that we are looking over a long period of time; and it is, in part, due to the fact that the legal requirements have changed over the years.

In this context, the petition filed by the Indiana Medical Device Manufacturers Council has given us a vehicle to review the agency's policy with respect to guidance documents. As we testify here in the middle of that review, we expect to complete it by the end of October, within the 180 days. I don't know what the results will be, but what I would like to do is spend the next few minutes just giving you an overview of what some of the key considerations are. There are five points I want to make; I will make them very quickly.

The first is what I have already said: guidance documents are not binding on the industry or on the FDA. Having said that, I would also say that we haven't always done an adequate job in communicating that fact to our employees and to the industries. That is an important consideration we have to look at.

Second, guidance documents are extremely valuable, both to the industry and the agency.

Third, formal notice-and-comment rulemaking is neither practical nor feasible. It is not legally required. It is not consistent, in some cases, with the speed with which technology advances with regard to some of the products we regulate, and there are resource considerations that we would have to take into account. The risk of requiring notice-and-comment rulemaking is that we will end up with less guidance and, thus, less help to both our employees and the industry.

Fourth, having said that, I would also say that public comment on guidance documents can be very useful and that most guidance documents would benefit from this kind of input. Again, although we have done this more in recent years, we recognize that we haven't been totally consistent on this.

Finally, I would say that we need to ensure we have an effective appeal mechanism, so that, if a company is unhappy with a guidance document or thinks that it should not apply to its product, there ought to be an effective way, within the agency, that it can seek review of that decision and not just a rubber stamp.

In conclusion, Mr. Chairman, guidance documents are essential, we feel, both to the industry and the agency; however, we agree that improvements can be made in the procedures that the agency uses to develop, issue, and implement guidance documents that are consistent with the public health. In developing a policy on this matter, we will take into account both the extent that the industry and the agency need the documents and the extent to which public participation will be helpful.

[The prepared statement of Mr. Schultz follows:]

STATEMENT BY

WILLIAM B. SCHULTZ

DEPUTY COMMISSIONER FOR POLICY

Good afternoon. My name is William B. Schultz, Deputy Commissioner for Policy. With me this afternoon on the panel are Mr. Ronald G. Chesemore, Associate Commissioner for Regulatory Affairs; Dr. Bruce Burlington, Director of FDA's Center for Device and Radiological Health (CDRH); and Ms. Ann Wion, Deputy Chief Counsel for Program Review of the Office of General Counsel.

Thank you for this opportunity to speak about FDA's policy of providing guidance documents to the FDA-regulated industry.

FDA's mission to help ensure the safety of the nation's food supply and the safety and efficacy of the nation's drugs, biologics, and medical devices derives principally from the Federal Food, Drug, & Cosmetic Act (the "Act"). Although the Act provides the basic framework for FDA's mission, it provides little specificity with respect to the regulation of products subject to FDA's jurisdiction. For example, section 510(k) of the Act directs medical device manufacturers to report to FDA, the regulatory class of a device or that the device is not classified, at least 90 days before first introducing that device into interstate commerce. The Act does not, however, tell manufacturers exactly when they would be first introducing a medical device and thus, when they would be required to file this premarket notification.

FDA's regulations provide more detail of the Act's requirements. For example, the regulations that set forth the 510(k) procedures state that a manufacturer must file a premarket notification when it is introducing a medical device into commercial distribution for the first time or when it is reintroducing a device with a significant change or modification.

In many respects, however, even FDA's regulations do not provide industry members with the kind of specific, detailed guidance that they need in their efforts to comply with the law, nor do the regulations always provide Agency staff with the kind of specific criteria that are essential to a consistent application of the law. Recognizing that both the industry and the Agency benefit from more direction, FDA has issued various guidance documents such as guidelines, points to consider documents, guidance memoranda, and compliance policy guides.

With respect to the 510(k) notification example, our regulations state when a change to a device would require submission of a notification. However, the criteria that the regulation sets forth (i.e., "significantly changed or modified," "could significantly affect the safety or effectiveness," and "major change") are relative terms and subject to varying interpretations. In an effort to provide more direction, FDA has developed a draft guidance document that helps manufacturers determine when medical device modifications would likely require

filing of a premarket notification. The draft document presents a flowchart model that can be used by manufacturers in their decision-making to analyze how changes in devices may affect safety or effectiveness. Last year, the Center for Devices and Radiological Health (CDRH) provided a draft of this guidance document to industry groups for comment. The Center recently has completed a second draft of the guidance, which incorporates industry comments and suggestions and which is being provided in draft for an additional round of public comments.

As the above example illustrates, guidance documents can help to clarify requirements that have already been imposed by Congress or promulgated by FDA pursuant to notice-and-comment rulemaking. These documents provide useful information about what the Agency considers to be the important characteristics of preclinical and clinical test procedures, manufacturing practices, scientific protocols, and other matters.

Guidance documents help industry by explaining how to comply with the Act and regulations and by explaining how to avoid enforcement actions. For example, many of the guidance documents disseminated by CDRH are directed to small businesses. These documents explain the regulatory requirements and advise small businesses on how to comply with the regulations. Compliance policy guides, which address a variety of compliance issues,

often set forth the types of factors and criteria that are used to evaluate whether to initiate legal action against a company.

Guidance documents also respond to requests for clarification regarding specific statutory and regulatory requirements. For example, in response to a request for clarification, the Center for Biologics Evaluation and Research (CBER) developed a guidance document concerning the use of pilot facilities for the development and manufacture of biological products. Similarly, when industry and FDA reviewers sought a list of the container closure information that should be submitted with ANDAs/AADAs, the Packaging Advisory Group in the Office of Generic Drugs compiled lists of recommendations. Finally, when food companies needed clarification on the food labeling regulations promulgated under the Nutrition Labeling and Education Act of 1990, the Center for Food Safety and Applied Nutrition issued a lengthy set of Qs & As to address the issues most commonly raised.

Guidance documents such as those I have just described give industry a "heads-up"; they provide examples of the types of activities that would violate the Act and regulations and they provide pointers on how to comply with affirmative requirements of the Act and regulations. These documents do not establish legally enforceable rights or responsibilities. Rather, they explain how the Agency believes the statute and regulations apply

to industry activities. In the absence of guidance documents, certain activities still would be prohibited by the regulatory scheme, but a company would be less likely to know that it was not in compliance. Nevertheless, FDA could proceed with an enforcement action. Similarly, the absence of guidance documents would not change the standards for applications -- it would just make it more difficult for industry to know how to comply with them. Accordingly, the FDA-regulated industry seeks and relies heavily on FDA's guidance documents for assistance.

Guidance documents also are essential to the efficient administration of FDA's duties. They help to ensure that our employees implement the Agency's mandate in a fair and consistent manner. Thus, when FDA staff are reviewing applications and petitions, they will be looking for the same kinds of supporting evidence from all submitters. Likewise, when field enforcement personnel are reviewing companies' activities, they will have guidance in determining which activities comply with the law and which do not. This benefits industry because it helps to ensure a level playing field.

GUIDANCE DOCUMENT REVIEW AND THE INDIANA MEDICAL DEVICE COUNCIL CITIZEN'S PETITION

In recent months, questions have been raised about FDA's use of guidance documents and the process by which they are issued.

In May 1995, the Agency received a citizen's petition filed on behalf of the Indiana Medical Device Manufacturers Council, Inc. (IMDMC), which raises questions about the Agency's process for issuing guidelines. The IMDMC petition requests that FDA amend its rulemaking regulation to require notice-and-comment rulemaking for all interpretive rules and rules of Agency practice and procedure.

In conjunction with preparing a response to the petition, the Agency is undertaking a comprehensive review of its use of guidance documents. As part of that review, we will evaluate methods to ensure that guidance documents are developed, issued, and implemented in a way that is fair and reasonable. At the same time, we will take steps to ensure that guidance documents do not supplant notice-and-comment rulemaking when the need for the latter is evident. Today, I will give you an overview of the principles that we believe should guide our review and any changes to the program.

First, we recognize that guidance documents are not and cannot be binding on industry or on FDA. The only binding requirements are set forth in the statute and FDA's regulations. In fact, when FDA trains its reviewers and compliance personnel, it communicates the non-binding nature of guidance documents. Moreover, FDA has willingly departed from the recommendations set forth in its guidance documents. For example, although a

guidance document disseminated by the Center for Devices and Radiological Health recommends that stress testing be used to demonstrate long-term durability of heart valves, CDRH has agreed with at least one manufacturer's rationale for demonstrating long-term durability based on a different (fatigue) type of testing.

Similarly, although CDRH guidance requests flow rate testing for ureteral stents, which are used to keep the ureter open, it has permitted at least one sponsor to omit this testing. In fact, in light of that sponsor's justification for omitting the test, CDRH is now considering revising its guidance to remove the recommended flow rate test. One last example relates to intraocular lenses. Although CDRH guidance recommends using four different substances to test for toxicity, CDRH has accepted a manufacturer's justification for using just two of those substances.

Despite FDA's efforts to communicate the non-binding nature of guidance documents and FDA's willingness to depart from its guidance, part of industry's dissatisfaction with guidance documents must be the result of our failure to communicate the non-binding principle consistently -- both to industry members and to our own employees. Our goal is to ensure that FDA personnel understand the non-binding nature of guidance documents and that industry has a meaningful opportunity to persuade FDA

that, in a particular case, an approach that is different from the approach described in a guidance document satisfies the statute and regulations. The idea behind our first guiding principle is to ensure that guidance remains just that and that guidance documents can be challenged by a particular manufacturer before they are applied to that company's product.

Our second guiding principle is one that I have already pointed out -- and that is that FDA's guidance documents are extremely valuable to both the industry and the Agency. Guidance documents provide industry with specific details that often are missing from the statute and the regulations and help to ensure a consistent application of the Act and regulations by FDA. Even the petition filed by IMDMC "support[s] FDA's efforts to disseminate useful guidance."

This brings me to our third guiding principle. We welcome comments on all guidance documents, but notice-and-comment rulemaking for each guidance document simply is neither necessary nor feasible. So long as guidance documents are treated as non-binding, the Administrative Procedure Act does not require notice-and-comment rulemaking. Moreover, because technology in the medical products area advances so rapidly, many guidance documents would be obsolete by the time notice-and-comment rulemaking was completed. In addition, FDA does not have the resources to undertake the cumbersome notice-and-comment process

for each and every guidance document it issues. If notice-and-comment rulemaking were required, resource limitations would mean that considerably fewer guidance documents would be available. As a result, the flow of important information to industry regarding the Agency's position on specific issues would be reduced and the assistance that these documents produce would be eliminated. The remedy would be worse than the problem the petition has identified. No one, including the regulated industry, supports this outcome.

Despite the impracticality of full notice-and-comment rulemaking for guidance documents, our fourth guiding principle is that in many, and probably in most cases, guidance documents could benefit from at least informal public input. In fact, we currently solicit public input in connection with the development of many guidance documents and we have found this input to be useful. For example, the Center for Biologics Evaluation and Research has sought public input for its guidance documents during workshops, advisory committee meetings, and other public meetings. CBER's current policy is to issue a Federal Register notice of the availability of certain guidance such as guidelines and points to consider. When publishing such notice, CBER has solicited comment on its guidance documents.

Similarly, the Center for Devices and Radiological Health has increasingly solicited public comment during the development

phase of its guidance documents. Again, the public comment has been solicited both in writing and during advisory committee meetings and workshops. In fact, over the past two years, 49 device-specific guidance documents were developed for which CDRH solicited outside input. Last month, for example, the first day of the Ophthalmic Devices Panel meeting was devoted to public comment on an panel discussion of a proposed document entitled "Draft FDA Guidance for Photorefractive Keratectomy Laser Systems." Comments were presented from ophthalmic professional organizations, excimer laser manufacturers, and practicing ophthalmologists. In March 1995, CDRH solicited comments on draft guidance for liquid chemical germicides from the Centers for Disease Control and Prevention, the Health Industries Manufacturers Association, and the Chemical Specialties Manufacturers Association.

As the above examples illustrate, FDA has increasingly solicited public comment in connection with the development of its guidance documents. Nevertheless, we recognize that the Agency has not been totally consistent in soliciting public input when formulating guidance documents. We plan to look at ways to assure solicitation of public input and to look at different methods (short of notice-and-comment rulemaking) to determine the most efficient way to ensure meaningful public participation.

Finally, we think one of the most important guiding principles is the existence of an effective appeals process. Such a process will assure industry that there will be genuine reconsideration of guidance policies. The process would further ensure that guidance documents are not being applied as binding requirements.

FDA's regulations already include a number of vehicles that industry may use to seek an appeal of an Agency employee's decision. Under the general provisions set forth in Part 10 of Title 21, an interested person may request internal Agency review of an Agency decision or may petition the Commissioner to review an administrative action. In addition, there are specific provisions that apply to the FDA Centers. For example, FDA's regulations provide procedures for dispute resolution regarding new drug applications. These procedures include informal meetings with the division reviewing the application, meetings with an ombudsman, and referrals to advisory committees.

To the extent that the appeals processes currently in place are not sufficiently understood by industry or do not provide meaningful reviews of Agency decisions, we are seeking ways to implement changes that will address these problems. Our goal is to ensure that industry is aware of its right to an appeal and to ensure that this right is meaningful.

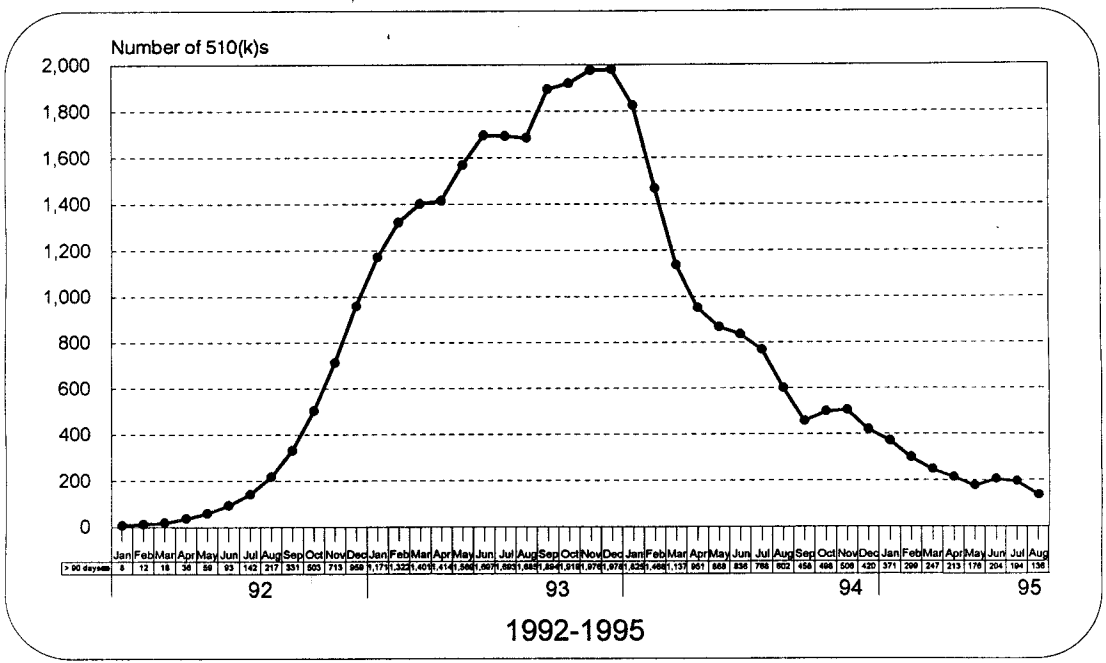
CONCLUSION

In conclusion, guidance documents are essential both to industry and to FDA. However, we agree that improvements can be made in the procedures FDA uses to develop, issue, and implement guidance documents. We want to ensure that there is meaningful public participation but that FDA can continue to provide industry with detailed and useful guidance as to how FDA intends to proceed under the laws it administers.

I would be happy to answer any questions you may have.

Backlog

510(k)s Under Review More than 90 Days*

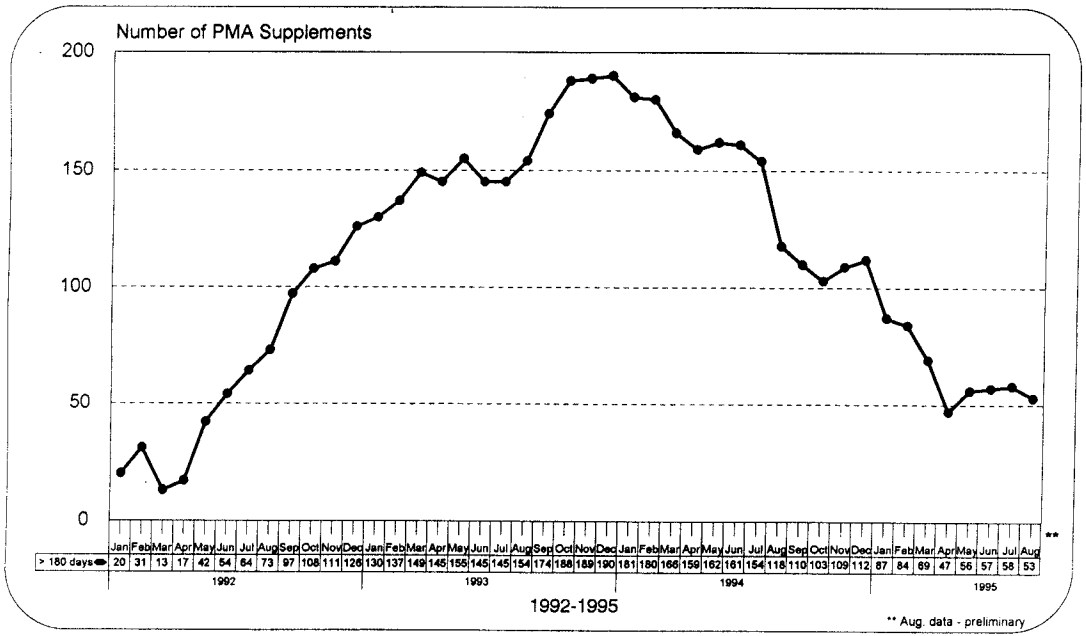


*Reflects the FDA days in current review cycle, not cumulative FDA days
note: data reflects each month's close of business total, therefore annual totals, based on monthly data above, are not equivalent to ODE's annual report

(from ODE Report 5)
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Backlog

PMA Supplements Under Review More than 180 Days*



*Reflects the FDA days in current review cycle, not cumulative FDA days
note: data reflects each month's close of business total, therefore annual totals, based on monthly data above, are not equivalent to ODE's annual report

(from ODE Report 5)

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Mr. SCHULTZ. Mr. Chairman, the invitation letter indicated that the committee is also interested in issues related to the uniformity of compliance with requirements applicable to devices. If you wish, Mr. Chesemore is prepared to speak for a few minutes specifically on that topic.

Mr. SHAYS. Would that be a request that he testify?

Mr. SCHULTZ. We would request it, if you wish.

Mr. SHAYS. We are happy to have him do that.

Mr. CHESEMORE. Thank you, Mr. Chairman.

Throughout its history, FDA has been concerned about uniformity in its compliance activities, enforcement applications, and the application of the law.

Mr. SHAYS. Let me just interrupt you. I'm sorry. We are just not picking up your voices well. The silver mike is the one that magnifies your voice.

Mr. CHESEMORE. Is this better, sir?

Mr. SHAYS. I think so. If you could have a nice booming voice, that would help.

Mr. CHESEMORE. Yes, sir.

Over the years we have a comprehensive approach to our activities based upon the establishment of national compliance programs, compliance policy guides, and standardized operating procedures.

In addition to the examples that Mr. Schultz gave, I would like to address two other issues that I believe go to the heart of what we believe helps us in our uniformity of operations in the field, of FDA. These two examples are: written guidance and training.

In the area of written guidance, three areas: First, all field and center personnel use the same compliance program manual and compliance policy guidelines. These written documents, which we do share with the industry, clearly delineate what is to be inspected and analyzed, both foreign and domestic, why, how and what regulatory or administrative action should or should not be appropriate, based upon the inspectional and analytical findings.

Second, all of the field investigators and their supervisors utilize the same investigations operations manual, the inspection guides, and import alerts.

A third example of written guidance which we utilize to help achieve uniformity is a written regulatory procedures manual. Again, both headquarters and field personnel utilize this manual for guidance in such areas as the issuance of warning letters, the conduct of recalls, and the recommendation of formal agency compliance actions. These formal agency compliance actions, such as seizure, injunction, and prosecution, are also reviewed by appropriate headquarters staff, as well as the Office of General Counsel, to ensure uniformity.

In the area of training, Mr. Chairman, we would like to say that to be a consumer safety officer or an investigator in the Food and Drug Administration requires a minimum of 30 semester hours of science at the college level. The vast majority of our investigators do have bachelor's or higher degrees.

Once hired, investigators around the country participate in uniform basic classroom and on-the-job training. Examples include classes in basic food and drug law and investigative techniques. We

also have a standard written training manual. We offer courses in basic device good manufacturing practices, and we also have advanced courses in such areas as auditing against the Mammography Quality Standards Act.

We are also, Mr. Chairman, in the process of developing a formal investigator certification program, which we believe will also help to increase uniformity across the country. This particular program will include both formal training, on-the-job experience, and tests will be required of our investigators.

We believe that these particular activities go a great deal in helping us assure uniformity.

Thank you, Mr. Chairman.

Mr. SHAYS. Thank you.

Mr. Schultz, any other comments?

Mr. SCHULTZ. No.

Mr. SHAYS. OK. Then what we will do is, I will open it up first to Mr. McIntosh, and then I will go to Mr. Towns.

I'm sorry. Before doing that, I would like to welcome Mr. Waxman.

Mr. Waxman, would you like to make an opening statement of any kind?

Mr. WAXMAN. I will submit my opening statement for the record.

Mr. SHAYS. Thank you. I appreciate that. We will have time for questions in just a second. I thank the gentleman.

Mr. McIntosh.

Mr. MCINTOSH. Thank you, Mr. Chairman.

Let me note that the notion that these policy statements are nonbinding is in the context of an industry that must get approval from the agency in order to take any action in marketing its product or, in fact, in changing its product and the way it is manufactured. So while there may be no legal indication that they are binding on either the agency or the manufacturer, the absence of compliance can effectively be used against them.

Now whether or not the agency says it does that consciously, there is certainly a perception in the regulated community that that is what happens. So to simply say they are nonbinding, I think, does not answer the question, especially in the context of life-threatening decisions that are being made.

My first question would be, do any of the policies that are out there, that have not been developed through notice and comment, fit the definition of having general applicability and having future effect?

Mr. SCHULTZ. I think they do, yes. I think that some of them apply more than to a specific company, and they certainly have future effect, but they are not binding in the sense that a company could not be prosecuted for violating one of those policies. A company has the opportunity, of course, to argue that it should not apply or that a different rule ought to apply to that company.

Mr. MCINTOSH. My understanding of the Administrative Procedures Act is that, when you meet those two criteria, you have what is referred to as a rule.

Mr. SCHULTZ. That's correct. But that does not necessarily—in a minute, I'm going to turn it over to Ms. Wion, who is our lawyer. I should ask her if she wants to add to this. That does not nec-

essarily mean the agency is required to go through notice-and-comment rulemaking.

In other words, there are some rules that require notice-and-comment rulemaking, and the courts have said, basically, it's those that are binding. There are some rules that don't.

Mr. MCINTOSH. Let me make sure I'm following you. It's the agency's position that it meets the general definition of a rule, but there is one of the exceptions that would allow them to not go through notice and comment for these policy guidelines?

Mr. SCHULTZ. I'm saying some of these policies could fall in that.

Ms. Wion, do you want to add?

Ms. WION. We agree that the definition of "rule" in the Administrative Procedures Act is a very broad definition. In fact, some courts have said it could cover virtually any statement that an agency makes. So it is important, when we talk about when notice-and-comment rulemaking is required, to go to section 553 of the act and, as you note, look at the exceptions to notice-and-comment rulemaking, which include interpretive rules and general statements of policy, the categories that cover, generally, the kinds of guidance documents that we're talking about today.

Mr. MCINTOSH. Now, if you had a situation where something is a general statement of policy, and in order for somebody to submit an application for approval, a 510(k) form, they have to follow those, isn't that, in effect, a regulation, if they are being told, "You must consult this statement of policy before we're going to consider your application"?

Mr. SCHULTZ. What we're saying is that the word "must" never goes along and should never go along with guidance, that it's not a must at all. But very often, to get consistency among reviewers, for example, we will tell our reviewers, as you go through this type of application, here is what the agency's view is as to what the company needs to do to meet the standard. Companies are, understandably, often very interested in what our policies are, as well, but it's not a must, because it's guidance.

Mr. MCINTOSH. Then my question is, what would ever justify developing these broad policies or interpretive documents in secret? Why not include the public in the procedures that are laid out under current law, in a way that would allow that type of input into the agency?

Mr. SCHULTZ. In general, I think we can benefit from public participation. There certainly are cases where speed mandates that we have to do something quickly, but even then there's always an opportunity—I mean, once it's out there, the public always has the opportunity to come back to us, or an industry, or a company, and say, "You ought to do it this way," or "You ought to consider redoing it."

One of the advantages of guidance is, it's much easier to change than a regulation. It can be changed much more quickly.

Mr. MCINTOSH. But it's my understanding what is being asked for in this petition is that FDA change its process so that, for these general guidelines that are future in effect and have broad applicability, they will go back to the rule that they used to have of using the notice-and-comment process in developing those.

Mr. SCHULTZ. The petition seems to say that, but I think it misunderstands where the agency has been, historically. If you go back, historically, you will see, over the last 20 years, there are many times the agency has used guidance, and not through notice-and-comment rulemaking, to inform the public as to what it's view of certain requirements were.

What I see, though, in addition to what you said, is, the thrust of this petition is saying to the agency, "You ought to consider getting more public input on guidance documents, because whatever you say, FDA, these guidance documents have real meaning and significance to the industry, and the regulated industry ought to have the opportunity to participate." I guess I would say to you that we see that as a very valid point, and, as we review this petition, we're going to seek ways of doing that.

Mr. MCINTOSH. Mr. Chairman, I will have additional questions, but I will defer to others.

Mr. SHAYS. I thank the gentleman.

Mr. Towns.

Mr. TOWNS. Thank you very much, Mr. Chairman.

Before I move forward, let me just sort of clear up something. It didn't sound too good, so I want to make certain that—I know you are anxious and eager to correct the problems, and I'm convinced of that. I think that some of these problems have gone on for many, many years.

When the chairman indicated that you were not prepared to stay, that didn't mean you're not going to leave somebody back here to hear what is being said. You are saying you are not prepared to engage in a debate, but you are going to leave somebody here, I hope.

Let me tell you why I say this, because industry feels that you are not listening. And I would hate for you to do that, because it would only confirm what industry is saying, that you are not listening; you don't intend to listen. And I don't think that; I think you want to listen. The way this was said, the way it was framed here and the way you responded, you know, it appears to me that industry is right, and I don't think that's the case.

Mr. SCHULTZ. We will certainly have somebody here. We will review the transcript. We are prepared to respond to any questions. We would be prepared to come back again. But we were asked—well, I don't want to go through it all, but something was just sort of thrown at us yesterday that was very much a change in what we had been told before.

But, as you say, we're certainly very interested in this hearing. I assume that some of what comes out of this hearing will be useful to us in responding to the petition.

Mr. TOWNS. At this point, I would yield to the chairman of the Health Subcommittee, who also serves on this committee, Mr. Waxman, for any questions he might have at this time. Let him use my 5 minutes, and I will wait his turn.

Mr. Waxman, I yield to you.

Mr. WAXMAN. I thank you for yielding to me. I do want my own time, as well, but if you are yielding me the balance of your time, I appreciate it.

You are listening to what we have to say at this hearing. I think it's important for Congress to hold hearings, get points of view, and try to be constructive. The key point, I believe, is to be constructive. But as I look at this issue, it seems to underscore the very difficult job that you have at the Food and Drug Administration. We want to approve drugs and devices, and oversee the safety of the food supply; we want all of these things done right away, but we want them done right.

Therefore, it if takes time for you to get all the information about, for example, as we're talking about today, a device, that means sometimes a delay in getting that device on the market. But it's a delay I think the public will understand, if it means we're not going to get a device that's going to do harm to the public out before we know all the facts.

As I understand what's going on, rather than go through an extensive rulemaking, you're using guidance documents to give the information to the industry involved and also to tell other industries what FDA is going to expect from them in order to get a device approved. Is that what this is basically about, Mr. Schultz?

Mr. SCHULTZ. Yes. It could be approval, or it could be guidance so, when we do an inspection, this is what our inspector is going to look for.

Mr. WAXMAN. Now, the guidance documents, I presume, take a lot less time than if you went through a whole formal process of rules and regulations, and Federal Register, and notice and comment; isn't that accurate?

Mr. SCHULTZ. That's correct.

Mr. WAXMAN. So, in effect, you're being criticized for not going through the formal procedures for establishing the rules and regulations and taking a shorter route. That's one level of criticism. But then I'm sure you could also be criticized for taking too long, if you went the other way.

Mr. SCHULTZ. Right.

Mr. WAXMAN. So it really is a dilemma. Now, if you do take a shorter route, then the question is, how do you incorporate public participation and comment so that you can make the best guidance documents that will be applicable, not only to the case before you, but for others to understand, to move the process forward?

Mr. SCHULTZ. That's correct. I can tell you some of the things we do today. Sometimes we will put guidance documents out for public comment; sometimes we will have them discussed at advisory committee meetings; and sometimes we will have separate public meetings on them. Of course, every time, the public is entitled, after the document is out, to come back and comment to us. Because it's guidance, it's very easy for us to change the guidance, if we think that's warranted by the comments.

Mr. WAXMAN. So you are aware, then, you want the input from—you say, "public comment," but it really is comment from the industry which is important to have.

Mr. SCHULTZ. Yes, it could be the industry or anybody. We do this today, but what we don't do is do it necessarily consistently. Part of what we're looking at is looking across the agency to see what sort of policies we ought to adopt to ensure that our policy is consistent.

Mr. WAXMAN. So you need public input. You need to make sure your guidance documents are consistent. You don't want to tell one industry one thing and the next day tell another industry another thing. You want some consistency and some uniformity in your policy so people will know what the rules are.

Mr. SCHULTZ. Right.

Mr. WAXMAN. And I guess the questions that we're raising today in this hearing are, how good a job are you doing and how can we give you the tools necessary, if you need it, legislatively, to do a better job? And I think it's in everybody's interest.

I understand that we're going to hear other witnesses that are critical of the FDA, and that's appropriate to hear from them. Then it's appropriate to hear from you in response, but I think you ought not to be called in the same day. You ought to have a chance to evaluate what they have to say and give us your best judgment as to the issues in debate, and narrow the difference and learn from this, rather than use this hearing as a process simply to blame each other, or whatever. That's certainly not constructive.

Mr. SCHULTZ. I appreciate that, Mr. Waxman. This issue has come up in other contexts, as well, and what can happen is, at a hearing, certain allegations will be made against the agency that we, sitting here, have no information about. What we need to do is go back, examine the record, and then we're happy to come back to the committee or to respond in writing, however the committee desires.

Mr. WAXMAN. I think it's very important that the Congress act responsibly. I have sat through many meetings when witnesses have come forward and said things that just weren't accurate, without maybe, even, intending to say things that were untrue. I've heard anecdotes used by Members of Congress to justify policies that didn't make any sense, and the anecdotes turned out to not have been accurate either.

So I think we need to deal with this in a way that gives everybody a chance to be heard, evaluate what they have to say, and then think through the best policies, not simply react quickly, because sometimes the quickest reactions or the most emotional reactions are not the most thoughtful.

I thank you very much for your presentation.

Thank you, Mr. Chairman.

Mr. MCINTOSH [presiding]. Thank you, Mr. Waxman.

It's our hope that, with Mr. Shays voting first and me voting last, we will be able to continue uninterrupted on this vote.

Let me turn now to Mr. Souder.

Mr. SOUDER. I wanted to comment just briefly on Mr. Waxman's last point. It has been helpful in a number of hearings, however, to have the agency late in the hearing, as well, understanding that some comments may be made that you don't understand, but most of the people here today are pretty public in their objections. You could have anticipated and probably have heard those objections many times.

For those of us who may not be as detailed in the field, it's helpful to get the exchange during the process of the hearings. But we will certainly take you up on coming back again, I'm sure.

I have some questions related to the guidance, as well. In the guidance documents, are those usually followed through in the final regulations? How often are they reversed later on?

Mr. SCHULTZ. Well, very often there will be a guidance document that will be issued that is really much more detailed than would typically be appropriate in our practice in issuing regulations. So they would not be followed up through a regulation; they would simply be available as guidance.

One of the things that we're looking at is whether we do a good job in making them available, so that somebody who is interested in guidance has a single place they could go to find out what the agency has said.

Mr. SOUDER. So, if you are a manufacturer deciding what to put on the market—so I can try to understand the process—a guidance document, while it's not a must, certainly, at the very least, is some sort of a potential threat of legal action if you don't follow it? In other words, if the guidance is that you shouldn't do this, and you do it, while it might not be an enforcement, isn't there a possibility of future action against you?

Mr. SCHULTZ. Yes, just as there would be if there were no guidance document. At times the manufacturer is in a vacuum, and is trying to decide whether it needs to come to the FDA or, if it comes, what has to be in the application, if it has no information, it's in jeopardy; and if it has the guidance document and doesn't follow it, it's in jeopardy. But at least, if it had the guidance document, it has the opportunity to come to the agency and have the discussion.

Mr. SOUDER. But isn't it true it's certainly at greater risk of jeopardy if it knows the risk and still goes against it. In other words, I agree with you, there's risk being blind, and there's also risk—but the more you know, and then you go against it, it becomes more likely that you're going to have a problem; is it not?

Mr. SCHULTZ. The only thing I would say is, it's hard, at some point, to discuss this in the abstract. You really need to have the specific example, because there are times when it's appropriate to deviate from guidance because of a special case, or whatever, and there would be no legal jeopardy.

Mr. SOUDER. And in saying that there is no legal jeopardy and it's not a must, does it not bias regulators? If you had a company that continually didn't follow the guidance documents, numerous times, wouldn't that kind of give you a warning maybe to keep your eye on that company? Would it be any kind of internal signal to regulators to keep an eye on a company?

Mr. SCHULTZ. It would really depend. We also would have to talk about how we would even know. Certainly, if our inspectors go in to inspect, what they are really looking for are violations of the regulation or the statute. If we consistently see that, then that is a red flag, yes.

Mr. SOUDER. That comes back to the core question of input into those guidance documents, because if, in fact, they are quasi-official, it puts a little more—I mean, certainly, you would grant that, at the very least, it's like a strong warning sign and that it would be pretty risky to put a lot of capital into something if you had pretty strong signals that it wasn't.

Mr. SCHULTZ. They are significant. We wouldn't go through the trouble if they didn't have some significance. So I agree with you, it is important, in terms of fairness to the regulated industry and just to get the document be the best it can be, to get input from the public.

Mr. SOUDER. In the Hudson study and in documents before the release of this current study today, they have made charges, and I think it's pretty logical to assume that lives are lost by not approving certain devices, as well. Do you disagree with that premise, that lives are lost by delaying certain devices from coming to market?

Mr. SCHULTZ. I do disagree with the basic theme of that study. Dr. Burlington, who runs the Device Center, is really the one I would like to have respond to it, if you want to go into it more than that.

Mr. SOUDER. I would like to, because if something is not a direct, clear threat to somebody's life, and yet having that device could potentially save their life, why would it not be true that delaying access to that device could be costing lives in America?

Dr. BURLINGTON. I'm having trouble following all the negatives, with due respect, in your question, but I think I get the point.

Mr. MCINTOSH. If I may interject. Mr. Burlington—and I apologize that you have a question that you now can't respond to, but can I ask you to hold that? We have to go vote.

Here's Mr. Shays. I will let him continue.

Mr. SOUDER. I will come back, or I'm going to miss the vote.

Dr. BURLINGTON. Do you want me to hold my answer, then?

Mr. SHAYS. Yes.

My basic question centers around the concern I have that the FDA, in order to deal with its environment as it sees it, ends up writing its own rules of conduct for itself. We see that in terms of the whole issue of time requirements, which, candidly, aren't realistic, so the FDA has amended them and, as a result, chooses its own timeframes for regulatory decisions.

So in some cases it may take 10 years for a product to be approved. In some cases, it could be the manufacturer who thinks that it's not going to like the agency's decision, so it's not going to push for a decision quickly. So there are a lot of factors.

But the bottom line to this informal guidance process is that it enables you to not have to have public comment and avoid the impact that it should have. So maybe you could just address that issue.

Mr. SCHULTZ. The point about deadlines I think is a valid one on both sides. The ones in the statute, I think everybody recognizes that some of them, anyway, aren't realistic, and therefore, then, we have no deadlines. We had, I think, a very good experience in the drug area that maybe we can build on in other areas.

In 1992, in conjunction with the industry and Congress, the FDA had 6 months or so of discussions with the drug industry to come to agreement about what would be realistic in terms of resources and what would be realistic in terms of approval times for new drugs. We ended up with very ambitious times: 6 months, for important drugs, for review, for making a decision; and a year, for all drugs, for making a decision. We were given 5 years to get to that

goal. I can say that we are very much on track. We have met all the interim goals.

So I think you have identified a real problem. I think that there may be ways of coming to a solution. But what we learned from that experience is, it's very important to have all three parties involved: Congress, the industry, and the agency employees. Because if goals are set that aren't realistic and that the agency hasn't said it can meet and the employees aren't committed to, then none of us are getting what we want.

Mr. SHAYS. Let's just focus on interpretive rules. Right now that is an informal process; is that correct?

Mr. SCHULTZ. Yes.

Mr. SHAYS. And the formal process requires you to do what?

Mr. SCHULTZ. It requires us to put out a proposed rule, publish it in the Federal Register for notice and comment, receive the comments, and then, in the final rule, actually respond to every comment, explain every substantive comment, and explain what we did to accept it or why we rejected it. Then that would be subject to judicial review. Major rules go through a review, not just at the agency, all the way through the agency, but through the department and the Office of Management and Budget.

Mr. SHAYS. And explain once again why that process isn't acceptable for you, why you have to use the interpretive process.

Mr. SCHULTZ. It's acceptable when the regulation is going to be binding, and we use it constantly. The Federal Register is full of regulations the agency has issued. But we don't think it is realistic to use that for all the guidances that we issue. We have probably 1,000 to 2,000 pages of regulations in the Code of Federal Regulations. We have, I think, now close to 1,000 guidances that have been issued over the years.

Mr. SHAYS. I understand and I think I appreciate that you don't think it's realistic. Given that you don't think it's realistic by what authority, have you developed this process?

Mr. SCHULTZ. The Administrative Procedures Act, as interpreted by the courts, says that if the regulation, or action, is not binding, then we don't need to go through that formal process, and we don't need to go through any process.

What I'm suggesting here is that, particularly in recent years, we go through an in-between process where we do generally accept public comment. Somebody just gave me a note that, in the device area, we have sent 49 of these guidances to advisory panels in the last 2 years. We have public advisory panels that we get advice from on the guidance.

So what I'm suggesting is, there's an in-between where we can get the public input but not go through the full rulemaking process. Now, I should say, in some cases, for both regulations and guidances, you have a matter that is so important that, in the public interest, you need to get it out and get the public input later. We always want to reserve for that.

But, in general, we do accept the point of the Indiana petition that the public ought to be able to comment on these.

Mr. SHAYS. So based on the courts' interpretation of your rulemaking authority, since it's not binding, they say that you can follow this process. In following this process, though, what you have

effectively done is cut out the opportunity for petitioners to utilize a formal comment process, whereby they can make comment. What is the solution to that?

Mr. SCHULTZ. What I'm suggesting is—there are two parts: one is, I think we should have a consistent policy across the agency for guidances, A, making it clear these aren't binding; B, in general, allowing public comment; and, C, providing for an appeals process. So if somebody isn't happy with a guidance, they have somewhere else in the agency they can go to appeal it.

Mr. SHAYS. Without giving it the kind of thought I would like all three of those sound sensible. How have you started to implement that?

Mr. SCHULTZ. We haven't started to implement it, but we are basically using the deadline for the petition as an internal deadline, for ourselves. So we would expect to have something thought out that we could make public by the time the response to the petition is due, which is the very end of October. That's our goal, and I expect to at least come close to meeting that.

Mr. SHAYS. This committee is going to give a great deal of attention to the whole practice of the FDA, basically, in our judgment, inventing its own rules and then using them in what I sometimes think is an arbitrary way, or certainly not a consistent way. I like bureaucracies to have some flexibility, so I have to think that through. But it allows you to pick and choose in ways that I don't think are always fair. So we're very interested in following up on this, obviously.

Mr. Fox, are you prepared to ask a question?

Mr. FOX. Yes, I am.

Mr. SHAYS. I am going to also give you the chair for a second, because I will be gone for a second. So you are in charge.

Mr. FOX [presiding]. OK, I will call on myself. Thank you, Mr. Chairman. I've never had this much power before or since.

Mr. Schultz, thank you, you and your staff, for attending today this important hearing. I just have a few questions, if I could, and to the extent you want to answer them, otherwise, defer to the other experts, I would appreciate it.

In the administration's reinventing government proposal, 125 categories of class 1 medical devices are nominated for exemption from the premarket notification process. Have those categories of devices been identified?

Mr. SCHULTZ. I believe the answer is yes.

Dr. Burlington, do you want to add to that? I believe we issued a notice, didn't we?

Dr. BURLINGTON. Of the exemption.

Mr. SCHULTZ. Of the exemption. Yes, we've issued a notice in the Federal Register.

Mr. FOX. What administrative procedures were used to identify these categories, if you know?

Mr. SCHULTZ. Rulemaking, notice-and-comment rulemaking.

Mr. FOX. And has the regulated community been afforded an opportunity to comment?

Mr. SCHULTZ. Yes.

Mr. FOX. OK. The FDA has proposed that device manufacturers establish quality assurance systems that identify who is respon-

sible for various aspects of the design and manufacturing process. Does the FDA have any such system to monitor its own business, and, if so, who is responsible for seeing that the 510(k) applications are processed within 90 days and that PMAs are processed within 180 days, as mandated by the Food, Drug, and Cosmetic Act?

Mr. SCHULTZ. I would like to ask Dr. Burlington to respond to that, since he is the director of the Center for Devices.

Mr. FOX. That was a difficult question. I would have delegated that one myself.

Dr. Burlington.

Mr. SCHULTZ. I was going to say to take a crack at it.

Dr. BURLINGTON. Thank you, Mr. Fox.

That responsibility is delegated to the Center and to the Office for Device Evaluation within the Center. We seek good management principles in order to get decisionmaking at the lowest level that is feasible, with a reasonable level of control of the quality of the decisions, and we seek quality control mechanisms so that we know what's going on and that we can do a better job in matching resources with work flow, in order to get to those statutory directives and timeframes.

We have in the past, in fact, fallen short of that, as you are aware. We have made, however, significant progress over the last couple years toward reapproaching those goals, particularly in the case of 510(k)'s and PMA supplements. We are beginning to make progress, as well, on PMAs, and this year have made significant progress on investigational device exemptions, in terms of getting them cleared on the first cycle. We have been fairly consistent in meeting our goal of getting those acted upon within the 30-day statutory directive.

We seek consistency. We monitor what's going on. We meet among the delegated officials who have the responsibility to review decisions seeking exactly the sort of quality control that was anticipated in your question, I believe.

Mr. FOX. H.R. 2290, which is my bill to try to speed up the device approval process, I hope that someone from FDA might—I don't know whether it's Mr. Schultz—tell us who might be looking into that bill, as far as the agency's involvement in recommendations of changes or what their feelings are.

Mr. SCHULTZ. We will look at it. My office will look at it. The Center, Dr. Burlington's center, will look at it. Our Office of Legislative Affairs will look at it. We will be happy to discuss it with you or your staff.

Mr. FOX. Let me ask a question regarding the Administrative Conference of the United States. They had a letter on September 24, 1990, I guess it was from Marshall Bregger, chairman of the Administrative Conference, to James Benson, then Acting Commissioner of the Food and Drug Administration, in Rockville, MD.

In that letter, the thrust of the comments and of the conference recommendation, interpretive rules of general applicability and statements of general policy, is that FDA should reconsider its seeming all-or-nothing approach with regard to using the notice-and-comment procedure. In the last part of the letter he says, "For these reasons, I urge you to seriously consider adopting the proce-

dures set forth in conference recommendation 76–5 in your amended rule."

Why then did the FDA abandon its policy of putting interpretive rules through a notice-and-comment rulemaking over the objections of the Administrative Conference letter?

Mr. SCHULTZ. I haven't seen that letter, but I can tell you why we made that change in our regulations. I would like to see the letter.

Mr. FOX. I'll be glad to give you a copy.

Mr. SCHULTZ. It may be that what we're talking about here and what we have been doing since 1990, is to a large extent, but maybe not enough, providing an opportunity for public comment, in many cases, on guidelines, is consistent with what that letter was saying.

As I said before, before and after 1990, the agency consistently used guidelines as a way of informing industry of what it was doing, without going through the time-consuming notice-and-comment process. The reason we made the change in 1990 is, the case law changed in such a way that some courts suggested that they might be construing our regulations as requiring us to go through the full notice-and-comment process in situations where we had never intended that to be the case and had never in the past done it.

But I would like to see the letter, and we could respond to you either here or at another time.

Mr. FOX. We're going to give you a copy of the letter, Mr. Schultz.

Mr. SCHULTZ. OK.

Mr. FOX. Let me say, in following up on your comment, on the notice-and-comment procedure, wouldn't that give industry, that is at the front line, a better chance to give you input by maintaining that procedure?

Mr. SCHULTZ. It would certainly give them a chance to give us input. What we're saying, I think, is, in most cases, we can afford the opportunity for input, either through advisory committees that are public or other kinds of comment, without incurring the delay and disadvantages of the full-blown rulemaking process. Since we don't intend for these guidances to be binding, it really doesn't seem to be necessary or a good use of our resources to go through the full-blown process.

Mr. FOX. Let me ask you this: Within the Office of Device Evaluation, who decides when a guidance is final and signs off on it?

Mr. SCHULTZ. I will let Dr. Burlington answer that, since it's about his center.

Dr. BURLINGTON. Procedural guidances used in that office that affect the office and are cross-cutting are decided by the office director or one of her deputies. Vertical guidances, guidances that are product-specific, or product area-specific, I should say, tend to be done at the division level.

Mr. FOX. OK. And, finally, within the Office of Device Evaluation, which members of the public get to see the draft guidance, and who decides that?

Dr. BURLINGTON. The individuals who are responsible for signing off on guidances are the ones who make decisions about at what

stage the public input will be received. We inevitably seek public input. We have, in fact, invited members of industry and the public at large to submit their proposals for guidance to us and that we would use those as starting documents.

As Mr. Schultz mentioned, we have, 49 times in the last 2 years, discussed with advisory committees guidances in evolution. And we take seriously comments received after guidances are initially put forward in draft. So we have a uniform policy of seeking that input. The time at which it is done, in the development of a guidance, is at the discretion of the person who has responsibility for issuing it.

Mr. FOX. The last thing I would make a comment on is that I hope that the FDA will work closely with Congress and all other interested parties, because I think, when it comes to medical devices, we're trying to make sure we get them to market faster without sacrificing quality and efficacy of standards.

Dr. BURLINGTON. I absolutely agree with you, Mr. Fox. The members of the Center, just as the members of this committee, clearly want us to be both fast and decisive, as well as consistent, and also open, with a high level of procedural input, in terms of the promulgation of guidances and in getting these guidances so that they make sense for industry. But we also recognize there is tension among that need for speediness, consistency, and openness.

Mr. FOX. Yes.

Thank you, Mr. Chairman. I appreciate the opportunity.

Mr. MCINTOSH [presiding]. Thank you, Mr. Fox.

Let me turn, Mr. Schultz, to one of the examples you used in your written testimony, the 510(k) modification guidance, and I think it's entitled, "Deciding when to submit a 510(k) for a change to an existing device."

If it is, in fact, the case that these are meant to be a heads-up to industry but not enforceable and not creating any legally enforceable rights or responsibilities, then how do you or how does the agency explain to Star Dental in their Dental-ease modification, which was documented in the medical device approval letter dated August 1995—and I will submit the newsletter to the record—in which they were told by the inspectors who were slapping them on the hands, at least, for making a modification in their product, that they should review that document in deciding whether to make that type of modification?

That, to me, sounds as if it has pretty significant legal consequences, if there might be an enforcement action taken against someone.

Mr. SCHULTZ. I'm at a disadvantage because I haven't seen, I don't think, the document that you have there.

Mr. MCINTOSH. It's a newsletter.

Mr. SCHULTZ. But what I would say is that the reason companies want guidance is because they want to be able to review them in conjunction with making decisions. That is different from saying that the guidance could be the basis for any kind of prosecution, which it could not be. Guidance could not be the basis for a prosecution; it is not binding.

Mr. MCINTOSH. And I think that's the fundamental problem we have here is that FDA's regulatory process is structured so that a regulated entity can't make a move without approval. So the prob-

lem is, the guidances become, effectively, legally binding for people, in order to take an action. What was told to this company was, "Look, before you do this in the future, read this guidance and make sure you have followed it in deciding whether or not to come in and seek a formal modification under the 510(k) proceeding."

Mr. SCHULTZ. I think, if they had read the guidance, they would see that it is guidance; it is not binding. If they don't want to follow it, they can come.

Mr. MCINTOSH. I think you're not understanding what I explained happened.

Mr. SCHULTZ. OK.

Mr. MCINTOSH. They didn't read the guidance. They were slapped on the hands and told they should have read the guidance. Now, presumably, they weren't reading it just to see they don't have to read it. I mean, somebody wanted them to read it for the substantive requirements and follow those when they made their decisions.

Mr. SCHULTZ. I don't know the facts of this. I mean, it could well be—and I'm just speculating—that the inspector said, "Well, look, you're doing it wrong. Have you seen this guidance? You ought to look at it," and walked away, without any sort of penalty or consequence. Or it could be the inspector made a mistake. I just don't know the facts.

Mr. MCINTOSH. OK. Well, if you could go back and find out for us on that. But let me ask you, are there written instructions to the field inspectors or guidance, internally, on when to refer to guidance when you are dealing with the regulated community?

Mr. SCHULTZ. I would like to ask Mr. Chesemore to answer that, since that's his area.

Mr. CHESEMORE. Mr. Chairman, there are written guidelines and instructions on this guidance, and the guidelines clearly state that, with respect to the list of observations, the 483 that perhaps you have heard about, investigators are not supposed to cite a firm when they do not follow guidance documents. We encourage the investigator to mention this to the firm during a close-out session, but it's not supposed to be on the 483.

As such, we mentioned a little while ago or someone brought up, I think, encouraging industry, at the time of these investigations and these inspections, to make their objections known to the investigator, to challenge the investigator. If they disagree, certainly we are encouraging them to come in and talk to the local district management about how they interpret these guidance documents.

So, while this is standard in our training, and investigators are given guidance with respect to how to utilize these things, from time to time, perhaps, someone will stray away from what we ask them to do.

Again, I don't know the specifics on this particular firm either, sir.

Mr. MCINTOSH. I just saw it in the newsletter. I have to say, though, this has an Alice in Wonderland type quality to this whole discussion. Because what we're saying is, in order to avoid the necessity of getting public input before we develop guidance, we don't publish anywhere for people to refer to in making decisions. We've

developed this elaborate procedure, internally, at the FDA, to tell people that they can talk about this guidance.

But nonetheless, it's there, it's sitting at the agency, and it's something that they are using in making decisions day-to-day. Wouldn't it be a lot easier just to say, "We're going to go through the steps, get public input; we're going to have a list that's published in the Federal Register of these guidance documents; and we're going to follow these procedures and not have to create an elaborate construct to discipline ourselves internally to not use them?"

Mr. SCHULTZ. I agree with you that, as a general matter, we should get public input. And I agree that they ought to be published in some place where they are easily accessible. But that doesn't necessarily mean formal rulemaking, and I don't think it necessarily means in the Federal Register. We're open to thoughts on this. We've thought about whether or not it should be put on the FDA page on the Internet. Actually there may be ways where we can get it out faster and more efficiently than the Federal Register.

I don't think we disagree with your basic points.

Mr. MCINTOSH. I welcome the fact that you want to use the petition as an opportunity to develop that, and I do recommend you consult with people over at ACUS. They have thought a lot about the notice-and-comment requirements in this and other regulatory areas. They are not partisan, particularly, and they would be helpful in doing that. Also, see Sally Katzen over at OIRA. I mean, she's thought a lot about these issues herself and is very, very good on that.

Let me turn to another question, and then I have to go vote. What is the agency's response to, really, the fundamental question raised by the Hudson study that, in the United States, with the changes in the device approval process in the last 4 or 5 years, we are behind Europe, and the consequence of that is that it's less safe, less healthy, in fact, costing us lives of people who could benefit from these devices if the approval process moved quicker?

Mr. SCHULTZ. Dr. Burlington is prepared to respond to the specifics of that petition. I think, in general, though, we are charged, appropriately so, with protecting the public health by ensuring that devices have a reasonable assurance of safety and effectiveness before they are approved. We are also charged with doing that in a timely manner. And we recognize that, particularly if it's a breakthrough device, we need to do that as quickly as we can. We need to make these decisions in an expeditious manner.

Dr. Burlington has been director of the Center for Devices for about 2½ years, and I think, if you look at the performance during that period of time, he has made very significant strides in achieving those goals. He can talk to you, in general, about what I just talked about, but also about the specifics of that article, I think many of which are misleading.

Mr. MCINTOSH. Let me call a recess now, and I would like to hear that when we get back.

Mr. SCHULTZ. OK.

Mr. MCINTOSH. And I will tell you one other question so you can think about which direction you want to go on it. Should there be

a formal process or some way in which the agency consciously considers the downside effect of taking an extra step in the approval process?

Maybe, after the fact, they say, during the 7 years or 5 years or 4 years, whatever it was, there were these many people who could have benefited by this and didn't, but we think it's reasonable because we had to ensure safety and efficacy. Right now, that fact is never put into the equation, at least in a public fashion. Think about whether there is something beneficial there.

The committee will stand in recess until either Mr. Shays or I return.

[Recess.]

Mr. MCINTOSH. If everyone could please take their seats.

I appreciate the FDA folks for waiting as we went through both of those votes. I understand that my question has been asked a couple times, and you haven't had a chance to answer it. So before we dismiss you—and I have no other questions, or if I do, I will put them in writing—Mr. Green, I understand has one—but Dr. Burlington, would you proceed with the agency's response on this, and then we will see what Mr. Green's question is.

Dr. BURLINGTON. Mr. Chairman, thank you. I appreciate the opportunity to address the question that you and Mr. Souder have raised regarding the Hudson Institute report.

Without going into full detail—and we would be glad to provide full detail for the record, if you wish—I would like to say, in general, that there is a thesis here that when a product is safe and effective, that it was probably also safe and effective the day before and stretching some time before that, and any time lost denies those benefits to the individuals during that time that was lost.

We certainly see the sense of that argument and agree with it, in fact, but we all have to understand that the safety and efficacy of a product, whether it's a pharmaceutical or whether it's a medical device, is not just in the article itself; it's also in understanding how to use it properly so that one can select which patients it's going to benefit and which ones that won't. That is one of the things that is learned during the development process and, in fact, refined during the review process that takes place at the agency.

In addition, you can't look at only the successes. One also needs to consider those products which offer great hope initially but turn out to falter in the development process and not bear through that promise. When you take these things together, we think that there is a benefit to having regulatory review, to the independence, to the winnowing of the hopes, and the looking and saying, where is there objective evidence that practitioners can use to guide medical decisionmaking?

Incumbent on us, also, is that when we have something where we have the evidence in front of us that it's going to make a difference in health care, that we move speedily to move that to market, so that the public will then get that benefit. I have taken this seriously throughout my career at FDA. Certainly, I took it seriously in the Center for Drugs when I was there, both directly approving products and working with the Division of Anti-Infective Drug Products to speed up our review times.

I have certainly taken it seriously in the Center for Devices these last 2½ years. After I had been there just a couple of months and realized one of the categories of products that was discussed in Dr. Murray's paper, the endovascular leads for automatic implantable cardioverter defibrillators, were in the agency, looking at the data and saying that these have evidenced that they make a difference in patient outcomes, I said, we have got to put in place a policy where we take those things out of queue, where we deal with these things as expediently as possible.

When you know something makes a difference, then you can no longer afford to wait and hold it in line. And we did that and are proceeding to continue to do that with important products that have a medical benefit.

We also have to be cognizant of the fact that we shouldn't make that decision—we shouldn't make it on unsupported hopes of a manufacturer, because each manufacturer has that hope. We have an obligation to manufacturers for fairness and consistency in how we handle their applications, so that we're not taking them out of line or out of their turn in the review queue until we have that evidence that they make a medical difference.

But then, when we do, Dr. Alpert, director of device evaluation, and I are committed to putting in place processes to get those things reviewed and approved expediently.

Mr. MCINTOSH. How many devices pose serious health risks on the magnitude of causing someone to die if they are treated with them?

Dr. BURLINGTON. I don't have a count of devices that pose serious health risks. In general, when you are using a device as an intervention in a life-threatening illness, you can almost count on it having a health risk attendant to it.

For instance, some of the products that are discussed in Mr. Murray's paper, one of the cardiac valves, I mean, cardiac valves are certainly a category of products where there are complications that are life-threatening. Placing intra-arterial stents in people with threatened heart attacks, when you put a metal cage inside of an artery supplying blood to the heart, if something goes wrong, the chance the patient may die is very real and palpable. So the higher the benefit of the products, often the higher the risk, as well.

Mr. MCINTOSH. This will be a debate that I'm sure will continue over time.

Let me ask Mr. Green, you indicated you had one question for the FDA panel.

Mr. GREEN. I have one question. Again, like a lot of members, I apologize for not being here earlier, but I was looking forward to the hearing and some of the issues that have come up.

One of the things that caught my attention—again, not knowing some of the other questions that were asked, if you had a chance to answer them before members ran to vote—was that in the Indiana Medical Device group citizens' petition they cite a number of cases where the FDA developed rules without public participation and then announced the rules though speeches, press releases, and things like that.

They cite the example of using the reference list to determine where the agency would clear a 510(k) submission. The Indiana Medical Device group alleged that this policy was developed without public participation. It was announced in July 1992 in a speech by Ronald Johnson, then director of the Office of Compliance at the FDA Center for Devices and Radiological Health.

I would ask for your comment, but I would hope we would have a better structure than announcing policy at a speech, simply because I would hope that the Federal Register would be more apropos to do that instead of using speeches or press releases. I can see where you would use those to publicize, but the actual information should be available to everyone, and there should be some other, better way to do it.

If you could just comment on if that happened, from Mr. Johnson, and there wasn't any other public notice on that.

Mr. SCHULTZ. Let me comment first on the general point and then talk about the specifics of the reference list, if that's useful.

On the general point, what we have said is, as we look at the petition and look at our process and our use of guidances versus regulations, while we don't agree with the exact request for relief in the petition, we do agree with the basic thrust of it, which is to say, we ought to look at getting public input more consistently on guidances and figuring out a way to publish them and make them available to people. I don't know that that's necessarily through the Federal Register, but there ought to be one place companies can go to find out what the guidance is.

We are, in the context of responding to the petition, doing a review of all these issues and will have a response relatively shortly.

In terms of the reference list, let me tell you what the problem was, what we did, and then how we changed it, because we don't think we did it quite right the first time. The problem was that we had 510(k) applications, where a company comes in to us and says, "I want to sell a medical device because it is substantially equivalent to a device already on the market, and my job is just to convince you that it is basically the same as something already on the market."

So you had that practice going on in the Center for Devices, while at the same time you had our inspectors going into the plant and, in some cases, finding very serious good manufacturing practice violations which raised questions about whether the company was capable of consistently making the same product, thus raising questions about whether it would, in fact, be substantially equivalent.

For some period of time, the left hand didn't know what the right hand was doing. The theory of the reference list was, we ought to get the information that the inspector found to the people reviewing the devices so they could take that into account in reviewing the application. That's what Mr. Johnson announced in that speech.

Now, the policy was very much criticized by the industry as being secret. They said they didn't know whether they were on the list; they didn't know how to get off, and so on. So, as part of the President's reinventing government initiative last spring, we made

some very clear statements, and I think they have been very satisfactory to the regulated industry.

First of all, we said, we will only hold up the application if there is a connection between what we found at the plant and the ability to make the product. Second, we said, if you are in that category, we will tell you right away. We won't wait until we're ready to approve the application and tell you; we will tell you right away. Third, we said, if you tell us you have fixed the problem, we will get back within 60 days and reinspect. If we don't meet that deadline, then we won't hold up your application because we weren't able to get back to reinspect.

As I said, I think that has been satisfactory.

Mr. GREEN. Thank you.

Mr. MCINTOSH. Thank you, Mr. Green.

Let me ask unanimous consent that we hold the record open for 3 days, if there are any other written questions for this or the subsequent panel.

I appreciate the agency officials for joining us today and look forward to seeing the resolution on the petition on this matter.

Mr. SCHULTZ. Thank you very much. Mr. McIntosh, we will have somebody here in case there are other questions you want responses to on the record.

Mr. MCINTOSH. I appreciate that. Let me mention one thing, Mr. Schultz. I think people may have misinterpreted one of your characterizations of the petition that I think we're in agreement on, that it doesn't apply to all policy statements or guidelines, but it's narrowly drafted to request those of future effect and general applicability.

Mr. SCHULTZ. The interpretive rules.

Mr. MCINTOSH. That's right. That aren't product-specific. I think that was my reading of their request.

Mr. SCHULTZ. I think that's right. We should go back and look at it.

Mr. MCINTOSH. Thank you all for coming, and we appreciate your staying through the rest of the hearing.

At this point, if there is no objection, I think I would like to combine the second and third panels and ask all of those witnesses to come forward at the same time.

[Witnesses sworn.]

Mr. MCINTOSH. Let the record reflect that each of the witnesses answered in the affirmative.

The first witness on this panel is Bradley Thompson, who is an attorney with Baker & Daniels and counsel to the Indiana Medical Device Manufacturers Council.

I would like you all to summarize your testimony for the record.

STATEMENTS OF BRADLEY M. THOMPSON, ESQ., BAKER & DANIELS, COUNSEL, INDIANA MEDICAL DEVICE MANUFACTURERS COUNCIL, INC.; LARRY PILOT, ESQ., McKENNA & CUNEO, COUNSEL, MEDICAL DEVICE MANUFACTURERS ASSOCIATION; EDWARD R. KIMMELMAN, BOEHRINGER MANNHEIM CORP.; DAVID C. MURRAY, REGULATORY ANALYST, THE HUDSON INSTITUTE; THOMAS M. LENARD, PH.D., DIRECTOR OF REGULATORY STUDIES, PROGRESS & FREEDOM FOUNDATION; AND JEFFREY A. BRINKER, M.D., DIRECTOR, INTERVENTIONAL CARDIOLOGY, JOHNS HOPKINS UNIVERSITY HOSPITAL

Mr. THOMPSON. Thank you, Mr. Chairman. Thank you for inviting me to testify today and for placing on today's agenda the subject of FDA's rulemaking and guidance procedures.

My name is Brad Thompson, and I serve as general counsel to the Indiana Medical Device Manufacturers Council and as a partner in the law firm of Baker & Daniels.

Rather than proceed along the lines of my written testimony which I have submitted, I would like to respond directly to what the FDA has said this afternoon.

I would like to start out by acknowledging what I heard to be positive remarks that FDA made about the agency's intentions to critically examine this area and to make the changes that are appropriate. I find that very encouraging, and I was very pleased to hear that.

What I would like to do is, at the very outset—because there is some confusion about what the Indiana petition requests—spend just 30 seconds and explain that at the beginning. We request, essentially, three things:

No. 1, we request that the FDA's administrative regulations be amended so that interpretive rules and rules of agency practice and procedure will undergo notice-and-comment rulemaking just as substantive rules do. What we did is, we took the exact same language that was deleted in 1991 and proposed adding it back so what FDA did from 1977 to 1991 would again be the law.

For other documents, and I will call them "guidance documents," that includes a whole variety of things: speeches, warning letters, points to consider documents, any number of things which communicate a regulatory expectation, we ask that a different procedure be adopted, not formal notice-and-comment rulemaking, but what we call "good guidance practices".

We borrow that name from good manufacturing practices which, as you know, are the FDA's requirements for quality manufacturing. Good guidance practices, in our view, would simply be a set of standards that FDA would use to judge whether it is turning out quality guidance.

The third change that we would ask is simply one of monitoring, that FDA do a more systematic job of making sure that it is complying with those two prior changes, that it is complying with the good guidance practices and that they are complying with the rulemaking requirements. That means, rather than rely on training an individual reviewer to understand and hopefully not announce new policy without going through those procedures, that some central

office at FDA, to the extent it can, review these materials to make sure that the system is, in fact, functioning the way it should.

That is what we are requesting. It isn't terribly different from the situation that existed before 1991, except that we would ask, for these guidance documents, which do include a tremendous volume of documents, that the FDA take a more systematic approach to ensuring public participation. There is a real lack of procedures at FDA to ensure that the public is involved when these guidance documents are developed.

Having said that, I would like to respond to the five guiding principles that the FDA announced as guiding its review. I find them, by and large, encouraging, but I also have some comments on them.

The first one is that guidance documents cannot be binding. That is, obviously, true. That is, in fact, the law. We would point out, however, that the disclaimer approach is not a viable way of ensuring that guidance documents are not binding. What I mean by the "disclaimer approach" is, you go through, if you're the FDA, 10 pages of very detailed requirements, and at the end you say, "And by the way, this is an internal document."

That disclaimer at the bottom of page 10 doesn't change the fundamental nature of that document. It is the way the FDA behaves in using that document which controls whether or not it is binding. So we ask FDA to acknowledge that and do more than add disclaimers, but No. 1, make sure that the documents are not used in that fashion, and, No. 2, as I said, use good guidance practices in developing those documents to ensure that they have the appropriate amount of quality.

FDA's second guiding principle is that guidance is good. We agree. The only caveat I would suggest is that we say, "quality guidance is good." Guidance lacking quality does no good. It wastes resources, and it causes confusion. The systems we are talking about today are designed to ensure that the documents have quality.

Now, one of those systems is to ensure that there is public participation. One of the main criticisms of the documents has been that they lack clarity. They are written without necessarily understanding the situations to which they are to be applied, or maybe they are just written inartfully. But when you solicit comments you learn that, and you can change the language.

Mr. Chairman, in your opening remarks, you mentioned the Price Waterhouse survey, and I think that survey speaks to this point quite well. The objective of the survey was to find out what industry thinks is the cause of significant delays in product approval. As you mentioned, 75 percent of the respondents in the device industry found that the guidance documents were so unclear that they were either not helpful or actually harmful. Considering the amount of time and effort that FDA puts into the guidance documents, FDA isn't getting a very big bang for its buck.

The third guiding principle at FDA is that they believe that notice and comment should not be followed for guidance documents. Based on what I have said before, you can already tell my response to that. We don't either. We think that notice and comment is important for interpretive rules. Interpretive rules, frankly, aren't

that voluminous. All you have to do is look at how much rulemaking activity was going on before 1991, and you realize that there are not that many.

But if a guidance document inappropriately includes an interpretive rule, then that interpretive rule should be subject to notice and comment. I would hope that very few, if any, guidance documents would include interpretive rules. That would be, under our scenario, inappropriate. But the guidance documents could still and would still be welcomed.

The fourth guiding principle is that most guidance documents would benefit from comment. The only suggestion I would have is that he revise it to say, "all guidance documents." Guidance documents, by their nature, are indications to the public as to what they are supposed to do. If nothing else, clarity is important.

The fifth one, that the appeal process be used, we approach that with mixed feelings. Obviously, an appeal process is no substitute for quality guidance in the first place, and I have yet to see an effective appeal process that can adequately insulate against possible retribution.

Those are my suggestions as to ways, perhaps, to rethink some of the guiding principles that FDA will be operating under. With that, I would be happy to respond to questions now or later.

[The prepared statement of Mr. Thompson follows:]

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**TESTIMONY OF BRADLEY MERRILL THOMPSON,
SECRETARY AND GENERAL COUNSEL,
INDIANA MEDICAL DEVICE MANUFACTURERS COUNCIL, INC.**

BEFORE A JOINT HEARING OF THE

**SUBCOMMITTEE ON NATIONAL ECONOMIC GROWTH,
NATURAL RESOURCES & REGULATORY AFFAIRS**

AND THE

**SUBCOMMITTEE ON HUMAN RESOURCES
AND INTERGOVERNMENTAL RELATIONS,**

BOTH OF THE HOUSE COMMITTEE ON GOVERNMENT REFORM AND OVERSIGHT

September 14, 1995

Thank you for inviting me to testify today, and for placing on today's agenda the subject of FDA's rulemaking and guidance procedures. My name is Brad Thompson, and I serve as General Counsel to the Indiana Medical Device Manufacturers Council and as a partner in the law firm of Baker & Daniels.

The IMDMC, as it is called, is a nonprofit association of over 30 large and small Indiana medical device manufacturers and about 15 associate members in allied industries. As such, our members are significantly affected by new rules -- both official and unofficial -- that FDA adopts. And as evidenced by the Citizens Petition we filed at FDA on May 2 of this year, we consider the reform of FDA's rulemaking and guidance procedures to be one of the most important issues facing medical device manufacturers and other companies producing and selling regulated products.

I believe that your briefing book contains a copy of that petition. I will not repeat the observations contained in it, nor will I describe today all of the evidence that we supplied in support of our position. Your book contains copies of those materials. Rather, I would like to spend my time suggesting some ways in which FDA can improve the processes it uses to develop and impose regulatory standards. These improvements, we believe, would greatly help to protect the public welfare, speed lifesaving products to market and minimize the cost of health care.

Broadly speaking, there are two areas in which FDA should improve its development of regulatory standards. First, the agency should expand its use of notice and comment rulemaking for significant requirements imposed on an entire industry. And second, FDA should adopt what we call Good Guidance Practices to better control the process for developing and announcing product-specific and other standards that do not merit rulemaking. I will address those two areas separately.

I. The Use of Guidance Documents

Before I do, however, I would like to explain what we mean by "industry-wide requirements" and "product-specific standards." Industry-wide requirements include any regulatory requirement that affects a whole industry such as the medical device industry or a substantial sub-industry such as the in vitro diagnostic device industry. An example of such a requirement is the FDA's sudden decision in 1992 to deny product clearances under the 510(k) procedure for firms to which FDA has sent a warning letter for asserted violations of the Good Manufacturing Practice regulations. FDA announced this broad rule affecting the entire device industry in a speech.

A product-specific standard, in contrast, only affects companies making or selling products in a relatively narrow product category. In the case of devices, for example, such a category might include products in a specific FDA device classification such as intravascular catheters. FDA develops these standards in both the enforcement and product approval contexts.

These industry-wide requirements and product-specific standards can be found in various forms of guidance issued by FDA. As we use the term, "guidance" refers to any oral or written vehicle that FDA uses to communicate a regulatory requirement or standard to the public. Examples include FDA speeches, warning letters, industry-wide letters, press releases, and so called "points to consider" documents. Usually in the context of product reviews, FDA issues documents that it calls "guidance," and those documents also fall within our definition of guidance. FDA uses all of these communication vehicles to announce new industry-wide rules and other regulatory standards.

Indeed, that's the problem.

II. Industry-Wide Requirements

A. The Problem.

As you know, the Administrative Procedures Act requires federal agencies to undertake a well-defined process of notice

and comment rulemaking for new substantive rules. This rulemaking usually entails at least the publication of a proposal in the Federal Register, the solicitation of comments and the publication of a final rule together with a statement of basis and purpose for the rule that responds to the comments.

Unfortunately, for many new, significant industry-wide requirements, FDA uses the guidance documents as a surrogate means of rulemaking. FDA's procedures for developing and issuing these guidance documents, however, do not include any of the statutory safeguards designed to ensure public participation in the process.

The benefits to FDA and to the public of using notice and comment rulemaking for important, industry-wide rules seem clear. Public participation invariably leads to more sensible rules. Rules cannot be developed in a vacuum, and the insights and wisdom offered by consumers, academics and those upon whom FDA will impose the rules can often lead to more effective and efficient regulatory approaches. Since both healthcare technology and the structure of the healthcare industry are changing at an incredibly rapid rate, FDA by itself simply cannot be expected to keep abreast of those changes and their implications for new rules.

In addition, the notice and comment rulemaking process results in greater acceptance and compliance by the regulated community as the agency develops a consensus approach. Regulations take on an air of legitimacy if the public has had an opportunity to help fashion the requirements. Moreover, the process of notice and comment itself helps to publicize the requirements, educating the regulated community with respect to what will be expected of them. The process also results in more transparent regulatory requirements that the public is better able to find and understand.

While some agency officials have relationships with trade groups, professional societies and individual companies that may allow for informal comment on guidance documents, these relationship-based opportunities for comment should not replace the more well-defined notice and comment procedures that allow the general public equal opportunity to participate in the rulemaking process. The agency's casual approach simply does not facilitate the quantity and quality of comments obtained by the more formalized publication in the Federal Register, and therefore also does not result in the most effective and efficient rules.

While we can only speculate, the agency's current approach to rulemaking may simply be the result of limited financial and manpower resources, as well as the agency's apparent frustration with the somewhat cumbersome and lengthy procedures that have

developed for notice and comment rulemaking. Among other things, the lengthy aspects of rulemaking limit FDA's ability to change its mind quickly. Given these factors, the tendency of FDA personnel to avoid notice and comment rulemaking may be less the result of any specific decision by an FDA official, and more the result of an evolutionary process brought about independently throughout the agency by these common pressures. They are nonetheless troubling for the public.

B. The Solution.

To help solve this problem, we have requested that FDA amend its administrative regulations so that both substantive and interpretative FDA rules must undergo notice and comment rulemaking. Indeed, while not required to by the APA, FDA for many years used notice and comment for both types of rules. In 1991, however, FDA amended its administrative regulations to delete the requirement that the agency use rulemaking for interpretative rules.

As you know, the APA generally only requires notice and comment rulemaking for substantive rules. The statute provides little guidance in making the determination of when a particular rule is substantive, and instead leaves courts to fashion their own tests.

In perhaps oversimplified terms, a substantive rule is one that creates a new, binding requirement usually not apparent on the face of a statute, while an interpretive rule reflects what an agency thinks a statute means. In practice, making this distinction can be difficult since it must be made on the basis of the specific facts, including the agency's sometimes veiled intention to make the rules binding. Evidence of that intention can include the actual language of the requirement and the agency's practice of enforcing it.

FDA for many years avoided the problem of distinguishing between substantive and interpretative rules by requiring notice and comment rulemaking for both types. But since FDA changed that practice in 1991, the agency has aggressively sought to limit its obligation to undertake the effort of notice and comment rulemaking by routinely concluding that new, significant rules are merely interpretative. Our Citizens Petition describes several examples of new substantive rules adopted without rulemaking. Given the agency's built-in financial incentive to conclude that a new rule is only interpretative and the consequence that many substantive rules have not undergone proper rulemaking since 1991, we suggest that the agency eliminate that temptation by returning to the agency's pre-1991 approach.

III. Product-Specific and Other Regulatory Standards not Subject to Rulemaking

A. The Problem.

As already explained, the second FDA practice in need of reform is FDA's approach to developing product-specific and other regulatory standards that do not need to undergo rulemaking. In both the approval and enforcement arenas, FDA develops these regulatory standards without public input through "draft" guidance and "points to consider" documents. In fact, we understand that any unit within FDA may develop such guidance for its own purposes. And before a guidance document is released to the public, an FDA official with the appropriate rank may or may not have even seen or signed-off on it.

In the case of the Office of Device Evaluation, for example, any level from the individual reviewer on up can develop guidance. The extent of public participation through advisory panel input or distribution to specific industry trade groups or companies is largely left to the discretion of the individuals developing the guidance. Moreover, there exists only an informal understanding that an FDA reviewer should not release a guidance until at least a Division Director has accepted it. And since there are no mechanisms to ensure that the guidance documents are disseminated to the appropriate people, companies submitting product approval applications are routinely surprised to find out, after submitting the application, that FDA has a guidance or an updated guidance explaining what the agency expects for those submissions.

The result of this disarray is poor quality guidance which, as often as not, actually impedes the product-approval process. This summer, Price Waterhouse released the results of a substantial survey of the drug, device and biologics industries designed to identify the factors which, in the opinion of those industries, contribute to the delays in the FDA approval process. In its report entitled "Improving America's Health: A Survey of the Working Relationship Between the Life Sciences Industry and the FDA", Price Waterhouse found that one of the principal causes of the delay in product approvals is the lack of clarity in FDA guidelines. According to the report, "[t]he important point that emerges from these figures is that a significant number of companies of all kinds saw the guidelines as confusing or as hindering their submissions." In fact, among the device companies responding to the survey, almost one-quarter of the companies indicated that the FDA guidelines impeded or stopped the approval process. About one-half felt that the guidelines had no impact, and only about a quarter believed that the guidelines were helpful or very helpful. A copy of the summary section of the report is attached. Considering the resources

that FDA invests in these guidelines, it is disappointing that the result is at best neutral.

To be sure, these guidance documents have the quite laudable goals of increasing consistency among reviewers and improving communications with industry. But while the agency says that they are living documents that describe only one acceptable approach among perhaps many, in practice the industry finds that reviewers often treat these guidances as specific, inflexible legal standards. As a result, since FDA has no written procedures controlling how guidances are developed, approved, or implemented, and since some of these guidances become at least de facto standards, FDA in effect produces some very important requirements with very little public input.

Compounding that problem is the fact that the public plays no role in deciding when the development of a guidance document should be initiated and when existing guidance documents need to be updated. While these decisions involve the allocation of scarce agency resources and thus should be made by FDA, the public can offer valuable insights that will help FDA evaluate the need for the initiation or revision of guidance.

B. The Solution.

Given the volume and nature of these product-specific and other guidance documents that do not announce substantive or interpretative rules, the notice and comment procedures simply are not appropriate. For new regulatory standards that do not merit rulemaking, FDA instead should adopt Good Guidance Practices that apply regardless of the type of guidance document in which the standard is found. These GGPs should ensure:

1. public participation in FDA's decision to initiate guidance;

2. an appropriate level of public participation in the guidance development;

3. uniform processes for guidance document sign-off by FDA to ensure reliability and consistency with other guidance issued by FDA;

4. processes for determining, with public input, when guidance documents need to be updated; and

5. greater centralized tracking to help the public participate in the development process and to facilitate the public dissemination of completed guidance.

Adopting these GGPs would result in higher quality guidance documents. While these procedures would be certainly less involved than notice and comment rulemaking, the guidance documents would benefit from public input in much the same manner as rules that undergo rulemaking. Moreover, the guidance would represent an official FDA view rather than perhaps only the whim of a small group of individuals within the agency. FDA also would initiate and revise guidance documents according to need, with the public having an opportunity to comment on that need.

FDA's adoption of these GGPs should not have the effect of reducing the amount of guidance that FDA issues. Over the last several years, industry representatives have asked FDA for more guidance in order to facilitate the product review process. While FDA has responded by increasing the quantity of guidance, FDA now needs to focus on the quality of that guidance. Voluminous poor-quality guidance does not advance anyone's interest, and is only a waste of time that can actually impede the regulatory process. We hope that FDA will be able to maintain or even increase the volume of guidance at the same time it initiates these quality control procedures. The ultimate shared goal of FDA and the public remains speeding up the approval process.

It is important to emphasize that FDA need not reinvent these GGPs. We are familiar with a number of voluntary organizations like the Association for the Advancement of Medical Instrumentation that have very effective procedures for standards development that FDA could borrow. I understand that Mr. Edward Kimmelman will expand on this subject.

It is also important to emphasize that our concerns do not extend to the level of one-on-one advice from an agency official to a particular company. FDA has shown a willingness to counsel individual companies on the agency's interpretation of the law, and that system seems to be working well particularly in the Center for Drug Evaluation and Research. Indeed, FDA's efforts in that area are greatly appreciated by the public.

IV. Monitoring

These solutions to the failure to use rulemaking and Good Guidance Practices will only work if FDA monitors the agency's compliance. To accomplish that monitoring, FDA should require that a central FDA office review and clear industry-wide letters, warning letters and other such broad communications that in the past have contained new regulatory requirements. The office should ensure that these communications do not announce new regulatory standards that should either undergo rulemaking or be developed through GGPs. As a related task, FDA's Office of General Counsel should conduct training programs for FDA personnel to sensitize them to when a particular requirement must

undergo notice and comment rulemaking or is subject to the GGPs. In this way, FDA could better ensure that new requirements benefit from the appropriate level of public input before the agency puts them into effect.

Conclusion

During this age in which the public is asking the Federal government to reinvent itself, we certainly subscribe to the philosophy that needless bureaucracy should be eliminated where ever it exists. The procedures advocated in our Citizens Petition obviously do not represent bureaucracy, but rather relatively simple, organizational steps designed to safeguard the public's involvement in the development of rules and guidance. GGPs could include such easy steps as the creation of an electronic bulletin board to track the development of guidance documents. Indeed, just as in manufacturing, systems to ensure quality can actually speed the process up by bringing order to the chaos. It is organization and quality that we desire.

Since this is certainly a subject worthy of considerable discussion, we hope FDA will choose to solicit public comment on the solutions that we propose, and consider those comments in designing systems to improve the quality of the guidance the agency provides. We appreciate the interest expressed by members of the subcommittees, and are grateful for the opportunity to present our views at this hearing. I would be happy to respond to any questions that you may have.

Summary Findings and Conclusions

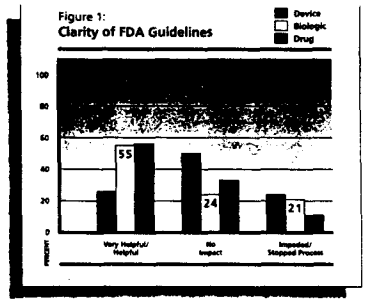
The data gathered in this survey are both extensive and varied, and not easily summarized. However, a good deal of the information does address four issues that are especially pertinent to the nature of the FDA-industry relationship: factors involved in delays of the approval process, communications between these parties, production and costs, and overseas activities. These areas are discussed below, together with the conclusions that emerge from the data.

Factors Delaying the Approval Process

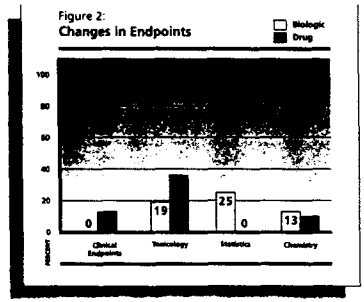
It is widely agreed that the FDA product approval process takes too long. Many indeed argue that this has a detrimental effect on human health by restricting the range of products available to physicians and their patients. There exists a formidable literature that seeks to explain why this is so and what could and/or should be done to remedy it. Nevertheless, it was believed that it would be useful in this survey if the companies themselves were asked to relate their experiences in the product approval process. Thus, the companies were requested to rate the effect of several factors on expediting the approval process. Among them were the following:

- FDA guidance on submission requirements
- Changes in endpoints
- Clarity and appropriateness of FDA requests for additional data
- Changes in personnel at the FDA
- Technical knowledge of the reviewer
- Quality of the companies' initial submission

FDA guidance on submission requirements. Although more than half of the biologic and drug companies rated the FDA's submission guidelines favorably, only a quarter of device companies agreed. The important point that emerges from these figures is that a significant number of companies of all kinds saw the guidelines as confusing or as hindering their submissions. Biologic and drug companies also indicated that about half the time the FDA's regulatory position changed during the approval process, and that these changes usually resulted in delays.

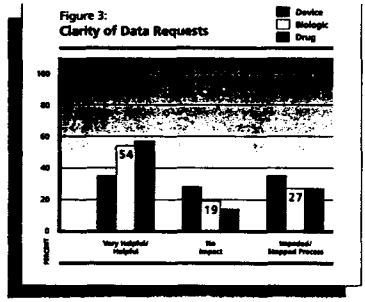


Changes in endpoints. Endpoints, the criteria that the FDA requires to judge the safety and efficacy of products, often change during product development and clinical trials. Biologic and drug companies reported that changes such as clinical endpoints, toxicology, statistics, and chemistry were frequently required by the FDA during the approval process.

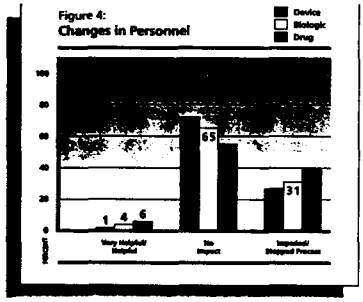


Of those companies for which changes in endpoints were required, in approximately one third of the cases the company believed that the communication of the changes by the FDA was not appropriate (either not timely, up front, or fairly communicated).

Clarity of FDA requests for additional data. The experiences of the companies with regard to demands for additional information, clinical trials, analyses, and the like were similar to those concerning FDA guidelines. An even larger proportion, one quarter of the biologic and drug companies and one third of the device firms, found these requests to be detrimental.



Changes in personnel at the FDA. With regard to personnel changes at the FDA, many companies found that such changes had essentially no impact (55-72%). However, such turnover seldom helped, and either impeded or stopped the process approximately one third of the time (27-39%).



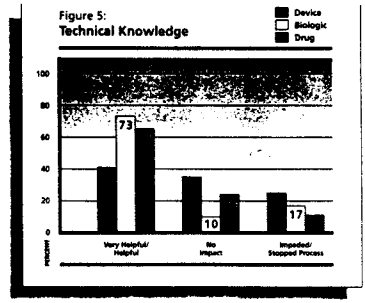
Technical knowledge of the reviewer. The expertise of the reviewers was judged to be an asset by a majority of the biologic and drug companies, but was somewhat less favorably viewed by device companies. A lack of technical knowledge by the FDA reviewer was believed to be detrimental to the review process in 11-25% of the cases.

On compliance inspections...

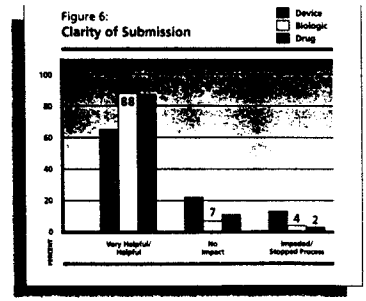
In addition to product review, a major responsibility of the FDA is to carry out periodic compliance inspections to ensure that companies are adhering to Good Laboratory Practices, Good Clinical Practices, and Good Manufacturing Practices. This issue was not a primary focus of the survey, but it was touched upon in a number of questions asking for the companies' experiences with these inspections.

Only device companies provided enough answers to these questions to make the data useful, and about two thirds had undergone these inspections. Three quarters of these companies felt that the training and knowledge of the inspectors who visited were poor or only fair (none were judged excellent), and only a third indicated that their inspectors' consistency with CDRH guidelines and policy was better than fair.

Half of the companies submitted comments concerning their experience with CDRH compliance. All were negative.



Quality of the companies' initial submission. Clearly, the companies have discovered that the quality (completeness and clarity) of their submissions to the FDA is of critical importance. The biologic and drug companies were especially aware of this, and only infrequently found the quality of their submissions to be a major problem, whereas device firms had more difficulty in this regard.



Another question, this one directed only at biologic and drug firms, asked about the value of computer-assisted submissions, CAPLAs for the biologics and CANDAs for the drugs. Although the number of responses to this question was small, about 75% were in favor of these tools.

Finally, in response to the question, "Can we streamline the FDA process for product approval without jeopardizing patient safety," over 99% of the companies said yes. This response might be seen by some as self-serving. Still, the virtual unanimity of the answers can be viewed as a clear indication that the life sciences industry believes that faster reviews are possible without patient safety being put at risk, and that the industry is very willing to work with Congress and the FDA to find ways to achieve this goal.

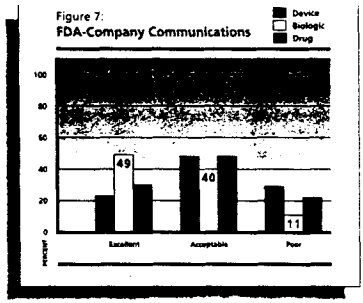
Conclusion: These data emphasize some steps that both the FDA and the life sciences companies can take to make the approval process faster and more efficient. On the part of the agency, improved written and oral guidelines at the outset and throughout the entire review process are vital. Similarly, the agency must take care to ensure that their requests for additional data also are clear, necessary, and timely. Needless to say, this is intimately related to the desirability for expert reviewers who remain with the product review process longer. On the part of the companies, clear, succinct, well-organized, and complete submissions are critical. Also, the companies must make serious efforts to determine what constitutes a good submission from the FDA's point of view and not just from their own. And, in the area of joint efforts, more and better computerization of submissions and data analysis is clearly desirable.

FDA-Industry Communications

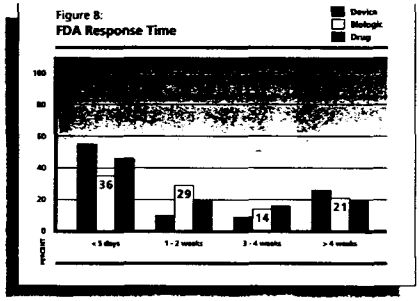
Effective communication is the key to understanding and progress. And so it is with the interactions between the FDA and the life sciences companies. Of all the factors that hinder and delay the product approval process, none is more detrimental than poor or confusing communications, and perhaps none is, or could be, more easily avoided. For this reason, a substantial number of the questions in the survey were designed to provide a comprehensive picture of the state of communications between life sciences companies and the FDA.

A very general question was asked at the outset: "How would you rate the quality of communications your company has had with the FDA with this submission?" The data indicate that only about one half of the biologic and roughly one quarter of the drug and device companies felt that their communications with the FDA were excellent.

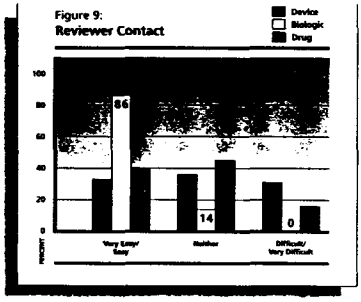
Figure 7:
FDA-Company Communications



Another question concerned the average response time for questions submitted by the companies to the FDA reviewer/CSO. Two points emerge. The most common experience for all three types of companies was a fast response, under five days. However, this bit of good news must be balanced against the bad: Roughly a quarter of the time it took one month or more to get a reply.



An important factor in industry-FDA communication is the degree of difficulty companies have in contacting their reviewer during the approval process. Here again, the experience of the companies appears to depend on the FDA center with which they are dealing. Most of the biologic companies reported that communications with the CBER were good, whereas only one third of the device and drug firms had comparable experiences with their review centers, CDRH and CDER, respectively.



Pertinent to this issue of ease of communication is the fact that, by far, telephone contact was most common (~75%), followed by letter. Faxes were used very little and E-mail not at all.

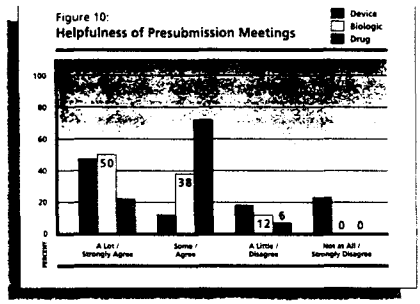
Finally, there is the matter of presubmission meetings. This process, when properly done, has a significant favorable impact on subsequent communications. This practice is not consistently applied as part of the approval process.

Of the biologic and drug companies that had these meetings, the great majority found them to be helpful, and none considered them a waste of time. In contrast, fewer device firms found these meetings helpful, and about 23% deemed them to be of no help.

On the approval queue...

The companies were asked to evaluate the usefulness of their ability to determine from the FDA their ranking in the queue.

About a third of the device companies indicated that the ability to do this was very useful, and some of the accompanying comments indicated that this information was often very useful in corporate planning. Nearly all the rest, however, stated that queue determination had little or no value. For example: "Position in queue can drop dramatically without explanation," "The information is useless; it provides only relative, not real, information on a submission's position in the queue," and "It is frustrating to sit #1 in the queue for over 3 months!"



Conclusion: These findings indicate that the quality of communication between the life sciences companies and the FDA depends very much upon the FDA center involved. On the whole, biologic firms were very satisfied with their contact with the CBER. In contrast, the device and drug companies appeared to have generally unfavorable experiences; only one quarter reported excellent communications. Regardless of the overall figures for each type of company, in too many instances communications were poor.

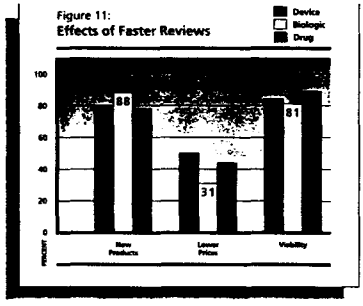
Production and Costs

Irrespective of how long the FDA product approval process takes, whether it is expeditious or delayed, one thing is certain: Each day costs life sciences companies money, and a lengthy process can be economically stressful or even fatal to companies with no product income and limited cash flow and equity. Such a loss of small companies, which are among the nation's most fertile sources of new ideas, could only have a detrimental impact on health care. Medicines and equipment that might prove extremely valuable to physicians and their patients could be lost.

The question in the survey asking the companies to estimate the percentage of total product development cost that could be attributed to the FDA produced relatively few answers. In all likelihood, such a question is difficult to answer with any certainty; current accounting procedures in small companies may not make such a distinction.

A more specific question did produce a large number of answers: "How would a reduction in product approval time impact your company's plans?" In particular, the question sought to determine whether such a reduction would (1) increase the number of products developed, and (2) reduce the price of products. About 80-90% of all companies indicated that faster review times would enable them to bring more products to market, become more competitive, and thereby provide more choices to physicians and their patients. One third to one half indicated that quicker reviews would reduce the price they would eventually charge for their products. The great majority of the companies also felt that faster approval would improve their viability in the U.S. market.

Figure 11:
Effects of Faster Reviews



On User Fees...

One of the newest developments in the FDA approval process is the imposition of user fees on the companies seeking product review, a practice long used in other countries. These fees, to be collected for each separate product submission, are to be used by the FDA to support the hiring of more staff and generally expedite the review process.

Such, at any rate, is the theory; by and large, the life sciences companies are skeptical. In answer to the survey question, "To what extent do you feel user fees will help reduce product approval time," only 4% indicated that it would help "A Lot." Most, over 70%, felt that the impact of such fees would be "A Little" or "None."

This was one of the few questions in the survey that invited written comments, and here the cynicism surfaces. Over half of the comments expressed no confidence that the fees would help. For example: "We fear that user fees will be offset by a reduction in other FDA support," "I do not believe that the FDA staff or turnaround time will be improved by fees," and "User Fees will have a short-lived effect and will be imposed primarily to placate Congress."

Conclusion: The life sciences companies and the health care professionals and patients they serve would stand to benefit in several ways if the FDA product review process were to become faster and more efficient. In particular, a streamlined approval process would, in each company's view, enable them to bring more products to the market.

Approval and Manufacturing Abroad

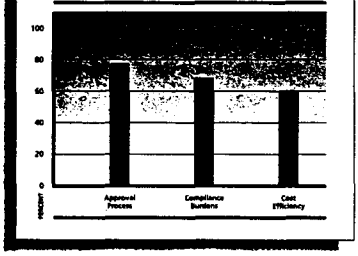
An argument often made in connection with the length of FDA product approvals is that U.S. companies are being encouraged, indeed forced, to seek product approval abroad in order to get their products on the market. Because of this, the claim continues, they are more likely to set up manufacturing abroad, with a concomitant loss of American jobs.

This issue is difficult to evaluate. To some extent and in some instances, it may certainly be true. However, life sciences companies are aware that they operate in a global economy, and, more importantly, that people in other nations also get sick and need medical services. Many companies plan to set up manufacturing offshore for strategic business reasons that have little or nothing to do with the FDA approval process. FDA requirements other than product approval, such as compliance and good manufacturing practices, may play a significant role in company plans to manufacture offshore.

Accordingly, the life sciences companies were queried about their plans for seeking approval and setting up production outside the U.S. for each of the product submissions they had made to the FDA. Whereas, all three types of companies said that they plan to sell some of their products abroad, for the most part this marketing would be based on export rather than overseas production. When asked where they plan to manufacture these products, in the U.S. only, abroad only, or both, a majority of companies indicated that they planned to produce the bulk of their products solely in the U.S., while one quarter planned to manufacture overseas.

Still, the fact that even a minority of companies plan to set up manufacturing abroad begs the question as to why. Thus, the companies were provided with reasons that might have influenced their decision to manufacture overseas. As shown, about three quarters of the companies indicated the regulatory approval process is generally faster in other countries than in the U.S. However, the cost efficiencies of producing closer to intended markets and reduced compliance burdens were also very significant factors.

Figure 12:
Decision to Manufacture Abroad



Conclusion: The evidence supports the notion that many U.S. life sciences companies are actively seeking product approval abroad. Some are planning to manufacture abroad because of the slowness of the FDA approval process and the FDA's compliance and exporting regulations. However, it is probable that many of these companies were planning to seek foreign approval in any case and that manufacturing decisions are influenced by many business considerations.

Mr. MCINTOSH. Thank you, Mr. Thompson. What I think we will do is hear from each of the witnesses and then open it up for questions.

Our next witness will be Mr. Larry Pilot, who is an attorney with McKenna & Cuneo and counsel to the Medical Device Manufacturers Association.

Welcome, Mr. Pilot.

Mr. PILOT. Thank you, Mr. Chairman.

On behalf of the Medical Device Manufacturers Association, which I will refer to as MDMA, I thank you for the opportunity to verbally summarize our interest in FDA's enforcement standards for medical devices and, in particular, the citizens' petition filed by the Indiana Medical Device Manufacturers Council. I have provided a prepared statement which I request be made part of the record of this hearing.

I believe every manufacturer of a device intends to comply with laws administered and enforced by FDA. Explicit provisions of the Federal Food, Drug, and Cosmetic Act make it quite clear what the expectations are for compliance and what the penalties are for violations of the act. The historical performance of the device industry, which is dominated by small and very creative manufacturers, supports a reputation of compliance.

Very few disputes about compliance result in litigation. However, there have been an increasing number of FDA enforcement activities during the last several years which would create for the public the false impression that the device industry is riddled with violators. I believe many of the FDA enforcement initiatives are not supportable in law and are the product of misunderstanding on the part of both industry and the FDA. Often, in my opinion, this is due to a "shoot first, ask questions later" attitude by the FDA.

The Indiana citizens' petition seeks to reduce the possibility of misunderstanding by emphasizing the importance of rulemaking to make clearly specific what is required for compliance. MDMA supports this initiative. Additionally, MDMA, as part of the National Medical Device Coalition, which represents approximately 700 manufacturers, has prepared a comprehensive blueprint for FDA reform.

Now, the concerns that we express to you today relate directly to FDA enforcement activities that begin with inspection in the field and often result in some type of enforcement implication. In my testimony, I refer specifically to activities relating to FDA inspections, warning letters, recalls, medical device reporting, good manufacturing practices, export certificates, and civil penalties. Each of these topics is laden with negative enforcement overtones which rarely relate to real or potential problems with the expected performance of a device.

For example, many warning letters charge violations for which there is little likelihood that FDA would prevail in litigation. Just prior to coming here today, I looked at the agency's history in this area, with reference to regulatory letters in 1984 and warning letters in 1994, as well as seizures and injunctions.

I won't go into that, but you will be surprised and impressed with the implication that is associated with the comments that I am making here; in particular, on the implications of warning let-

ters, which I believe are not a good indicator of either compliance or enforcement.

It is fair to assume that the public reaction to these communications, and I'm referring to warning letters and inspectional observations, is to conclude that the FDA is right, and the manufacturer is wrong. MDMA suggests that greater and more candid dialog between FDA and those who are inspected would stimulate a better understanding and respect for opinion differences as to what is compliance.

An atmosphere that encourages sharing, as opposed to a strident "FDA knows best" attitude, would clearly be more beneficial to the consumer than FDA threats. After all, the FDA is not in the business of manufacturing devices. This is what manufacturers do, and they do this superbly. The competitive marketplace demand for the highest quality device is a much greater incentive for manufacturer excellence than any subjective demand by government employees who do not have the daily responsibility to manufacture safe and effective devices.

If the FDA would revise current procedures to allow for greater due process as part of the enforcement process, the enforcement decisionmaking process, there would be much fewer but possibly better enforcement initiatives.

For example, before deciding whether to issue a warning letter or label a responsible activity on the part of a manufacturer as a recall, if the FDA would release less to the public and more to the affected manufacturer before announcing a decision, I believe the administrative record would contain the balance that is essential to responsible decisionmaking. If this is done fairly, I predict that compliance will remain at the highest possible level, and FDA enforcement activities will decline substantially.

Finally, it is essential to the proper conduct of the FDA that Congress implement the public expectation of responsible oversight. I believe that prior absence of conscientious and balanced oversight by Congress may have contributed to some of the current problems associated with FDA performance.

We are pleased with the interest of the subcommittees, appreciate the opportunity to be here today, and are anxious to cooperate with the subcommittees, the FDA, interested members of the public and the health profession to accomplish beneficial FDA reform. And I thank you.

[The prepared statement of Mr. Pilot follows:]

Testimony of:
Larry R. Pilot, Counsel
Medical Device Manufacturers Association
(MDMA)

I am Larry R. Pilot, a partner in the law firm of McKenna & Cuneo, L.L.P., and Counsel to the Medical Device Manufacturers Association (MDMA).

By way of introduction, I have been directly and intimately involved in issues relating to regulation of the medical device industry since 1970 when I was an employee of the Food and Drug Administration (FDA). From 1970 through June of 1979, I had responsibility for development and implementation of voluntary and mandatory programs relating to compliance with requirements of the Federal Food, Drug, and Cosmetic Act (the "Act") prior to and after the passage of the Medical Device Amendments of 1976. As the Associate Director for Compliance in the Bureau of Medical Devices, regulations relating to Good Manufacturing Practice, Administrative Detention, Registration and Listing, Hearing Aid Devices, and Banned Devices were among the activities for which I had responsibility. Likewise, I was responsible to assure compliance with, and enforcement of, the Act and regulations promulgated under the Act. As a result of that experience, I am familiar with the entire enforcement process -- from the initiation of an inspection/investigation through the litigation of disputes in federal court. Since 1979, much of my law practice has been devoted to counseling and, if necessary, litigating disputes to assure that clients comply with applicable provisions of law and are treated fairly by the FDA.

On behalf of the MDMA membership, I appreciate and thank you for the opportunity to present views on the subject of FDA enforcement activities. The MDMA represents approximately 100 manufacturers and distributors of medical devices. The majority of MDMA members are small and medium sized firms. Most of these firms are very small; 72% employ less than 50 employees. These companies are still under the management of the entrepreneurs who gave birth to innovative medical devices -- these same entrepreneurs are responsible for the subsequent growth and development of medical device companies that now support employment

of considerable numbers of people. Although this hearing focuses on a vital issue: FDA enforcement policies, it is imperative that the interests of smaller companies be represented in the ultimate goal -- comprehensive and fundamental reform of the FDA's Center for Devices and Radiological Health. All told this industry, which employs 270,000 people, boasts a $5 billion manufacturing export surplus; one of the few manufacturing sectors left in the U.S. recording such an accomplishment.

While all businesses are subject to various types of regulation by local, state, and federal governments, the medical device industry is subject to considerable pervasive regulation by the FDA. Under provisions of the Act, the determination regarding whether a device can be made available for domestic or foreign distribution is subject to considerable control by the FDA. Additionally, the determination regarding the availability of devices in commercial distribution from domestic or foreign sources to American consumers is also subject to considerable FDA administrative discretion. Finally, the very ability of domestic manufacturers to do business in the United States can be jeopardized by FDA enforcement initiatives - some of which are without foundation in law either through administrative or judicial due process.

I believe I speak for most medical device manufacturers as I compliment the members of the Subcommittee on Human Resources and Intergovernmental Relations and National Economic Growth, Natural Resources and Regulatory Affairs for conducting hearings on this very important issue. Often, the public assumes that regulatory agencies such as the FDA always function on our behalf correctly and lawfully. Unfortunately, this is not always true. As taxpayers, we expect that our investment to support the FDA and its enforcement efforts are comparable to the performance we expect of any business enterprise we elect to support through our personal financial investments. However, unlike an investment made in a public corporation, taxpayers have very little information to determine

the value of FDA enforcement activities. This is where the Congress has a major responsibility, and I am hopeful that hearings such as this will begin to probe FDA performance, identify valid questions, and obtain the answers which will determine the future course of FDA enforcement policy. If there are individuals at the FDA who have broken the law or have gone beyond their statutory limitations, they must be held accountable by Congress. This new Congress has changed the attitudes of many at the FDA but clearly more continued oversight is needed.

It is the understanding of the MDMA that these hearings were inspired in part by the May 2, 1995 Citizens Petition initiative submitted by Baker & Daniels and the Indiana Medical Device Manufacturers Council, Inc. This petition seeks to halt certain FDA practices and assure that the FDA applies notice and comment rulemaking to develop new rules. The MDMA supports this initiative and seeks to encourage every reasonable effort to assure that the FDA makes its compliance expectations known to the device industry with precision and clarity. As the FDA expectations are made known through lawful means, the MDMA expects that the FDA will maintain a level playing field that will reject arbitrarily selective enforcement initiatives.

I believe that nearly all medical device manufacturers are motivated to do good and avoid the possibility of participating in any harm to consumers using its devices. This motivation is both altruistic and legalistic. From the legal perspective there is the constant recognition that a successful plaintiff in products liability litigation can destroy a company. In addition, there is the further recognition that the FDA can seek judicially enforced civil and/or criminal penalties. These legal considerations are adequate to discourage those who are unscrupulous from becoming part of the medical device industry. On the rare occasions where violations of the law have occurred, those who are responsible deserve punishment without sympathy. Fortunately, the history of the medical device industry is

exemplary. Daily testimony of this fact is supported by the experience of millions of Americans using hundreds of thousands of devices manufactured by thousands of different manufacturers. Yet, there has been an effort over the last several years to disparage the efforts this industry; and, the FDA has been a major contributor to this disparagement through enforcement activities that are arbitrary, capricious, and abusive of discretionary authority. Most device manufacturers know their responsibility for compliance under provisions of the Act and applicable regulations. They are eager to obtain useful guidance and direction from the FDA. They want to comply, and they invest considerable resources to comply. However, this is very difficult, sometimes impossible, if the FDA obsession is directed toward enforcement.

Since passage of the "Safe Medical Devices Act of 1990," and the appointment of the current Commissioner, the level of FDA hostility toward the device industry has increased significantly and dramatically. Yet there is a paucity of credible evidence to support any claim of a public benefit derived from increased FDA enforcement initiatives. The very definition of enforcement is to compel obedience by threats and many FDA initiatives are guided by this attitude. Moreover, there is literally no due process attached to FDA inspired enforcement accomplishments. Generally these FDA proclaimed accomplishments are identified through the FDA release of information relating to Warning Letters, Recalls, Medical Device Reports (MDRs), and alleged Good Manufacturing Practice (GMP) regulation violations. Because many of the enforcement actions of the FDA begin with the initiation of an inspection by inspectors who are located throughout the 21 FDA District Offices, I offer an explanation of this process as well as some suggestions for the FDA and the subcommittees to consider. I will also use the same approach with regard to the FDA enforcement actions identified above and issues related to the recently abandoned "reference list" and the subject of civil penalties.

FDA Inspection

Under Section 704 of the Act, FDA inspectors have the authority to inspect device establishments at reasonable times, within reasonable limits and in a reasonable manner. Upon the completion of an inspection where objectionable conditions are observed, the FDA inspector will present inspectional observations on a Federal Form FDA 483. Management of the firm is provided with the opportunity to discuss these observations. If errors appear on the FDA 483, they generally will be corrected upon request.

The inspectional observations do not reflect actual violations of law. The determination of alleged violations is made by supervisory personnel in the District Office and/or personnel in FDA Headquarters. The observations of the FDA inspector and the discussions with management on the FDA 483 observations are generally incorporated into a document known as the Establishment Inspection Report (EIR). Whether the FDA decides to pursue an enforcement action is generally determined after review of any prior history of the medical device firm, the contents of the EIR, and any written response to the FDA 483.

Although FDA inspectors are instructed to avoid conveying their opinions or conclusions to firm management as part of the inspection process, it is not unusual that the FDA 483 is replete with statements reflecting personal opinions and conclusions. Irrespective of the quality of the oral or written response to the FDA 483 by the firm, the FDA may initiate an enforcement action on the basis of the EIR, the contents of which are unknown to the firm. While the FDA maintains that the EIR contains information supplied by and known to the firm, it has been my experience, and that of numerous manufacturers, that many times the content of the EIR was not correct. This incorrect information may have been the basis for

supporting the enforcement action. Clearly, access to the EIR may have prevented the need for an enforcement action if known by the firm and if the firm would have had the opportunity for further dialogue with the FDA.

Because the FDA 483 is disclosed to the public after presentation and the EIR is not disclosed until an enforcement action is initiated, I have three suggestions which I believe will encourage compliance through dialogue, reduce possibilities of misunderstanding, and provide due process that is fundamental to the American concept of fairness.

The first suggestion is to decline public release of the FDA 483 until after FDA decides whether enforcement action is indicated. Release of the FDA 483 serves no useful public purpose, because its contents are often misunderstood by the unsophisticated reader. The contents may be embarrassing to the inspected firm which is clearly placed on the defensive by public release of a document for which the contents may not support any violation of law.

The second suggestion is to provide the inspected firm with a copy of the EIR upon completion. This will enable the firm to analyze the contents and provide additional documentation to correct errors or misunderstandings conveyed in the EIR. Finally if indicated, the firm should have the opportunity to meet with District Office personnel to improve the likelihood of a mutual understanding.

If these three suggestions are accepted by the FDA, I believe useful dialogue between the parties will improve prospects for compliance and reduce the appearance of frivolous enforcement initiatives. There is no benefit to premature public exposure to FDA inspection results and no detriment to the FDA associated with disclosure of the EIR to management of the inspected firm. If valid enforcement action is necessary, neither

disclosure of the EIR to the firm nor non-disclosure to the public will deprive the FDA of the opportunity to seek administrative or judicial sanctions.

Warning Letters

Prior to 1991, if the results of the FDA inspection revealed objectionable conditions, the FDA would issue either a Notice of Adverse Finding (NAF) Letter or a Regulatory Letter. The NAF letter was issued at the discretion of the FDA District Director whereas the issuance of the Regulatory Letter was generally subject to the approval of FDA Headquarters. The reason for this approach was to limit issuance of a Regulatory Letter to those situations where the FDA had evidence to support judicially enforced seizure and/or injunction actions. The history of this approach indicates that these letters served their purpose. Few Regulatory Letters were issued and it was rare for a firm to receive a second Regulatory Letter. This respect for the Regulatory Letter was due to the fact that the FDA did indeed possess the evidence to support recommendations to the Justice Department for seizure or injunction.

In 1991, Commissioner David Kessler announced that the NAF and Regulatory Letter would be replaced by the Warning Letter and that the District Director could issue such letters without consulting with FDA Headquarters. The result of this change has been a disaster. Desirable uniformity has been lost because the decisionmaking is left to the discretion of 21 different District Directors. The number of Warning Letters issued has increased by orders of magnitude over the historical numbers associated with the Regulatory Letter. In my experience very few Warning Letters have been, or are being, issued with the strict criteria that were applied to Regulatory Letters. Yet, the transmission and public release of these Warning Letters causes great damage to the reputation of responsible firms and generates confusion among the public. In particular, for a small

company trying to raise capital, a Warning Letter can have catastrophic ramifications.

The ridiculousness of the Warning Letter is illustrated by the fact that some firms have received numerous Warning Letters in the course of a year with no subsequent enforcement action. The failure of the FDA to take subsequent enforcement action is either due to the fact that (1) there was no evidence to support an allegation of a violation; or (2) the mission of the FDA is simply to publicly embarrass the recipient of a Warning Letter. In either event, the Warning Letter serves no useful purpose for public benefit; and, the FDA should be directed to abandon this unwise expenditure of paper, postage, and resources.

Recalls

Since passage of the Safe Medical Devices Act of 1990, the FDA has had authority to order recall of devices. This procedure has been rarely applied, because most manufacturers will voluntarily recall a device if there is any reasonable possibility that harm could come to a user. Since at least the early 1970's, the FDA has applied procedures for device recalls where there is a nexus between a violation of the Act and correction by the manufacturer of a device either through labeling, field modification, or retrieval of the device. Clearly, if there has been a violation of the Act and the manufacturer is willing to implement a remedy, this process assures compliance without the need for costly application of enforcement resources.

The FDA publishes recalls on a weekly basis. The appearance of a manufacturer's is name in juxtaposition to announcement of a device recall is both embarrassing and costly. However, it is most unpleasant when the FDA announces a recall without the knowledge or participation of the manufacturer. The injury of this unilateral action becomes an insult when

there is no connection between the action taken by the manufacturer and any violation of law. This represents another area of enforcement activity for which candor between the FDA and the manufacturer before any public announcement would be beneficial and incorporate a concept of desirable fairness.

Medical Device Reporting (MDR) Regulation

Since 1984, the device industry has been subject to reporting requirements under the Medical Device Reporting (MDR) regulation. This regulation requires MDR submissions whenever the manufacturer receives information relating to death, serious injury or malfunction associated with any of its devices. Initial understanding of, and compliance with, this MDR regulation appeared to provide useful information to the FDA. However, aggressive and overly broad interpretations by FDA inspectors has prompted considerable confusion about this regulation. Many FDA 483s, Warning Letters, and other enforcement initiatives allege violations of this regulation. As a result the number of MDR submissions has increased substantially.

Many of these submissions are made because of a fear of retaliation by the FDA for alleged failure to submit the MDR. Many manufacturers are loath to exercise judgment decision making and simply submit all complaints to the FDA. Again, this attitude exists because of the fear that the manufacturer will be accused publicly of a violation for failure to submit the MDR. This fear is prompted by the possibility of FDA enforcement initiatives ranging from civil penalties to criminal prosecution.

Last year the FDA processed approximately 112,000 MDR submissions, and the year before it processed approximately 97,000 submissions. The FDA refers to these numbers with pride as accomplishments. Yet, there is no credible evidence to demonstrate that these 200,000 reports during this two

year period has produced any public health benefit. If the objective of this MDR exercise is to serve a useful purpose, then there should be evidence to demonstrate that direct correlation of this information has resulted in preventative measures that are related to human life or the quality of human life. This program consumes huge amounts of paper work and resources for government and the industry. The existence of these reports suggests an image of the device industry that is unwarranted. The enforcement implications can be illustrated through review of FDA 483s and Warning Letters, yet the bottom line benefit to public health protection has not been demonstrated.

The management of this program, in particular as delegated to FDA inspectors, represents another enforcement initiative that Congress should carefully examine. This is important if only to reduce paperwork.

Good Manufacturing Practice (GMP) Regulation

Since 1978, the device industry has been obligated to comply with the GMP regulation. The regulation itself has not changed since 1978, but the FDA interpretation has become increasingly subjective and questionably expansive. For example, FDA inspectors often cite in FDA 483 observations references to failure to validate. Many Warning Letters also accuse manufacturers of failure to validate and further accuse that these failures represent violations. The GMP regulation and its 1978 preamble provide no support for the requirement for validation.

The FDA did develop a guideline on "General Principles of Process Validation." This document clearly states that these are "principles and practices of general applicability that are not legal requirements." (Emphasis added.) Yet, FDA inspectors and officials often indiscriminately accuse manufacturers of violations for validation failures irrespective of the existence

of other GMP controls to assure the safety and effectiveness of the manufactured finished device as designed for its intended purpose. This reckless conduct by the FDA intimidates and disparages the efforts of responsible manufacturers. It also results in the expenditure of large sums of money to respond to FDA accusations or perform validation procedures of questionable benefit to the quality of the finished device.

The FDA has proposed a revision to the GMP regulation which identifies possible validation requirements. The statutory GMP Advisory Committee is meeting this week to receive testimony about this proposal and to make a recommendation to the FDA. The FDA must then decide whether to repropose the GMP regulation or to issue a final rule. Irrespective of the outcome of this process, Congress must appreciate that present interpretation by the FDA of the GMP regulation has created considerable anguish for a responsible device industry and there are very few adjudications supporting the position of the FDA. Finally, the present GMP regulation imposes a significant paperwork burden on manufacturers. This GMP regulation has approximately 40 requirements that require the creation and maintenance of documents. The proposed GMP regulation has more than 100 requirements for the creation and maintenance of documents. This represents another area of activity for which Congress needs to evaluate and ponder the benefit to the public.

Reference List and Export Certificates

For several years, the FDA maintained a secret "Reference List." Generally those who received a Warning Letter were placed on this list and subsequently denied the opportunity for required or optional FDA reviews of manufacturer requests. Some manufacturers who did not receive a Warning Letter were also placed on the "Reference List" and denied these

opportunities which related to premarket notifications, premarket approvals, and export requests. Most often, the reason for placement on the list was due to questionable observations about GMP conditions for which, as described previously, there is no due process opportunity for resolution of disputes.

Earlier this year the National Performance Review under the direction of Vice President Al Gore announced that this sanction, for which there was no congressionally authorized mandate, would be discontinued. This was a responsible initiative by the Administration and welcome news to the industry. Yet elements of this unfortunate approach, which borders on unlawful taking, remain in effect to the detriment of domestic manufacturers. This is particularly true for domestic manufacturers who have devices in lawful commercial distribution in the U.S., and who seek from the FDA an acknowledgment of this fact.

For several years the FDA has managed a voluntary program where it responds to manufacturer requests for "Export Certificates." These certificates are often requested by foreign distributors or governments to demonstrate that U.S. manufacturers are lawfully engaged in the manufacture of devices within the U.S. Many of the countries to which domestic manufactured devices are exported do not have government sanctioned regulatory controls. Under the FDA "Reference List" program, any manufacturer who received a Warning Letter or was otherwise identified on the list was not eligible to receive an Export Certificate. This denial was maintained even though the manufactured devices were available for domestic commercial distribution or for unrestricted export to foreign countries. Although the FDA abandoned the Reference List, it continues to implement its refusal to acknowledge that domestic manufacturers are

lawfully manufacturing devices within the U.S. for domestic and foreign distribution.

This punitive enforcement sanction is not authorized by Congress and simply does not make sense. Continued operation of this Export Certificate program is harmful to U.S. manufacturers, because FDA participates in the establishment and maintenance of trade barriers by foreign governments. For example, if a particular foreign government asks the manufacturer for an Export Certificate and there has been a Warning Letter issued, the FDA refuses to issue an Export Certificate. As a result, the foreign government denies entry of the U.S. manufactured device because of failure to produce the FDA Export Certificate. Yet, the devices for which the FDA has denied the Export Certificate are manufactured within the U.S. for domestic and international distribution without restriction. Other than issuing a Warning Letter, the FDA rarely seeks to lawfully detain devices or pursue court ordered seizure or injunctive relief to prevent distribution of the devices manufactured in the U.S. What is the rationale for such behavior by the FDA? Does this make sense? FDA denial of the Export Certificate under a program that has been developed by the FDA without Congressional approval is creating considerable harm to countless domestic manufacturers seeking to lawfully export devices to foreign purchasers.

This program and conduct by the FDA must be abandoned, because it clearly illustrates government action that is arbitrary, capricious, and abusive of discretionary authority. More importantly, it deprives international consumers of the public health benefits of U.S. technology.

Civil Penalties

The 1990 Safe Medical Device Act (SMDA) authorizes the Secretary of Health and Human Services (HHS) to impose civil penalties of up to $1 million

through an administrative process, the result of which may be appealed in federal court. It is regrettable that the device industry was saddled with this particular burden when the reason for this initiative related to abuses within the generic drug industry.

The FDA recently finalized procedural regulations to implement this authority. The MDMA objected to FDA management of this program, because the FDA has sole responsibility to function as investigator, prosecutor, judge, and jury with regard to application of this enforcement penalty. Rights that are afforded under the Federal Rules of Civil Procedures are absent and the accused is subject to total control by the prosecuting agency, namely the FDA.

The MDMA previously objected to FDA application of this enforcement sanction, because the HHS Secretary did not delegate the authority to FDA. The FDA and the HHS Secretary ignored this plea. The MDMA believes a more appropriate and fair application of this enforcement sanction would be to have the Secretary function as the decision maker after the FDA, as prosecutor, has provided its best evidence to the HHS Secretary. Under this approach, the Office of the HHS Secretary would function much like a federal grand jury to assure the foundation for probable cause and the court to supervise an impartial method of adjudication.

The MDMA, as part of the National Medical Device Coalition (NMDC) consisting of 10 trade associations representing approximately 700 device manufacturers, has proposed a revision to this process as part of its "Blue Print for FDA Reform." We hope that Congress as part of its oversight interest in FDA enforcement activities will carefully review and evaluate this subject, and support this NMDC position.

Summary

The MDMA is pleased to have had the opportunity to express its views about FDA enforcement activities. We believe in and support all reasonable efforts to assure compliance with provisions of law that are clearly understood. The hostility between the FDA and regulated industry that developed during the 1990s has not produced identifiable benefits to the American public. The medical device industry is proud of the contributions it has made to public health. Many of these contributions, through existence of 1,800 types of FDA classified devices, occurred before the 1976 Medical Device Amendments. Clearly the benefits of such devices as heart valves, orthopedic implants, and intra-ocular lenses, to mention a few, outweigh any detriment to consumers and health care practitioners.

The enforcement initiatives and attitudes inspired by the present FDA Commissioner must be radically altered; because, the device industry, consisting of approximately 270,000 employees, is dedicated to being the best. This attitude is essential to assure continued success and dynamic growth of an industry whose innovators, managers, and employees are confident about the quality of devices they manufacture to the extent that they are comfortable about the use of these devices both on themselves and by those that they love.

With the help and assistance of Congress, we trust that the FDA will adjust its attitude. The MDMA welcomes the opportunity to participate with the Congress and the FDA in this shift of priority from enforcement to advancement.

Mr. MCINTOSH. Thank you very much, Mr. Pilot.

Our next witness is Edward Kimmelman, who is an expert in this area, with Boehringer Mannheim Corp., located in Indianapolis.

I also want to thank you, Mr. Kimmelman, for the format you used for your testimony. When I was reading it last night, the little summaries off to the left are very helpful in looking at which paragraphs I need to pay close attention to. Thank you.

Mr. KIMMELMAN. I will bring that message back to the people who are pushing that format in my company.

Thanks for asking me to testify.

My company, BMC, is a large manufacturer of in vitro diagnostic products. They are often called "IVDs," and I will refer to them that way. My comments, however, reflect the experience and views of IVD manufacturers, both large and small.

I personally have been involved in medical device regulatory affairs since the mid-1970's, when FDA first got into the business, in earnest, of regulated medical devices. Briefly, in vitro diagnostics are products used to test body fluids and tissues that are removed from the human body for testing. I will focus on the effect of informal guidelines on the premarket clearance of IVDs.

The Division of Clinical Laboratory Devices, DCLD, is the FDA division that is responsible for premarket review of IVDs. While I am here to testify in support of the petition, I do want to make the point that BMC and its people have worked constructively with the FDA on many issues, and they appreciate the professionalism and good intent of the agency personnel. We recognize the theoretical benefits that informal guidance documents can bring to the premarket review process. Unfortunately, to date, we have experienced the opposite result.

This is what we have observed: It is my belief that IVD products are overregulated, due in part to the use of informal FDA policy and guidance documents. This overregulation subjects these products to a level of premarket review that is inconsistent with the risk associated with their use and is out of line with the level of review these products get in other parts of the world.

FDA's inflexible application of informal guidance documents also leads to overregulation. The uncertainties related to informal guidances have increased review times and costs, because they increase the number of review iterations and may result in costly reruns of product evaluations and recalculation of evaluation results.

The uncertainty introduced by informal guidelines and policies has the added effect of delaying access to new IVD technologies here in the United States. U.S. patients get the benefit of these technologies months and even years after patients in Europe and other parts of the world.

Let me give you two illustrative examples: First, one that affects the IVD industry, in general. Triage is useful to guide the application of limited resources to high priority areas. As announced by the FDA, triage, as they were going to use it, to determine the intensity of premarket review, was to be based on risk to patients, with the devices categorized into tiers of increasing risk.

In the late 1970's and early 1980's, FDA, in its advisory panels, went through an exhaustive—and exhausting, I might add—proc-

ess of product classification, mandated by Congress. This classification process also was based, in great measure, on risk to patients. Triage, as employed by FDA, is essentially an informal classification system that I believe is duplicative of the legislatively mandated classification process.

From a practical point of view, for most medical devices, the triage process yielded results that were consistent with product classifications. Unfortunately, DCLD apparently did not use the triage method as it was intended to be used, resulting in low-risk IVDs being subjected to a level of premarket review that should be reserved for moderate-risk devices, in effect, up-classifying them without the benefit of notice and comment.

Another major effect of DCLD's approach is to disqualify from exemption many IVDs that truly deserve to be exempted from the 510(k) submission requirement. In recent months, after much prodding from industry, DCLD has agreed to consider an industry-developed triage approach based primarily on risk. We are encouraged by this.

Among the many product-specific examples let me choose one. Several years ago, FDA developed a guidance document for 510(k)'s related to cholesterol measurement systems. In January 1995, buried deep within some handout material FDA offered to attendees at a video conference, related to IVD products, was a draft revision of this guidance.

This document significantly changed the premarket submission requirements, including a new performance standard for these products. There was no public announcement of its availability. Several weeks after the video conference, as a test, one of my regulatory affairs specialists requested a copy of the latest FDA guidance document on cholesterol. We received the old version of the guidance document.

During the summer of 1995, FDA unveiled yet another revision of this guidance document at the AACC meeting, again with no public notice and no opportunity for input from industry or the practicing laboratory professional community.

I offer three suggestions to address our concerns: One, as I mentioned earlier, FDA has begun to work more directly with industry on ways to lighten the review load and speed the premarket review process. These efforts are beginning to bear fruit and should be encouraged.

Two, FDA should implement a quality system for the initiation, development, implementation, and revision of guidelines. FDA should consider working within the consensus mechanisms currently available in standards organizations like NCCLS and AAMI. FDA representatives have, for many years, worked successfully within these organizations. While the consensus process generally moves slowly, it can be accelerated to accommodate FDA's need for reasonable turnaround of specially needed guidances.

Three, already cleared 510(k)'s will provide guidance as to FDA's current submission requirements. Unfortunately, it takes about 18 to 24 months to obtain sanitized copies of cleared 510(k)'s through Freedom of Information. Much of the present delay is due to the process used in removing confidential proprietary information.

Working with industry, I believe the FDA could develop a means to shorten the Freedom of Information turnaround time.

In closing, I reiterate that I support the citizens' petition and see it as a way to assure against the imposition of overly stringent premarket review requirements which, one, delay the introduction of new and beneficial IVD technology and, two, raise the cost of processing premarket submissions, without a commensurate benefit in improved safety and effectiveness of IVDs.

We appreciate any opportunity to work with FDA. And speaking for my company, we have demonstrated our willingness to work hard and constructively to achieve practical premarket review of IVDs. The solutions I propose for IVDs can all be effected without the need for new legislation. They can be accomplished with prudent action by FDA; hopefully, with effective input of industry.

We encourage Congress to continue the oversight efforts of subcommittees like your own. Thank you very much.

[The prepared statement of Mr. Kimmelman follows:]

Testimony - Edward R. Kimmelman

House Committee on Government Reform and Oversight

Subcommittees on National Economic Growth, Natural Resources and Regulatory Affairs

and

Human Resources & Intergovernmental Affairs

Thursday, Sept. 14, 1995

Introduction

Who I am; who I represent

Thank you for inviting me to testify this afternoon. I am encouraged by the subcommittees' interest in the Indiana Medical Device Manufacturers Council citizens petition and the problems illustrated within it.

My name is Ed Kimmelman. I am Vice President for Regulatory Affairs and Compliance for the Boehringer Mannheim Corp, located in Indianapolis. The major portion of my work and that of my group involves the development and prosecution of premarket submissions to the FDA.

Boehringer Mannheim, or BMC, provides a broad range of in vitro diagnostic (IVD) systems, ranging from large and highly sophisticated instrument-reagent systems for the hospital laboratory to "easy to use" home use glucose monitors for diabetes management. We also provide products for smaller laboratories, including the physician office lab.

Background

Viewpoint of my testimony

My testimony will represent the position of my company, those of my colleagues from other IVD companies with whom I have spoken, and IVD companies who are members of a number of trade associations that represent small, entrepreneurial IVD companies.

My examples and detailed information will be from the IVD industry; a number of them from the direct experience of BMC. They will focus on that aspect of FDA regulatory compliance related to premarket clearance of IVDs. The Division of Clinical Laboratory Devices (DCLD) is the FDA division that is responsible for premarket review of IVDs.

The FDA enforcement effect of informal guidances related to other regulations (e.g., those related to medical device reporting and GMP compliance) is the same for IVDs as for other types of medical devices. These will be covered by other members of the panel.

What are in vitro diagnostic products

Briefly, in vitro diagnostics are products used to test body fluids and tissues that have been removed for testing from the human body. In the vast majority of situations, the test results are used in conjunction with patient history and physical examination to assist medical professionals in diagnosing the state of a patient's health and in treating the patient. In a very few situations test results may be the sole determinant of medical treatment.

A number of IVDs are used to "type" blood that is intended for transfusion and to test it for the presence of infectious agents like HIV and hepatitis.

There is a very broad spectrum of IVDs. Some involve the use of sophisticated laboratory equipment intended to perform many different tests in a high throughput, economical way. Some, intended for smaller laboratories, use equipment designed for operation by less sophisticated personnel in a low throughput environment. Also, there are IVD's, which may or may not use equipment, for home testing.

Key points of my testimony

We support the citizens petition

My company and small IVD companies that are members of a number of national and regional trade associations support the IMDMC citizens petition.

We recognize the theoretical benefits that informal guidance documents can bring to the premarket review process. Such documents, if well developed, using input from the affected constituencies, and if issued in a controlled manner, have the potential to speed premarket reviews and ultimately reduce the costs associated with premarket clearance of new medical devices.

Unfortunately, to date, we have experienced the opposite results.

Detrimental effects of informal guidances on the premarket clearance of IVDs

It is my belief that IVD products are over-regulated due in part to the use of informal FDA policy and guidance documents. This over-regulation subjects these products to a level of premarket review that is inconsistent with the risk associated with their use and is out of line with the level of review these products get in other parts of the world.

Later in this testimony, I will discuss the FDA use of "triage" to align the intensity of review with the risk associated with a medical device. Triage was announced approximately two years ago as one of a number of FDA management policies intended to speed review of 510(k) premarket submissions. Triage as applied to IVDs resulted in lengthy and costly premarket reviews that are clearly out of line with the risk involved in the use of many of these products.

FDA's inflexible application of guidance documents, rather than tailoring the application to the nature of the new technology and the risk to patients is another example of how informal guidances lead to over-regulation.

The uncertainty related to informal guidances has increased review times and costs. The uncertainty is due to the informal manner in which these guidances are announced and the failure to obtain input from IVD manufacturers and others affected by the guidances before they are announced. The uncertainty lengthens the review times because it increases the number of review iterations and may result in costly reruns of internal and external product evaluations and recalculation of evaluation results.

The uncertainty introduced by informal guidances and policies has the added effect of delaying access to new IVD technologies here in the U.S. U.S. patients get the benefits of these technologies months or even years after patients in Europe and other parts of the world.

Continued on next page

Key points ... , Continued

FDA / DCLD is beginning to work with industry

If this hearing had been held as recently as one year ago, I would have coupled my current testimony with serious concerns about the apparent arrogance of FDA's regulatory attitude related to premarket submissions. There were many examples at the policy and individual issue levels of a philosophy that argued against FDA working with the medical device industry to work on these concerns.

For what ever reason, be it the make up of the new Congress, the Administration efforts to re-invent government, or an appreciation by FDA management that old approaches weren't working, FDA has recently been reaching out to industry. We appreciate this opportunity to work with FDA, and speaking for my company, we have demonstrated our willingness to work hard and constructively to achieve practical premarket review of IVDs. Our goal is to have a premarket review process that gets new IVD technology to U.S. healthcare providers in a time frame consistent with that of the rest of the world, while assuring the review is consistent with the potential risk presented by these products.

We encourage Congress through the efforts of subcommittees like your own to keep FDA in the mode of cooperative regulation.

Triage

A basically good management tool

The FDA Triage management initiative is useful to guide the application of the agency's limited resources to high priority areas. As announced by the FDA, "triage" was to be based on risk to patients, with the devices categorized into tiers; Tier 1 being the lowest risk; Tiers 2 and 3 containing devices with higher risks. The stated intention was to have **Tier 1** devices be subject simply to a review of labeling **by a single reviewer**; **Tier 2** devices subject to a review of safety, effectiveness data and labeling **by a single reviewer** ; **Tier 3** subject to a **team review** of safety, effectiveness data and labeling. The team involved in a Tier 3 review could consist of FDA medical officers, biostatisticians, other FDA technical experts, and outside consultants, including members of appropriate FDA advisory committees.

Continued on next page

Triage, Continued

Triage is duplicative of the medical device classification process

In the late 1970s and early 1980s, FDA and its advisory committees went through an exhausting process of product classification mandated by Congress in the Medical Device Amendments of 1976. The classification process was based on risk to patients, with Class I containing the lowest risk devices and Class II and II containing devices of increasing risk. Also, classification was intended to determine the level of premarket review the product would receive. Class I and II devices would be subjected to 510(k) substantial equivalency review; Class III devices subjected to premarket approval, a significantly more intense and comprehensive review.

One might argue that "triage" is essentially an informal classification system that is duplicative of the legislative classification process. Certainly it appears that policy decisions made on the basis of triage could just as easily have been made on the basis of classification. If so, it raises a real question as to whether "triage" represents an end run around the requirement to develop classification through regulation.

From a practical point of view, for most medical devices, the triage process yielded results that were consistent with the product classifications .

Use for IVDs inappropriate

Unfortunately, DCLD apparently did not use the "triage" method as it was intended to be used. On the premise that the FDA labeling and 510(k) submission regulations required the inclusion of product performance data, DCLD decided that almost all 510(k)s would require at least a Tier 2 review. **This premise shifted many products which the advisory committee placed in Class I (low risk) into the Tier 2 (moderate risk) category, thereby, in a way, "up-classifying' them without going through the process of developing regulations.**

Result of DCLD "triage"

On the following page I have developed a table which compares the distribution of device classification decisions to the "triage" decisions for devices reviewed by each of the FDA's device evaluation divisions.

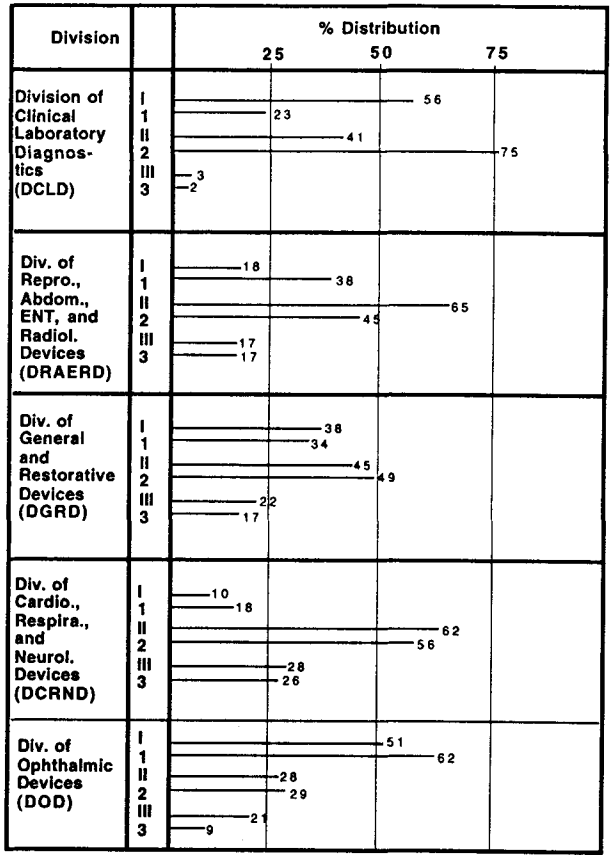
The table shows that "triage" resulted in a logical consistency between the device classification and the tiering level for all divisions except DCLD. In DCLD, while device classification panels placed 56% of all IVDs into Class I, the tiering process placed only 23% in the lowest risk category. Instead, triage resulted in lumping most Class I's in with Class II devices as Tier 2 reviews.

Triage, Continued

Result of DCLD "triage"

Fig. 1

% Comparisons among FDA Device Evaluation Divisions



Continued on next page

Triage, Continued

Effect of IVD triage was over-regulation

The effect of DCLD's apparent misuse of the informally constructed "triage" management tool resulted in low risk IVDs being subjected to a level of premarket review that should be reserved for moderate risk devices.

FDA is currently engaged in a process of exempting Tier 1 medical devices from 510(k) premarket submission requirements in an effort to lighten its review load. Another effect of DCLD's approach to "triage" is to eliminate many IVDs that truly deserve this exemption for consideration for exemption.

This result is inconsistent with the regulatory strategy for IVDs that is being developed in Europe, for example, and creates a situation where more and more IVDs are being developed in Europe, where these products are available to patients in Europe months and even years before they are available in the U.S.

The European regulatory approach

In Europe, the intention is to regulate IVDs with a relatively light touch, commensurate with the premise that most of these products do not constitute a risk of harm to patients. Those IVDs that do present a risk are specifically designated and are subject to higher levels of premarket review.

In September, 1991, in its working document describing the basis for developing an IVD Directive (European Community legislation describing the essential requirements for IVDs), the European Commission (the E.C. administrative body) said, "Contrary to other medical devices, IVDs do not generally present a direct risk of vulnerability to patients as they are, for the most part, intended for professional use."

As a result, the vast majority of IVDs are regulated by a system which requires that manufacturers "self-certify" that their products meet the essential requirements spelled out in the IVD Directive. A small group of IVDs, those used for blood typing, those used for the detection of HIV, Hepatitis B and Hepatitis C, and those used for self-testing (e.g., glucose monitors) are subject to premarket review and testing.

Current situation

In recent months, after much prodding from industry representatives, DCLD has agreed to consider an industry developed "triage" approach based primarily on risk to patients. A group of fifteen manufacturers conducted a pilot study of this approach with 150 IVDs and determined that the tiering results compared much more closely to the classification distribution for IVDs and to the approach being taken in Europe. The tiering distribution achieved in the industry pilot study compared to DCLD tiering for the same products is shown in the Fig 2.

We are encouraged by the opportunity to work with DCLD in the coming months, and will keep you informed of progress on this matter.

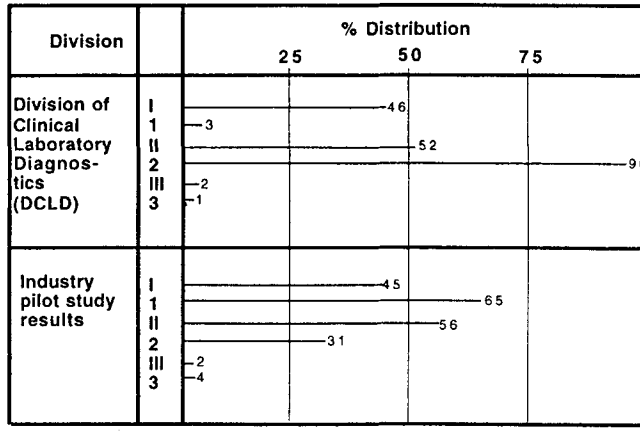
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Triage, Continued

Comparison of DCLD and industry pilot study

Fig. 2

% Comparisons between DCLD and industry pilot study



Poor communication of informal guidances

"... box of chocolates"

Because of poor communication by FDA during the development and implementation of informal guidances, the premarket review process for new IVDs has become a lot like dealing with Forrest Gump's box of chocolates, ... "You never know whatcha gonna git."

For the most part FDA treats the guidances as temporary documents, forever destined to be kept in "draft" status.

If the intent of the documents is to alert manufacturers to the premarket submission requirements, in general, and for specific products, keeping these documents in a constant state of flux does little good. If the intent is to provide submittors with sufficient guidance to assure that submissions are complete enough when submitted to allow for approval within the statutory guideline 90 days, they have been a dismal failure, ... even though FDA, with a bit of creative accounting, will tell you that the 90 day time periods are being met.

Continued on next page

Poor communication ... , Continued

Glucose monitor guidances

A number of years ago, FDA developed a guidance document for 510(k) submissions related to home use glucose monitors. This document formed the basis for submissions made by my company, supplemented by our own experience in filing 510(k)s for these products over the years.

The reality of the situation was that even though each new submission was patterned after the previous "cleared" submission, it was never complete enough to satisfy the "then current" review requirements. FDA requests for additional information during this period of time, coupled with the difficulty in communicating directly with reviewers, created an almost untenable situation that severely delayed the clearance of these devices. While, now, it is much easier to talk directly with reviewers due to a change in FDA communications policy, the stability of the guidance is still poor.

And to this day, if a manufacturer requests a copy of FDA guidance for glucose monitors, the FDA will forward a copy of a very "old" guidance document.

We hear there is work underway on a new guidance document, but even that information is not clear in regard to when that document will be available.

Cholesterol guidance document

Several years ago, FDA developed a guidance document for 510(k)s related to cholesterol measurement systems. In the intervening years, much publicity was given to the maintenance of reasonable cholesterol levels as a means to reduce the risk of heart disease. As a result, cholesterol testing became more prevalent, and there was much effort to "improve" the precision and accuracy of such testing.

In January of 1995, buried deep within some handout material FDA offered to attendees at a video conference related to IVD products, was a draft revision of the cholesterol guidance document. This document significantly changed the premarket submission requirements for cholesterol 510(k) submissions. There was no public announcement of its availability. Those companies preparing 510(k) submissions for cholesterol testing products, who didn't happen to "catch" the new guidance document, would have found out about it only after FDA's initial response to their submission. Such a submission could have been refused by FDA as incomplete, causing significant delay in its clearance by the agency.

Several weeks after the video conference, as a test, one of my regulatory affairs specialists requested a copy of the latest FDA guidance document on cholesterol. The FDA Division of Small Manufacturer Assistance (DSMA) Flash Fax system provided us with the "old" version of the guidance document.

Continued on next page

Poor communication ... , Continued

Cholesterol guidance

During the summer of '95, FDA unveiled yet another revision of the guidance document at the AACC meeting, again with no public notice, and no real opportunity for input from industry or the practicing laboratory professional community. Only those manufacturers who happened to participate in the FDA cholesterol workshop or stop by the FDA booth at the meeting would have been aware of the "new" revision.

"Points to consider - collection of data ..." document

The IMDMC citizens petition describes the situation related to FDA's informal development and announcement of the "Draft Points to Consider (PTC) for Collection of Data in Support of In-Vitro Device Submissions for 510(k) Clearance (September, 1994)

Possible answers

Work directly with industry

As I mentioned earlier, FDA has begun to work more directly with industry on ways to lighten the review load and speed the premarket review process. These efforts are beginning to bear fruit and should be encouraged.

Improve processes/Work through consensus organizations

FDA should implement a "quality system" for the initiation, development, and implementation of guidance documents. For models for such a system and when trying to clarify regulatory requirements for specific product groups, FDA should consider working through the consensus mechanisms currently available in standards organizations like the National Committee for Clinical Laboratory Standards (NCCLS) and the Association for the Advancement of Medical Instrumentation (AAMI). FDA representatives have for many years worked successfully within these organizations to develop voluntary consensus standards.

While the consensus process generally moves slowly, it can be accelerated to accommodate FDA's need for reasonable turnaround of especially needed guidances.

Continued on next page

Possible answers, Continued

Quicker public availability of "cleared" 510(k)s

Already "cleared" 510(k)s would also provide guidance as to FDA's current submission requirements. Subsequent submittors could learn by example how to avoid many problems that delay satisfactory processing of 510(k)s. But presently it takes almost a year to obtain "sanitized" copies of "cleared" 510(k)s through Freedom of Information. Legislation allows for the public distribution by FDA of non-proprietary information related to the safety and effectiveness of devices that are the subject of 510(k) submission.

Much of the present delay is due to the process used in removing confidential, proprietary information from the submission. Working with industry, I believe the FDA could develop a means to shorten the Freedom of Information turnaround time.

In closing

Summary of the impact of informal guidances

In closing, I reiterate that I support the IMDMC citizens petition. If FDA adopts the IMDMC's recommendations I believe it will ensure high quality guidance documents that meet the agency's goals of increasing consistency among reviewers and improving communications with industry. I also see it as a way to assure against the imposition of overly stringent premarket review requirements which:

- delay the introduction of new and beneficial IVD technology, and
- raise the cost of developing and processing premarket submissions without a commensurate benefit in improved safety and effective of IVDs.

Keep up the congressional interest

I believe in the effectiveness of Congressional oversight. I believe FDA's efforts to shorten premarket submission review times and to make their enforcement efforts more consistent and fair are a direct response to Congressional concerns.

I believe appropriate FDA use of informal guidances can result from Congressional support and action consistent with that outlined in the IMDMC citizens petition and continued Congressional oversight of FDA's use of such guidances.

Thank you

Again, I thank you for the opportunity to testify.

Mr. MCINTOSH. Thank you very much, Mr. Kimmelman. I appreciate that testimony and your coming here today.

Our next witness on this combined panel is Mr. David Murray. Mr. Murray and I were colleagues when I was at the Hudson Institute. He was laying the groundwork for the study that he is going to be describing to us today.

I must say that I was delighted to see the end product of the efforts that you had talked about back then. I think it will make a valuable contribution to an issue that has not gained much attention in this whole area, on what are the downside costs, in terms of safety and health effects of a regulatory review process.

Mr. Murray.

Mr. MURRAY. Thank you, Chairman McIntosh. First, let me begin by thanking you for inviting me to testify here today and also to thank Chairman Shays.

The testimony that I am delivering today is the result of research I have carried out as a member of the research staff of the Competitiveness Center of Hudson Institute in Indianapolis. I alone, however, am responsible for the views I express, and they should not be ascribed to Hudson Institute.

Medical technology has advanced at an incredible pace during the last 50 years. Physicians and scientists have harvested the fruits of explosive growth in electronics and the material sciences by applying revolutionary advancements in these technologies to medical science. These developments have fed upon one another, creating an environment of synergy and rapid innovation.

American consumers have been the ultimate beneficiaries of these technological breakthroughs. Treatments that we take for granted today, such as kidney dialysis, did not exist only a short time ago. Such advancements have benefited literally millions of Americans during the past decades and generated confidence that millions more will live longer and healthier lives in the decades ahead.

Although American physicians and scientists have developed most of these innovations in America, American consumers are no longer the first to benefit from these often lifesaving and life-enhancing products. All too frequently, Europe, Japan, and Canada approve new medical devices for use years before the Food and Drug Administration approves them for use in the United States.

The delay in introducing these new technologies in America has undeniable and serious consequences for American consumers, consequences that can be quantified in losses in the quality of life, and sometimes even of life itself, for thousands of Americans each year.

Proponents of the FDA system argue that these delays are the inescapable price of a system that ensures safety, but, really, very little evidence supports this view. The FDA has approved almost all the medical devices that have encountered serious postmarket difficulties worldwide.

The evidence that our paper presents indicates that, in certain instances, the FDA approval system is actually costing lives. Debates over the safety and efficacy of medical technology often obscure this basic, yet vital, fact. Rather, the public and the press have been well-sensitized to the dangers of premature approval of a medical device or drug.

Although premature approval is certainly a risk, minimizing this risk comes at the high cost of maximizing another risk, that of delaying the entry of safe and effective new technologies, with attendant loss of human lives. Conversely, the absence of all regulation would minimize the risk of delaying the availability of new technologies but would maximize the risk of allowing unsafe or ineffective products to reach the market.

Clearly, neither of these extremes is desirable as public policy. The risks of one must be balanced against the risks of the other to find a middle ground. To date, however, warnings about the risks of delayed availability of medical technologies have fallen on deaf ears.

Our study examined the regulatory histories of four lifesaving, high-tech medical devices that were approved in Europe before they were approved in the United States. Because each of these devices offered a substantial improvement in the quality of health care for the conditions that they were intended to treat, delays in their approval generated significant human cost. In other words, American consumers could have benefited from these devices earlier had the regulatory approval process been more efficient.

Let us take the example of the wire leads that are used to connect an implantable defibrillator to the heart. A physician can use either epicardial or endocardial, which are transvenous leads, to attach defibrillators to the heart. The clinical evidence in favor of endocardial leads, the transvenous ones, over epicardial leads is extremely strong.

A clinical study carried out on 125 participating hospital centers demonstrated that 4.2 percent of patients receiving the epicardial leads were dead within 30 days following surgery, and only 0.8 percent of patients receiving the endocardial or transvenous leads died during the same period. Endocardial leads became available in the United States in December 1993, but were first widely available in Europe in late 1991, 2 full years before they were widely available in the United States.

Given the improvements in patient survival for each generation of this device, this is hardly a trivial issue. Roughly 13,200 Americans received defibrillators each year over this period. By delaying their entry into the United States, American patients were denied access to medical technology that had the potential to save their lives. In fact, our study estimates that the 2-year regulatory lag in approving endocardial leads may well have led to over 1,000 deaths in American patients.

Similarly, the Cook coronary flex stents presented physicians confronting a life-threatening situation, the collapse of an artery during angioplasty, a far better alternative than they otherwise had. Patients who received the stent in clinical trials had up to a 40-percent chance of a heart attack if the stent had not been used.

Indeed, as Dr. Kessler noted upon the stent's approval, "It will be helpful for that small group of patients in whom balloon angioplasty might otherwise fail, causing heart attacks or even death." As a result of regulatory delay, we estimate that up to 2,900 American patients may have lost their lives as a result of the delay.

Mr. Chairman, my testimony here today and the report itself are not intended to be attacks on the FDA's management, or on the FDA itself, or the concept of the FDA itself. We agree that medical technology does need to be evaluated before it reaches the market. The purpose of my report is to bring to light the very real costs associated with regulatory delay.

Moving slowly in evaluating products may be good policy, but moving too slowly has dramatic human costs that are rarely considered in the policy arena. Without considering these costs, any attempts at enhancing the premarket review process, such as those being considered before Congress this year, are destined to be disappointing.

Thank you.

[The prepared statement of Mr. Murray follows:]

PREPARED TESTIMONY OF DAVID C. MURRAY

Before I begin, let me first thank both Chairman Shays and Chairman McIntosh for inviting me to testify today. The testimony that I am delivering today is the result of research that I have carried out as a member of the research staff of the Competitiveness Center of Hudson Institute in Indianapolis, which is chaired by former Vice President Dan Quayle. I alone, however, am responsible for the views expressed in the paper and in my testimony today. Those views should not be attributed to the Hudson Institute, its staff, trustees, or contractors.

Medical technology has advanced at an incredible pace during the last fifty years. Physicians and scientists have harvested the fruits of explosive growth in electronics and the material sciences by applying revolutionary advancements in these technologies to medical science. These developments have fed upon one another, creating an environment of synergy and rapid innovation.

American consumers have been the ultimate beneficiaries of these technological breakthroughs. Treatments that we take for granted today did not exist only a short time ago. Thirty years ago, patients suffering from kidney failure had little hope of survival,[1] but today nearly 500,000 Americans benefit from kidney dialysis, and the possibility of artificial kidneys is now on the horizon.[2] Until only ten years ago, an American whose heart spontaneously started to race or stopped without warning became just another statistic of sudden cardiac death, but today a defibrillator implanted inside a heart patient's body can save that person's life. When the heart stops beating normally, the defibrillator sends an electronic shock to the heart, bringing it back into a normal rhythm. Such advancements have benefited literally millions of Americans during the past decades and generated confidence that millions more will live longer and healthier lives in the decades ahead.

Although American physicians and scientists have developed most of these innovations in America, American consumers are no longer the first to benefit from these often life-saving and life-enhancing products. All too frequently, Europe, Japan, and Canada approve new medical devices for use years before the Food and Drug Administration (FDA) approves them for use in the U.S. The delay in introducing these

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[1] Susan Bartlett Foote, *Managing the Medical Arms Race* DAVE: NEED CITY AND PUBLISHER, 98-103.

[2] "Artificial Kidneys May Soon Be Reality," *Medical Materials Update* 3, no. 3. , page 3.

new technologies in America has undeniable and serious consequences for American consumers; consequences that can be quantified in losses in the quality of life, and sometimes even of life itself, for thousands of Americans each year. Proponents of the FDA system argue that these delays are the inescapable price of a system that ensures safety, but very little evidence supports this view. The FDA has approved almost all of the medical devices that have encountered serious post-market difficulties. The evidence this paper presents indicates that in certain instances, the FDA approval system is actually costing lives.

Debates over the safety and efficacy of medical technology often obscure this basic yet vital fact. Rather, the public and the press have been well sensitized to the dangers of premature approval of a medical device or drug. Although premature approval is certainly a risk, minimizing this risk comes at the high cost of maximizing another risk: that of delaying the entry of safe and effective new technologies, with attendant loss of human lives. Conversely, the absence of all regulation would minimize the risk of delaying the availability of new technologies but would maximize the risk of allowing unsafe or ineffective products to reach the market. Clearly, neither of these extremes is desirable as public policy--the risks of one must be balanced against the risks of the other to find a middle ground.

To date, however, warnings about the risks of delayed availability of medical technologies have fallen on deaf ears, and the costs associated with the very small percentage of unsafe FDA-approved medical devices have captured the limelight. This fact is partly due simply to the nature of the phenomena. When a device fails and individuals are hurt or killed, they are easily identifiable and they, their families, or their lawyers are more than willing to discuss it in front of news cameras. People who die because a device is not available due to a regulatory backlog, however, are much more difficult to identify. They simply die--no news coverage, no lawsuits, no investigation. In short, the public never hears about it. In the final analysis, though, a human life is a human life. Persons who die from the absence of a device that should have been available should count as much as the victims of a defective device when policymakers weigh the costs and benefits of our current policies governing the introduction of new medical technologies.

Our study examined the regulatory histories of four life-saving high tech medical devices that were approved in Europe before they were approved in the US. Because each of these devices offered a substantial improvement in the quality of health care for the conditions that they were intended to treat, delays in their approval generated significant

human costs. In other words, American consumers could have benefited from these devices earlier had the regulatory approval process been more efficient.

Let us take the example of the wire leads that are used to connect an implantable defibrillator to the heart. A physician can use either epicardial or endocardial leads to attach defibrillators to the heart. Epicardial leads are grafted onto the heart muscle by means of screw-in or stab-tab electrodes. This type of lead requires a thoracotomy, or open chest procedure. Endocardial leads, on the other hand, could be threaded through the patients blood vessels to the heart. Because these leads stay inside the blood vessels, there is no reason to open the chest.

The clinical evidence in favor of endocardial leads over epicardial leads is extremely strong. A clinical study carried out at 125 participating hospital centers demonstrated that 4.2 percent of patients receiving the epicardial leads died within 30 days following surgery, and only 0.8 percent of patients receiving the endocardial leads died during the same period.[3] Two years after surgery, 87.6 percent of the patients receiving endocardial leads were alive, but only 81.9 percent of patients with epicardial leads were still alive.[4] The medical characteristics of patients in both groups were similar. Other studies have also demonstrated the superiority of endocardial leads, exhibiting a differential in survival rates of about 4 percent.[5]

Endocardial leads became available in the US in December 1993. Endocardial leads were first widely available in Europe in late 1991, two years before they were widely available in the U.S.

It is evident that during the last several years, European consumers have had earlier access to the latest model of implantable defibrillators than American consumers. In fact, American consumers were one full product cycle behind their European counterparts for most of the past five years. Given the improvements in patient survival for each generation of the device, this is hardly a trivial issue as roughly 13,200

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[3]Sanjeev Saksena, "Clinical Outcome of Patients With Malignant Ventricular Tachyarrythmias and a Multiprogrammable Implantable Cardioverter-Defibrillator Implanted with or Without Thoracotomy: An International Multicenter Study," *Journal of the American College of Cardiology* 23, no. 7 (June 1994), 1521-30. These results were statistically significant at the .001 level.

[4]These results were also statistically significant at the .001 level, but when those who died in the thirty days following surgery were eliminated from the analysis, the survival rates at two years were similar.

[5]See also James M. Kleman et al., "Nonthoracotomy Versus Thoracotomy Implantable Defibrillators," *Circulation* 90, no. 6 (December 1994), 2833-42.

Americans received defibrillators each year over this period. In fact, the two-year regulatory lag in approving endocardial leads may have led to over 1,000 deaths in American patients.

The truth about implantable defibrillators and their lead systems is simply that the newer devices save more lives. By delaying their entry into the US, American patients were denied access to medical technology that had the potential to save their lives.

Mr. Chairman, my testimony here today and my report are not intended to be attacks on the FDA's Commissioner or on the concept of the FDA itself. Far from it. The purpose of my report is to bring to light the very real costs associated with regulatory delay. Moving slowly in evaluating products may be good policy, but moving too slowly has dramatic human costs that are rarely considered in the policy arena. Without considering these costs, any attempts at enhancing the pre-market review process for new medical technologies are destined to be disappointing.

Mr. MCINTOSH. Thank you very much, Mr. Murray. I appreciate that testimony.

Our next witness on this panel is Mr. Thomas Lenard, who is a senior fellow and director of regulatory studies in the Progress & Freedom Foundation.

Mr. Lenard.

Mr. LENARD. Thank you, Mr. Chairman.

I appreciate this opportunity to discuss the work we are doing at the Progress & Freedom Foundation to look at the effects of our current regulatory process and to develop a new framework for bringing medical products to market. Some of my comments are going to echo some of the themes raised by Mr. Murray and others, and I guess I should also add that the comments that I'm going to be making are my own and not necessarily those of the Progress & Freedom Foundation.

Mr. Chairman, the United States is currently the world's leader in biomedical research, but this lead is in danger of slipping away because America's procedures for bringing new medical products to patients are among the slowest and the most expensive in the developed world.

Nowhere is this more true than in the medical device industry. Major manufacturers increasingly are locating their research and manufacturing facilities offshore, and it is now routine for new medical devices developed by American companies to be available in other countries before they become available here. This means that American patients are increasingly receiving therapies that are two to three generations behind those available in Europe, for example, and this is solely because of the burdens imposed by the U.S. regulatory system.

The current regulatory scheme gives the FDA a statutory mandate to assure that drugs and devices are safe and effective, but this is combined with a monopoly on new product approvals. It is the second part of this framework, the monopoly element, that is the source of the current problems. As long as the only route to the American market is through the FDA, development of new medical products will continue to be plagued by unnecessary costs and delays and the other types of problems that are being discussed here today.

Meaningful reform must, therefore, address the FDA's certification monopoly and introduce competitive pressures into the device approval process. In this respect, as well as others, the new European Union system for regulating medical devices offers important advantages relative to our own and provides a model that we, in the group at PFF that is looking at this issue, have looked to in developing our own proposals.

The European system provides the manufacturer with the option of choosing a private notified body, based in any country of the EU, to certify that the device meets the essential requirements for safety, quality, and performance, and to gain entry into the entire EU market. For many simple medical devices, the manufacturer may self-certify compliance. The EU system has been in effect since the beginning of 1993 for active implantable devices, since the beginning of 1995 for other medical devices, and is soon to be phased in for in vitro diagnostic devices.

American medical device companies are well aware of the advantages of the EU system, in terms of providing a high degree of predictability that allows for rational planning and investment decisions. American manufacturers who export to Europe are fully subject to the EU system, and, in recent years, many American companies have relocated to Europe and are first introducing their products there.

The fact that the EU standards are often very stringent does not seem to dampen the enthusiasm American companies have for the European system. The EU system has a better balance of incentives than our own because much of the detailed work is done by competing private organizations.

Many of these organizations have a long history of functioning as independent test houses, and while, in general, they guard their reputation for independence carefully, they also have the incentive to help the manufacturer meet the standards needed for expeditious approval, as they compete with each other. American companies which deal with both the FDA and the EU system often remark that the difference is that the notified bodies "want to help."

The European system establishes competition at two levels: First, device manufacturers can choose which private notified body they wish to use to bring their product to market, and certification by a notified body in any of the EU countries is sufficient to enter the entire EU market.

Second, there is an element of jurisdictional competition, because the notified bodies are certified by the competent authorities in their respective countries. This provides an automatic check on any competent authority whose standards become out of line with those elsewhere.

The United States could benefit greatly by adopting the best of this system. The establishment of private device certification bodies, licensed by the FDA or another competent authority, would assure at least one level of competition. Device manufacturers could then choose the most efficient means of obtaining the necessary approval for getting their products to patients.

If we don't make fundamental changes along these lines, it seems to me that we are in danger of losing much of our medical device industry, which is already voting with its feet in favor of the European system. The ultimate losers, of course, will be American patients whose access to important therapies will be delayed or denied.

Thank you.

[The prepared statement of Mr. Lenard follows:]

Statement of

Thomas M. Lenard

Senior Fellow and Director of Regulatory Studies

The Progress & Freedom Foundation

Chairman Shays, Chairman McIntosh and Members of the Subcommittees, I appreciate this opportunity to discuss the work we are doing at The Progress & Freedom Foundation to develop a new framework for bringing medical products to market.

The United States is the world's leader in biomedical research. But this lead is in danger of slipping away, because America's procedures for bringing new medical products to patients are among the slowest and most expensive in the developed world.

Nowhere is this more true than in the medical device industry. Major device manufacturers increasingly are locating their research and manufacturing facilities offshore, and it is now routine for new medical devices developed by American companies to be available in other countries before they become available here. This means that American patients are increasingly receiving therapies that are two-to-three generations behind those available in Europe, for example -- solely because of the burdens imposed by the U.S. regulatory system.

These burdens are especially harmful for the hundreds of small, entrepreneurial companies that make up America's medical device industries. Eighty-eight percent of medical device companies have fewer than 100 employees, while their average expenditure on research and development as a percent of sales is more than twice that of the average of all manufacturing companies.

The current regulatory scheme gives the FDA a statutory mandate to assure that drugs and devices are safe and effective, *combined with* a monopoly on new product approvals. It is the second part of this framework -- the monopoly element -- that is the source of current problems.

As long as the only route to the American market is through the FDA, the development of new medical products will continue to be plagued by unnecessary costs and delays. Meaningful reform must therefore address the FDA's certification monopoly and introduce competitive pressures into the device approval process.

In this respect, as well as others, the new European Union (EU) system for regulating medical devices offers important advantages relative to our own, and provides a model that we at PFF have looked to in developing our own proposals. The European system provides the manufacturer with the option of choosing a private body (a "notified body") based in any country of the EU to certify that the device meets the "essential requirements" for safety, quality and performance. Compliance with applicable international standards is presumptive evidence of compliance with the essential requirements. For many simple devices, the manufacturer may self-certify compliance.

The EU system has been in effect since the beginning of 1993 for active implantable medical devices, since the beginning of 1995 for other medical devices and is soon to be phased in for *in vitro* diagnostic devices.

American medical device companies are well aware of the advantages of the EU system in terms of providing a high degree of predictability that allows for rational planning and investment decisions. American manufacturers who export to Europe are fully subject to the EU system. And, in recent years, many American manufacturers have relocated in Europe and are first introducing their products there. The fact that the EU standards are often very stringent does not seem to dampen the enthusiasm American companies have for the European system.

The EU system has a better balance of incentives than our own, because much of the detailed work is done by competing private organizations. It is they who certify that a manufacturer's products conform to the essential requirements and thus can be marketed. Many of these organizations have a long history of functioning as independent test houses. While in general, they guard their reputation for independence carefully, they have the incentive to help the manufacturer meet the standards needed for expeditious approval as they are all in competition with each other. American companies which deal with both the FDA and the EU systems often remark that the difference is that the notified bodies "want to help." In fact the converse may be true in the current FDA system where enforcement, not approvals, seems to be the highest priority.

Finally, the EU system provides flexibility. The degree of control is strongly related to the complexity and risk of a device. For Class I (the least risky) devices, the manufacturer is expected to self-certify, generally based on existing international standards. For active implantable devices, the notified body must approve the design itself and the manufacturer must present clinical data demonstrating efficacy and safety. For many devices, the manufacturer can rely primarily on either certification of the quality of his design and production processes, or alternately, on detailed testing of the individual product.

The European system establishes competition at two levels. First, device manufacturers can choose which private notified body they wish to use to bring their product to market, and certification by a notified body in any of the EU countries is sufficient to enter the entire EU market. Second, there is an element of jurisdictional

competition, because the notified bodies are certified by the "competent authorities" in their respective countries. This provides an automatic check on any competent authority whose standards become out of line with those elsewhere.

The United States could benefit greatly by adopting the best of this system. The establishment of private Device Certification Bodies (DCBs), licensed by the FDA or another competent authority, would assure at least one level of competition. Device manufacturers could then choose the most efficient means of obtaining the necessary approval for getting their products to patients.

If we do not make fundamental changes along these lines, we are in danger of losing much of our medical device industry, which is already voting with its feet in favor of the European system. The ultimate losers, of course, will be American patients, whose access to important therapies will be delayed or denied.

Mr. MCINTOSH. Thank you very much, Mr. Lenard. In the questioning, I would like to pursue that notion of competition some more, in this and other areas.

Our final witness on this panel is Dr. Jeffrey Brinker.

Welcome, Dr. Brinker, and I look forward to hearing your testimony.

Dr. BRINKER. Thank you, Mr. Chairman.

I am a practicing physician, director of interventional cardiology at the Johns Hopkins Hospital, and professor of medicine and radiology at the Johns Hopkins University.

Over the last 6 years, I have served on the FDA Circulatory Device Advisory Panel, including 2 years as its chairman. I have been engaged in the evaluation, regulation, and utilization of medical devices. I am an active member of a number of professional societies, including the American College of Cardiology, the North American Society of Pacing and Electrophysiology, and the Society for Cardiac Angiography and Intervention.

I have no financial interest in industry, nor do I have a vested interest in the FDA, per se. I did not actively seek the opportunity to speak at this hearing but accepted the invitation because I believe in this process and thus the responsibility to participate. My prepared testimony outlines general and specific views on the subject of device regulation. In the short time allotted to me, I would like to highlight them.

All of us would agree that society is best served when access to safe and effective new medical technology is provided in the most expeditious fashion. Controversy exists as to how this most effectively and efficiently can be accomplished.

While the present system of device regulation has a number of widely acknowledged shortcomings, most of which have been highlighted today, there is much that is right with it. I welcome attention that is directed toward optimizing the system but urge that we take care not to throw the baby out with the bath water. I would like to emphasize the following:

One, there is a need for device regulation, and this should be the responsibility of an impartial, knowledgeable body. These products have the potential to cause injury and death, which, for some devices, may be greater than for many drugs. In addition, device-related injury and failure result in a considerable financial burden to the patient, private insurers, and the government.

Two, effective regulation that is not unduly obtrusive may be accomplished under the present system without new law. A number of meaningful changes have taken place at the CDRH over the last 6 years which have been directed at facilitating approval of new technology, with particular attention to potentially important advances in medical care.

Three, I believe that it is the responsibility of the FDA to facilitate approval of safe and effective medical technology. This involves a change in philosophy but not of basic mission. I propose that the adversarial relationship between industry and the FDA be replaced with one based on communication and cooperation. Applications should be shepherded through the regulatory system by a continued interactive process.

Four, the FDA should have adequate resources to meet demands placed upon it. Toward this end, I recommend the imposition of user fees.

Five, a thoughtfully conducted clinical trial remains a cornerstone of device evaluation, especially for technology that claims to offer superior safety or efficacy.

Six, patients participating in FDA-sanctioned clinical trials of new devices must be protected from excessive financial burden. Insurers, including the government, should reimburse physicians and hospitals for services rendered, including the cost of the device. A quid pro quo for the insurers might be mandated collection of cost-effectiveness data which would become public domain upon device approval.

Seven, there should be a way for FDA sanction of investigator-initiated studies of off-label device use, such that approval for valid indications may be introduced into the labeling.

Eight, while I would not suggest that there is a medical-industrial complex, I do think that the objectivity of manufacturers and some physicians may be clouded by economic factors, as well as by an intellectual commitment to the technology.

I would like to remind all of us that "new" cannot be equated with "better." Few, if any, of the devices that have passed through the Circulatory Advisory Panel over the last 6 years were presented with any demonstrable benefit, in terms of lives saved, compared to available alternative therapy.

I do not feel that the conclusions drawn by the Hudson report are scientifically valid. In fact, I am convinced that the regulatory process imposed by the FDA has saved lives by insisting on important preclinical qualification and a limited initial clinical experience. Furthermore, in these days of limited financial resources for health care, I think it an absolute necessity that new technology demonstrate at least clinical effectiveness if not cost-effectiveness.

In conclusion, I think that the quality of medical care in the United States is the finest in the world. We provide the greatest number of our population with the most advanced technology in an expeditious manner. I am not against change but feel that it should be taken for the right reasons, with reasonable expectations that the end result will be an improvement for our greater society.

Thank you.

[The prepared statement of Dr. Brinker follows:]

Thank you for inviting me to participate in the joint oversight hearing on "Medical Devices: Enforcement Standards at the FDA." My name is Jeff Brinker. I am a practicing physician and Director of Interventional Cardiology at the Johns Hopkins Hospital. I hold the full time academic position of Professor of Medicine with a joint appointment in Radiology at the Johns Hopkins University. I have been active in the design and conduct of protocols involving the study of devices and drugs in patients and in animals for the last 20 years. Over the last 6 years, I have served on the FDA Circulatory Device Advisory Panel including 2 years as its Chairman. In addition, I have assisted the FDA as a mediator between it and industry on a number of occasions. I am currently Chairman of the Accufix Atrial J Lead Physician Advisory Committee to Telectronics Pacing Systems which is advising the company on the clinical management of patients with this recalled device. I have had a long interest in the clinical use of a variety of devices and have participated in discussion involving issues of approval and recall. I have no personal financial interests in industry and much of my work with the FDA is done on my own time and expense. I did not actively seek the opportunity to speak at this hearing but have accepted the invitation because I believe in this process and in the responsibility to participate in it. I hope my views are considered objective; they are based on my overall experience as a physician and the desire to see that society's best interests are served.

Society is best served when access to safe and effective new medical technology is provided in the most expeditious fashion. Much controversy exists as to how this might be best accomplished. Some would have us believe that any new medical device should be immediately available, with little or no regulatory constraint, to physicians who will determine its ultimate worth in clinical practice. Others suggest a trial by regulatory fire in which only the most determined sponsor with considerable resources could compete. This might include the necessity for extensive clinical trials which would yield scientifically valid evidence demonstrating superiority of the new product compared to alternative "approved" therapy. Underlying the differences in opinion expressed above are the operating definitions of "safe", "effective", and "expeditious". My opinion is that there is a need for an objective governmental device regulatory system and that the optimal methodology to accomplish this lies between these extremes.

Clearly, the present regulatory system has generated a considerable amount of discontent voiced predominantly by the medical device industry but with concern expressed by some in the medical community as well. The tripartite relationship between the FDA, the medical device industry, and medical community suffers from a lack of trust, communication, and cooperation. Typical complaints are that the FDA: changes its "ground rules"

places undue demands on the sponsor and physician investigators, is slow and uncompromising. The most frequent characterization of the relationship between the Agency and industry is "adversarial". Physician investigators further feel that the FDA is intrusive and unyielding in protocol design, interferes with their ability to practice medicine in the way they see fit, and delays the availability of important new technology to the practicing physician. While all of these complaints are valid to a degree, they can not be considered in a vacuum. Many in the medical device industry are looking more toward profit and the competitive edge than towards societal welfare. They, and on occasion their physician consultants and investigators, often have a prejudicial view of their product. This may hamper objective assessment of the technology. Clinical trials are often poorly designed, and there are problems with protocol compliance, data collection, and analysis. Physician investigators may be more interested in marketing the availability of new technology than in proving its worth. Industry often subtly, but occasionally overtly, encourages the off-label use of devices to circumvent the regulatory process. Physicians all too often forget the importance of the scientific method and fall back on a concept of medical infallibility to decide whether a device is safe and effective. This is often problematic because of the vested financial and intellectual interests that physicians may have in the product.

While acknowledging some of the perceived shortcomings of current regulatory system I would like to emphasize the following:

1. There is a need for device regulation. This is so for life sustaining and implantable devices as well as for "low risk" devices. For the former the potential for device related patient injury and death is considerable and may exceed that of many drugs. In addition to the risk posed by these devices, the financial burden to the patient, private insurers, and the Government in treating device related injuries and failures is substantial. There is also the cost to society of marketing devices which may be of low risk but are ineffective.

2. Effective regulation that is not unduly obtrusive may be accomplished without major changes in law. Over the last 6 years I have noted significant changes in the way the CDRH does business. This includes: the development of an expedited approval pathway for truly innovative technology which address definite clinical needs; initiation of an interactive process which brings the sponsor, physician investigators, the FDA, and advisory panel consultants together to address issues at various stages of the IDE and PMA process; increased reliance on postmarket surveillance to supply safety data; early establishment of performance standards which would simplify the approval process of devices similar to those being marketed; convening workshops

designed to facilitate communication between the FDA, the device industry, and physicians; and circumvention of the advisory panel process in certain situations (including by the reclassification of some devices) in which approval can be granted on the basis of established standards. These developments have accompanied a change in leadership at the CDRH and a responsiveness to criticism.

3. A fundamental obstacle in the relationship between the FDA and the medical device industry is philosophic; I believe that it should be the responsibility of the FDA to FACILITATE the approval of safe and effective medical technology. Towards this end, for PMA devices, I would suggest extension of the interactive process described above such that the agency, objective medical consultants (?members of the advisory panels) and the sponsor meet at regular intervals starting before the IDE process and continuing to market approval. The objective would be early identification of potential obstacles to approval and devising appropriate means of addressing these problems in an expeditious manner. In addition, review of all aspects of the device by the various sections of the CDRH should be done in a parallel rather than in series fashion; time lines for the entire process should be established and adhered to. Further I would suggest that there be an ombudsman available to industry which would mediate any potential disagreement between agency and sponsor. This does not obviate the necessity for the sponsor to clearly demonstrate safety and efficacy of the device by valid scientific means but it would facilitate the process. It also would require justification (usually based on a randomized controlled study) for labeling (or implied) claims of superiority or benefit compared to alternative therapy.

4. Non-PMA devices should be handled by the FDA in an expeditious manner. There should be a "user fee" assessed on the sponsor which would support the man-power necessary for efficient processing of applications. In certain situations some analysis may be contracted out to qualified third parties.

5. The thoughtfully conducted clinical trial is the cornerstone of device evaluation. It provides a mechanism for learning about device-patient interactions and allows for the demonstration of safety and efficacy in a controlled environment which limits the potential risk to the American public. It also allows for some evolution of the product and provides a means of defining the appropriate applications (indications) for device use. In an important concession to medical industry it sanctions the sale of an investigational device (under an IDE) that may or may not ever be proven to be either safe or effective, to the public. It also provides a protection for industry from certain aspects of product litigation. It is essential that we support the use of both pilot studies and safety/efficacy studies in the U.S.. Post market surveillance must also be accomplished such

that the long-term safety of devices, particularly implantables, be established. Further it provides a mechanism for initial approval of the device with limited clinical experience. All studies should be performed under proper regulatory oversight but this must be purposeful and not obtrusive.

6. There must be a reliable mechanism to ensure that patients participating in FDA sanctioned clinical trials of new devices are protected from financial burden. This should include the cost of the device, as well as any treatment required for injury during the study. Third party insurers and HCFA should be responsible for medical care and the costs of devices utilized under an approved IDE. There is currently debate as to the responsibilities of HCFA in this regard. As a result many hospitals and physicians have avoided using IDE devices in medicare/medicaid patients. This has inflamed the anti-regulatory feelings in the medical community with blame often, and incorrectly, directed at the FDA. Migration of investigational technology from the U.S. has been accelerated by this controversy. While there may be a reticence for insurers to pick up the obligation for "investigational therapy" it might be feasible to require that cost:benefit data be obtained as part of the clinical investigation and provided to the public for consideration after device approval.

7. There should be a way for knowledge derived from reliable studies to affect device regulation without the active support of the sponsor. This would allow information from properly performed investigator initiated studies on off-labeled uses of devices to be incorporated in the labeling. This would have fostered approval of such therapy as radio frequency catheter ablation for cardiac arrhythmia and stents for coronary bypass grafts at an earlier period of time. This would be a service to the entire medical community (i.e. those of us who wish to function within the bounds government regulations) and society as a whole.

8. No regulatory system will be perfect; devices will be approved which may over time be found unsafe. A pacemaker lead, approved by the 510K process 7 years ago, has been recently found to be prone to wire fracture and possibly heart perforation. Two deaths have occurred while 17 other patients have had life threatening complications. An additional 4 people have died and many more have had significant complications during attempts to remove this implantable device. Some 45,000 people (about 25,000 in the U.S.) are at risk. Every regulatory decision requires careful regard for the potential risks of the device versus the benefit it might bestow. In some situations only time will reveal device shortcomings. In the best of all worlds these unfortunate events would be rare. However, their likelihood may be increased by a less vigilent oversight mechanism.

I would urge the Committee to keep an open mind with regard

to claims, such as those in the Hudson report, that the present regulatory process is costing hundreds and perhaps thousands of American lives. The conclusions drawn are not scientifically valid and do not take into consideration a number of factors such as the lack of randomized controlled studies, and the paucity of any data showing statistically significant differences in mortality (including data submitted by Cook Inc. for its stent). Most importantly lay persons and physicians most be aware that "NEW" cannot be equated with "BETTER". The vast majority of products dealt with by the FDA are essentially "me too" devices in which there may or may not be small advantages to the physician or patient compared to marketed devices. In some instances the new devices are not as good as the best alternatives but are still approvable. No patient's life or health hangs in the balance of these devices. There are certain technologies that do offer significant advantages in terms of saving or prolonging life. In many instances these technologies offer the most formidable challenges to the regulatory system because they have the greatest potential for adverse (including life-threatening) events. Implantable defibrillators and intra-coronary stents are examples. The first clinical use of an intra-coronary stent was in Europe. While initial reports were favorable, a subsequent study revealed that the long term use of the device (as applied in practice) was associated with a high incidence of coronary occlusion and no apparent benefit (Serruys PW et al New England Journal of Medicine 1991;324:13). Even after approval of the Cook and Johnson & Johnson stents in this country medical opinion has been divided (Hearn JA et al Circulation 1993;88:2086, Serruys PW and Kean D Circulation 1993;88:2455, Topol EJ: New England Journal of Medicine 1994;331:539). Clearly we learn about the proper use of devices in clinical trials; our knowledge of coronary stenting including mechanisms of deployment and adjunctive medical therapy continues to grow. The FDA has taken a leadership role in this area by encouraging proper studies to be performed to allow devices to be used in an optimal fashion. The current trial evaluating adjuvant medical therapy for stenting is a good example.

In many instances the clinical trial allows for the identification of problems and limits their sequelae. Such was the situation with a pacemaker which had a defective connector block and was subject to unpredictable failure. This was noted just before market release in this country and allowed for a fix to be made in the device. A relatively small number of patients exposed to the device during the clinical trial had to undergo repeat surgery. If this process had not been taken, thousands of patients may have been at risk of repeat surgery or sudden death due to device failure.

Any regulatory process most straddle the boundary line of being too restrictive or not demanding enough. It is imperative that an impartial body be given the responsibility for these

decisions. This entity must have the resources and authority to do the job effectively and efficiently. Congress first empowered the FDA to regulate devices on a limited basis in the FFD&C act of 1938. The FDA's responsibilities have been clarified in the Medical Device Amendments of 1976, the Safe Medical Devices Act of 1990, and the Medical Device Amendments of 1992. The rationale for these changes included the perception that devices needed closer regulation not less.

It is my opinion that the quality of medical care in the United States is the finest in the world. We have the most advanced technology and provide it to the greatest proportion of our population in an expeditious manner. I am not against reform but feel that it must be undertaken for the right reasons and that it should be done only if it would result in a substantive improvement. The FDA has increased the consciousness of the need for drug and device oversight throughout the world. In many countries including those of the European Economic Community, regulatory bodies have become more like the FDA. Furthermore, because the U.S. is a major market for devices, most companies in and out of the U.S. direct their product development and evaluation in accordance with FDA standards even if they introduce them at an earlier phase outside of this country. Those responsible for device regulation in other countries realize that establishment of the safety and effectiveness of devices will ultimately be determined by the U.S. FDA and this may have an impact on their decision making.

There is much that is right about the way this country regulates drugs and devices. We all can agree that every government agency can be improved. Attention should be directed towards optimizing the system and care taken not to "throw the baby out with the wash water".

Mr. MCINTOSH. Thank you very much, Dr. Brinker.

Let me turn now to my colleague from Indiana, Mr. Souder, and then I will reserve my questioning to go after him, since he has been very patiently waiting.

Mr. Souder, do you have any questions for the panel?

Mr. SOUDER. Yes, let me ask a few, and I will go back to you, and may have a couple more later, too.

I wanted to ask Dr. Brinker, I was confused by a couple things. One is, is cost-effectiveness currently a test?

Dr. BRINKER. For the FDA?

Mr. SOUDER. Yes.

Dr. BRINKER. No.

Mr. SOUDER. And you're suggesting that that might be a test?

Dr. BRINKER. No, I'm saying that effectiveness should be. I'm saying, in the future, that someday, by legislation, cost-effectiveness probably will be. But a device now has to be proved safe and effective. I think that any variance from the necessity to prove a device safe and effective—and I underline the term "effective"—would be a burden that our society shouldn't have to bear.

Mr. SOUDER. If you believe that part of it is to prove clinical effectiveness, and if a product that is supposed to be lifesaving is effective, why wouldn't accelerating the process of approval save lives, and why wouldn't slowing down that process cost lives? Why would you question the Hudson report?

Dr. BRINKER. I question the Hudson report only in some of the conclusions that it draws. If a device can be proven safe and effective, then I think the time when that proof is obvious, scientifically valid, and accepted till the time that it is available on the marketplace should be as short as possible, a day, 2 days, whatever is necessary to train physicians in the proper use and to establish proper directions and labeling.

I think the problem comes in the time it takes to establish, with valid scientific proof, that a device is safe and effective. Some of the devices that we have discussed today are still controversial. Some of the devices that have been approved have been shown, in retrospect, not to be safe and effective. And some of the devices that never get to the FDA process, because they are piloted in Europe, are not safe and effective.

Mr. MCINTOSH. Would the gentleman yield for 1 second on that?

Mr. SOUDER. Sure.

Mr. MCINTOSH. Let me make sure I understand that last remark. You are saying, up until the point where it can be proved to somebody's satisfaction that it is safe and effective, there should be no consideration of how much time is taken?

Dr. BRINKER. No, I don't say that. I didn't think I said that. I said that the clock should start on excess time for a device that is safe and effective when it is proven to be safe and effective.

Mr. MCINTOSH. What happens prior to that? What should your standard be, in terms of watching the clock?

Dr. BRINKER. I think that all of these devices should be brought through the process as quickly as possible, with regard to patient safety.

The problem—and I've been able to look at some of these issues—the problem is that many of these devices, including

implantable devices, and I underline that, clearly, because taking out implantable devices is a terrible thing. We are trying to do that right now with a pacemaker lead that affects 45,000 people in the world, 25,000 in the United States, and it has an unfortunate defect which might result in the sudden death of people.

Unfortunately, extracting the lead can result in more deaths, or a higher rate of deaths, at least. So we are in a quandary of how to do this. It is not clear that stents, over a period of time, would be safe and effective. In fact, when the Cook stent was presented to the FDA panel, while it appeared to be able to reduce the incidence of emergency surgery and myocardial infarction, there is no statistical difference from controlled data, which was historical controls, that there was any resultant saving of lives.

Even after approval, a number of papers in respected scientific journals questioned whether the Cook stent is the most effective way of approaching patients with acute occlusion of a coronary vessel. These are not slam-dunk end points once they get through the FDA even.

I agree with everything that has been said about getting good things through the FDA. I think that there are hang-ups at multiple parts of the process. I also believe that many of the hang-ups are due to the industry and their physician investigators. There is a feeling of infallibility on the part of doctors who back some of these devices. There are economic and tunnel vision problems with manufacturers.

Poor studies are done. In fact, most of the studies that were done when I first came on the FDA panel were inappropriate for us to evaluate for scientific validity. There were no proper questions asked. There were no proper conclusions drawn. Improper data. Patients were enrolled incorrectly.

Mr. MCINTOSH. Let's assume we have a device that works, you're saying that all of the prospective patients have to bear the cost of the fact that there's a scientific review panel that is not happy with the data.

Dr. BRINKER. No, no. I'm not saying that.

Mr. MCINTOSH. You think they should go ahead and be available then?

Dr. BRINKER. No. You start with the premise that you have a device that works. What I would ask, as a physician who is going to use that device, is to just prove to me that it works and that it's safe, so that when I give it to a patient, that I'm not going to kill them. I've seen patients die with devices. I've killed patients with devices. Some of the devices were good; some of them were not good. Some of the indications were not clear.

This is not a black-and-white answer to these problems. But I think that we can't accept less than a reasonable indication that the device is safe and effective. I think that should be done as quickly as possible, but I think it should be done. And I think that industry and the FDA, together, should be held to the fire. Very often, industry shoots itself in the foot, unbeknownst to them.

Mr. MCINTOSH. I think we agree on that general principle.

I will yield the time back.

Mr. SOUDER. Time really isn't of a critical nature with the two of us here.

As I understand the basic construct—and I would like to have David Murray elaborate a little more on this and then anybody else who wants to pick up—we don't disagree on bad devices, because we don't want to put anything out there that's clearly harmful, with little redeeming value. And we have very little disagreement on things that clearly work. We need an accelerated process, and the only disagreement there may be how we make sure we identify those at the most rapid rate possible.

The real question is in the mixed group. In other words, they have potentially redeeming benefits, potentially harmful benefits, versus the person may have a condition that's harmful in and of itself. They may die whether or not they get the device. And that's really the area and how big that area is that we're in dispute of. Is that not correct?

And we can come back to Dr. Brinker, but let's hear from a couple of the others, too, with that.

Mr. MURRAY. I think that's—let me say first, I'm encouraged to hear that we should look to having a reasonable assurance of safety and effectiveness. I think, actually, that's what our study does. Our study—the excess lag times in our study—the clock only starts after the device was approved abroad by a competent authority, either through the European community-wide process, depending on the device, or through an independent country.

Remember who we're talking about here. We're talking about European countries such as Germany, England, et cetera. These are governments, you know, First World countries, who have meaningful processes, and the new community-wide regulations are certainly meaningful and coherent.

What I'm saying is that, by approval in Europe, I think that does give us a reasonable assurance of safety and, indeed, efficacy.

Mr. SOUDER. May I ask you a couple questions related to that? Then you can finish.

Mr. MURRAY. Sure.

Mr. SOUDER. Is there a difference in the European—I assume, from what I've read, that there's a difference in that Europeans make more risk-awareness notification to their consumers and tell you that it may not be completely sure, or whatever, and we don't have that in America. In other words, what I understood us saying is that we hold these things until we're clear that, over a number of years, they are safe; whereas, in Europe, they put them on the market, if there's a probable indication, and people are aware.

Is there a difference in the standards?

Mr. MURRAY. The systems really are so different they are almost not comparable. However, the European system does hold devices to quality. There are standards and specifications that devices are built to. They are reviewed. There is clinical review for implantable devices, for high-risk devices. The devices are classified in a manner similar to which they are classified under the FDA system.

To say that the European system does not deal with safety or clinical evidence would be misleading. What we recommend is that we move toward a European-style system, which, indeed, the track record shows that the number of devices approved in Europe that have come back to hurt people that have not been approved in the United States is very small.

As a matter of fact, FDA was asked that question in an appropriations hearing in the spring. The only device they could come up with was one that was approved 15 years ago, before the community-wide regulations were in place, and when regulation by national governments was only in its infancy in Europe.

Mr. SOUDER. So what you're saying is that, of the devices that have been held up in this country that have been approved in Europe, the only one that they came up with was early on in the process. Was it a high-risk?

Mr. MURRAY. Yes, it was a high-risk device. I'm speaking in terms of high-risk devices.

Mr. SOUDER. OK. And did the FDA discover that that one device that they—I mean, could you elaborate?

Mr. MURRAY. The FDA did not approve it.

Mr. SOUDER. OK. Does anybody else want to comment on the earlier exchanges, the points with Dr. Brinker?

Mr. PILOT. I'd like to offer an observation from the perspective of the manufacturer, and particularly the entrepreneur, because I don't know of any manufacturer, large or small, that undertakes to generate income from the sale of devices so that income then can be used to support plaintiffs' attorneys in product liability litigation. And that would be the logical outcome of some of the statements that Dr. Brinker suggests, that industry is irresponsible in its approach.

The FDA has a responsibility, for these premarket approval types of devices, to assure reasonable assurance of safety and effectiveness, that's the statutory criteria, by virtue of valid scientific evidence.

The types of devices that Dr. Brinker is referring to are those that are generally subject to intervention by a licensed practitioner, a qualified surgeon, a qualified physician, a therapist, a licensed practitioner who functions between the patient and the device itself. It's oftentimes the skill and the judgment of that practitioner which determines the success of the outcome.

Now, you made a reference to acceptance or knowledge in the European system as part of your question. I believe that risk acceptance is part of the equation and that better communication between practitioners and those who are subjected to the use of a device will provide the type of benefit that consumers are looking for and the participation that they deserve.McIntosh. Let me turn now to something in Mr. Lenard's testimony about the European feature, and that was the concept of competition among different possible entities that can grant approval.

Do a lot of these problems, both in terms of secret policy guidance being developed by the agencies and the failure to respond quickly to the potential of a new device, do those fall out in a competitive system? And, if so, what are the potential downsides, in tt process.

Mr. MCINTOSH. Let me turn now to something in Mr. Lenard's testimony about the European feature, and that was the concept of competition among different possible entities that can grant approval.

Do a lot of these problems, both in terms of secret policy guidance being developed by the agencies and the failure to respond

quickly to the potential of a new device, do those fall out in a competitive system? And, if so, what are the potential downsides, in terms of, perhaps, more risky products being put onto the market? And is there any way to quantify those trade-offs, if we were considering policy options?

Mr. PILOT. Well, I mean, I think a lot of the bad effects that you're talking about do fall out as a result of the competition.

First, I should say that the European system is relatively new, so there's not a lot of experience with it. But it has been in effect for more than 2 years with the most risky class of devices, the active implantable devices, and there is no evidence at all that I can see that they have bought a more responsive, more efficient, and quicker system at the cost of higher risk. There just doesn't seem to be any evidence of that at all. They seem to have bought a more responsive and more efficient system, without any increase in risk.

The standards they have are quite stringent; they are not easy standards. The private notified bodies compete with each other, but they all have reputations that they want to protect, in terms of the fact that their certification actually means something. In addition to that, the national competent authorities supervise quite closely.

But it's really an entirely different system than our own, and the notified bodies are very cognizant of the fact that they both have to make sure that their certification means something, they have to satisfy their competent authority, but they also have to get business, and they have to retain business, so they have to satisfy their customers.

Mr. MCINTOSH. Any comments from any of the other panelists on this notion of competition as a possible way of improving the regulatory system?

Dr. Brinker.

Dr. BRINKER. Thank you. I'd like to address that one question.

I feel that we should all be open to potential changes that might make any system better. Competition—let me digress a second and say that the European system, in many countries, was almost no system of regulation of devices until very recently. In fact, they have tended to, from especially some very lax countries, to become more stringent, using the FDA as a model, having talked to a number of physicians and regulators. So where they are now, in a great measure, for many of the countries, at least, in this union is stricter than where they were 5, 6, 10 years ago.

Mr. MCINTOSH. So do you think the presence of a competing entity allows them to be stricter but more efficient in processing the applications?

Dr. BRINKER. I think that they are coming from a scenario where they were less strict, so it's easier to go into an area where we'll be a little bit more strict, but we'll give this method of compensation, and that is that you can deal with competitive device regulatory bodies.

I don't know whether that would be an effective way. I don't know whether we would, for instance, like the FCC or the FAA, or any of the other commissions, to be really a number of competitive private enterprises running them, so new airplanes, new computerization of flight paths, and new engines would be under any one

of a number of competitive bodies. I don't know whether that could work; it might.

If it could and would work better than the system we have now, I would support it. If the system that we have now could be fixed—and I personally think it could, and I think it could be changed for the better—I think that there's a lot to recommend it.

The first thing to recommend is a feeling of impartiality. This institution, the FDA, doesn't have to compete for business. And there are certain benefits of not competing for business, one of which is, you don't have to give the impression that you do something better for the company that might not be better for society as a whole.

I think there would have to be a whole unique, new set of regulations for these bodies, for instance, to make sure that they go along with the strict guidelines that the FDA employees have to have about associations with industry and things of that nature. So I think that this would open up a whole new bag of worms, and I'm not against doing that.

I hope the members of the panel read my written testimony. Nowhere does it say that I'm not for change. I also would like to take exception to the term that it's really the doctors; you know, devices don't kill patients; doctors who use them do. I've heard that said before. Like guns don't kill people; people kill people. To a certain extent, that's true, but there is a responsibility that the device manufacturer has to ensure that devices are properly labeled, that the indications are clear, that adjunctive medication is obvious, and that physicians are trained appropriately.

Mr. MCINTOSH. I think that's a battle with some other people, because I think all of us would agree we want to make sure we've got the right information in the hands of the people using these devices, so that they can do the best possible job.

Dr. BRINKER. But that's part of the regulatory process, because the FDA, as part of the approval process, mandates those things, mandates, in fact, certain physician training, and certainly the labeling.

Mr. MCINTOSH. Assuming they get it right. I mean, that's helpful.

Let me switch tacks slightly and ask a different question. One alternative method other than competition is to try to build more accountability into the agency actions. I asked the agency to think about it and comment, and we didn't get back to it, so hopefully they will do it in their written responses.

What about incorporating into their approval process a post mortem that measures how long it took, how many lives were lost, what is the downside to the fact that we had to go through this approval process and, over time, building a body of information that says, yes, roughly, when we've got a high-risk device, we know it's going to take longer, and this is within the norm of what we think it takes. We're willing to accept that in society because we're weeding out the riskier devices. Low-risk devices had less potential harm for the delay but also less potential risk, and so that was an area.

Would that type of accountability for each of the individual decisions be something that would be helpful in this process? I will throw that open to anyone on the panel.

Mr. PILOT. I believe, over time, it would be useful to have that information to analyze what the result of a regulatory process is. And I believe those opportunities exist now for the agency.

In my comments, I talked about medical device reports, for example, where manufacturers are expected to supply information to the agency as it relates to death, serious injury, or malfunction. In the last 2 years, over 200,000 of those reports have been transmitted to the agency. And the agency recognizes those as accomplishments, processing all this paperwork.

But I have asked the question repeatedly, what is the preventive benefit that comes out of all of that? Since 1984, the agency has been managing this program and expecting manufacturers to supply information to the agency. Presumably, it's evaluated for some public health benefit, a reason that you can tie into prevention. But I've yet to receive an explanation. I'm not the only one asking this question. Certainly, it's a question that Congress needs to ask. What is the benefit of some of these programs that you have in place?

I'd like to comment on the reference to competition. Without getting into a definition, but assuming that competition is a reference toward the direction of excellence, excellence and not compromise by some other activity, I believe, in the United States, we could benefit from some type of third-party review system, at the option of the manufacturer.

For example, if the FDA were to recognize Johns Hopkins for some particular expertise that they have, and if Johns Hopkins were interested in applying that expertise to the review process, as a manufacturer, I could go to Johns Hopkins and I could ask them to review my clinical data in support of safety and effectiveness. If they give me a thumbs up, I would take that to the agency, and that would function as the scientific review process, in lieu of FDA bureaucrats managing the process.

So I think, if you're talking about competition in that sense, that's certainly something that MDMA and the NMDC support.

But on the reference to analysis, I believe it's important to do that, but we have tons, loads, lots of paperwork that the agency can use now to evaluate its performance. We talked about warning letters and the reference list. And, again, I take my shots at the warning letter, because I don't think it's helpful to anybody to have those issued under the present system.

The number of warning letters issued in relation to regulatory letters, over the 10-year period of time, have gone up twentyfold, I believe. Yet the number of seizures and injunctions that the agency has pursued during that period of time remains the same.

Mr. MCINTOSH. I appreciate that point. My thought was, when they finally issue an approval on a device, they make, as part of their announcement, we have calculated it. It has taken us 5 years to go through this process. There were 10 people who died each year; that's 50 people who died as a result of this approval process. But we think it's worth it, because you have to take a certain amount of time to do it.

Now, if they had to justify those numbers each time they made a decision, I think they would try to minimize it as much as pos-

sible in order to not look bad when they go to the press and make a positive announcement about a new device.

Mr. PILOT. And I would hope, on a regular basis, if there were that type of system, that Congress, in oversight, on a yearly basis, or whenever, would review the agency's performance.

Mr. MCINTOSH. See how they're doing.

Mr. SOUDER. Is there a current method to—when a product is hitting a market void, in other words, it's an innovative product that could actually save lives, for which nothing exists currently in the market, so that it is clearly more likely to be a net gain and the risk might be worth it, in other words, a higher percentage of the people, is there any sorting process that would accelerate that type of application?

Mr. PILOT. Perhaps better judgment on the part of the agency.

Dr. BRINKER. The FDA has implemented, over the last, at least, 2 years that I know of, a breakthrough device fast track, which actually Burlington described very briefly this morning. This has been used. In the advisory panel—at least the Circulatory Advisory Panel, which I think is good and not manipulated by the FDA, has advocated the fast track approval of at least two devices that we reviewed, one being the nonfluorocotomy leads, and the other being the stents.

Mr. MCINTOSH. Let me at this point, if I might, turn to the minority counsel, since there are no minority members present, and ask Kevin, do you have any questions for any of the panel members.

Mr. DAVIS. Yes.

Mr. MCINTOSH. Come forward and introduce yourself, and go ahead and ask those questions.

Mr. DAVIS. Hi. Kevin Davis, minority professional staff, Government Reform and Oversight.

Thank you, Mr. Chairman.

Mr. Murray, has your report undergone peer review outside of the Hudson Institute; and, if not, isn't that a standard practice where you have a report which makes serious allegations that FDA delays have led to hundreds of deaths?

Mr. MURRAY. Yes, it has undergone peer review outside of the Hudson Institute. No, it's not necessarily a standard function in think tanks for academic papers. Generally, that function is carried out if it's going to be published in a third-party journal, such as a medical journal or a law journal, something to that effect. It's generally done at that level. When it's being published privately, that's not always done, although sometimes it is.

I would also point out that all the clinical data that's contained in the report came from refereed medical journals, and those articles, in turn, are peer reviewed by physicians.

Mr. DAVIS. Thank you.

Mr. Thompson, as you know, guidance documents are often desired by device manufacturers to clarify statutory or regulatory requirements. Are you concerned that requiring notice and comment for guidance documents would lengthen the amount of time that it would take for the FDA to respond to industry's need for guidance?

Mr. THOMPSON. I tried to make clear that the FDA has mischaracterized our petitior as requiring notice and comment for

guidance documents. That simply isn't true. We don't even suggest that guidance documents undergo notice-and-comment rulemaking. What we suggest is that substantive rules and interpretive rules undergo notice and comment.

The vast majority of guidance documents don't contain either of those categories of information, and for those we suggest good guidance practices. "Good guidance practices," as we defined them, are something much short of notice and comment, but nonetheless designed or calculated to get the appropriate amount of public input.

So we don't have the fear that it will slow down the process.

Mr. DAVIS. Thank you. Just one last question for Mr. Thompson.

In Mr. Lenard's testimony, he suggests that many American firms are relocating their facilities to other countries where the regulatory climate is more favorable. Are you aware with this happening with any Indiana firms?

Mr. THOMPSON. I understand, just anecdotally or, I should say, through rumor, that it happened. I have not systematically surveyed our membership to find out what's going on. The Health Industry Manufacturers Association did do a nationwide survey that included Indiana companies and found a significant problem in that regard, and that would include, I suppose, Indiana. But we didn't do an independent survey.

Mr. DAVIS. Where are the results of that research available?

Mr. THOMPSON. From the Health Industry Manufacturers Association.

Mr. KIMMELMAN. I'm sure, if you called HIMA, they would provide you with a copy. It's the Wilkerson report. It was just released a couple of months ago. And if they won't, give me a call, and I will get you a copy.

Mr. DAVIS. Thank you.

Mr. SOUDER [presiding]. I want to thank all of you for coming today. It's obviously a very difficult issue, and I think one of the points that we're hoping to bring out is that there are risks in both directions: risks if you don't have the devices on the market, and risks if you do have the devices on the market. And there are concerns, if we accelerate it too fast, it's tough to take the devices back out. We have to be careful as we make the changes, in one direction, not to overcompensate that way, also.

But I am really pleased with the Hudson survey that is beginning to have a breakthrough to show there are risks on both sides of the equation by delays and holding up things as well as by accelerating.

Do you want to make a comment, Mr. Kimmelman?

Mr. KIMMELMAN. Just one last comment. I think you will find the same kind of information in this Wilkerson report, in a very dramatic way. There are over 100 specific examples of useful medical devices that are available elsewhere in the world but not yet available in the United States. So you can enter that into the mix also.

Mr. SOUDER. Thank you very much. I want to thank the staff of both subcommittees, and thank you all for coming.

The hearing is now adjourned.

[Whereupon, at 5:05 p.m., the subcommittees were adjourned.]

[Additional information submitted for the hearing record follows:]

CCBC
Council of Community Blood Centers

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Testimony of the Council of Community Blood Centers
House Government Reform and Oversight
Subcommittees on Human Resources and Intergovernmental Affairs
and
National Economic Growth, Natural Resources and Regulatory Affairs
September 14, 1995

Mr. Chairman and members of the Subcommittees:

The Council of Community Blood Centers (CCBC) submits this statement in support of the efforts of these Subcommittees to evaluate the manner in which the Food and Drug Administration (FDA) promulgates and enforces binding rules. Furthermore, CCBC generally supports the citizens petition of May 2, 1995, filed with the FDA by the Indiana Medical Device Manufacturers Council, Inc. and Baker & Daniels (Citizens Petition), which addresses this matter. This issue is of great importance to those regulated by FDA and to the American public.

CCBC is an association of 67 independent, not-for-profit community blood centers nationwide. CCBC's members are not part of the American Red Cross network. Our members collect approximately 40 percent of the total volunteer blood supply in the US, and provide various therapeutic, tissue banking, stem cell, and laboratory services.

CCBC's members collect and distribute a wide array of blood and blood components heavily regulated by the FDA's Center for Biologics Evaluation and Research (CBER). The standards for licensure of these products, as well as other regulatory requirements, are developed under the authority of the Public Health Service Act (42 U.S.C. § 262) and the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 321, *et seq.*). Both statutes provide rulemaking authority allowing FDA to implement regulatory rules. The rules governing the licensure of blood and blood components are principally contained in 21 C.F.R. Parts 600-680. Other rules throughout 21 C.F.R. Parts 1-1300 are applicable to blood and blood components as well. Thus, CCBC members have a keen interest in FDA's use of the rulemaking process.

The issue raised by the Citizens Petition is whether, in recent years, FDA has failed to utilize legally required rulemaking procedures when implementing new rules, choosing instead to convey rules in a wide array of guidelines, points to

consider, and other documents directed to regulated parties. CCBC agrees with the Citizens Petition that an unfortunate result of this practice is that FDA too often has formulated its "informal guidance" solely within the agency and has not brought the public into the process. Further, during the development of this informal guidance, on occasion, FDA personnel have treated such guidance as if it were a binding rule.

We have two fundamental criticisms of this approach. First, as the Citizens Petition observes, many of these pronouncements in reality are substantive new rules that legally are required to be promulgated pursuant to the public notice and comment procedures in the Administrative Procedure Act (APA), 5 U.S.C. § 553. Although the line between informal guidance and a substantive new rule is not always easy to draw, the Citizens Petition demonstrates that FDA indisputably has crossed the line on a number of occasions in the recent past.

Second, and equally important, the Citizens Petition shows that FDA's failure to reach outside the agency for public input concerning regulatory proposals is not sound policy, even in instances where the APA's notice and comment procedures are not strictly applicable. In the fast-changing world of medical science, FDA cannot possibly craft rules that make sense if FDA fails to take advantage of the rich knowledge, broad experience, and substantial expertise among those in blood banking academia, health professional and consumer groups. The Citizens Petition provides many examples of the impoverishment of FDA's regulatory approach that has resulted from its recent tendency to fly solo.

CCBC, over the last decade, has noted a disturbing trend at FDA of moving dramatically away from the use of rulemaking. In the area of blood and blood components, FDA's CBER has promulgated, at best, a handful of final rules. In contrast, from 1982 to 1994 CBER issued 112 informal guidances, including guidelines related to blood and blood components specifically. Increasingly, over the last few years, these informal guidance documents have been formulated with limited public input. For example, CBER has used guidance documents for blood donor testing (HTLV and hepatitis C tests), donor screening (hepatitis and risk behavior screening), error reporting requirements, and donor re-entry protocols. Furthermore, FDA has increasingly applied these guidelines as if they were rules, apparently losing sight of their "informal" nature. CCBC suggests that the Subcommittees look at this trend in CBER and throughout FDA and attempt to understand why it is occurring.

CCBC does not mean to suggest that FDA must (or even should) follow the APA's procedures each time the agency offers informal guidance either to FDA personnel or to members of the regulated community. Such guidance is a valuable tool for ensuring consistency among FDA personnel and for signaling

to the community FDA's likely enforcement approach in areas of uncertainty. The value of this flexible tool might be lost if FDA were in all cases forced to adhere rigidly to the APA's procedures. Nonetheless, the point is that even FDA's informal guidance would benefit greatly from public input. This input need not take the form of APA notice and comment. FDA could, for example, circulate proposed guidance to the affected parties for informal comment, or take other steps to foster a dialogue between the agency, the regulated community, and patients (such as negotiated rulemaking, or another form of consensus development).

In addition, FDA needs to better understand that much of the value of informal guidance lies in its flexibility. FDA must retain the discretion to depart from informal guidance in appropriate circumstances, and the agency must be willing to actually exercise this discretion. Otherwise, such guidance really amounts to a substantive rule, for which it is appropriate to apply the full panoply of APA notice and comment procedures. The agency sometimes has lost sight of this important distinction and has rigidly refused to tailor its supposedly informal guidance to fit the situation at hand.

Finally, the Citizens Petition requests three actions from FDA to bring meaningful public participation back into the development of new rules and guidance. First, the Citizens Petition proposes an amendment to return FDA's rulemaking regulations to the pre-1991 state, in which the agency had committed itself to following notice and comment procedures when issuing interpretive rules and rules of agency practice that ordinarily are exempt from the APA's requirements. Second, the Citizens Petition asks FDA to institute written procedures to guarantee some level of meaningful public participation in the development of guidance documents. Third, and finally, the Citizens Petition requests that FDA adopt written procedures to better control communications by agency officials with the public, in order to avoid the improper, unilateral announcement of new rules that should have undergone notice and comment rulemaking. CCBC supports all three of these proposals as an excellent start in the right direction. We recognize, of course, that there may be additional valid solutions to the problem. The key, in our view, is to focus on devising easy means of bringing the public into the process without thereby imposing a procedural straightjacket on FDA. We are confident that the Subcommittees' hearings will aid in the search for ways to achieve this important goal.

CCBC thanks the Chairman and members of the Subcommittees for this opportunity to present our views.

Attachments:

1. IN Medical Device Manufacturers Petition
2. Hudson Institute Report
3. Warning Letter
4. Talk Paper
5. Text of Commissioner's speech

Attachment 1

IMDMC

INDIANA MEDICAL DEVICE MANUFACTURERS COUNCIL, INC.

PRESS RELEASE

For further information,
contact Brad Thompson
(317) 237-1195

FOR IMMEDIATE RELEASE
May 2, 1995

Today, the Indiana Medical Device Manufacturers Council (IMDMC) and the law firm of Baker & Daniels filed a Citizens Petition at the United States Food and Drug Administration (FDA) asking the agency to halt its practice of developing new rules without adequate public participation. While the IMDMC and Baker & Daniels support FDA's efforts to create useful guidance documents explaining how to comply with the law, the Petitioners have become concerned by the growing tendency of the agency to use these documents to avoid the notice and comment procedures that federal agencies must follow to ensure public participation in development of regulations.

The timing of this Petition is motivated in part by the Petitioners' hope and belief that this year, to reduce the burden of unnecessary regulation, Congress will adopt statutes restricting the ability of federal agencies to promulgate new regulations. If Congress does, or even if FDA simply wishes to appear to embrace the anti-regulatory sentiment of the Congress, FDA may be tempted to expand even further its practice of announcing significant new rules through means other than regulations.

The Petition recites numerous examples of instances in which FDA has announced new requirements that were not developed with public participation. Not only do these practices violate the Administrative Procedures Act, FDA loses the benefits of that participation. Involving the public in rulemaking invariably leads to more sensible rules. Rules cannot be developed in a vacuum, and the insights and wisdom offered by consumers, academics and the regulated community can often lead to more effective and efficient regulatory approaches.

The Petition requests that FDA add back certain language that the agency deleted from its regulations in 1991 requiring notice and comment procedures for most rules. For guidance documents that do not impose new rules, the Petition requests that FDA implement a consensus-based approach to the initiation, development and issuance of those documents. In addition, to ensure compliance with the law, the Petition asks FDA to adopt greater internal controls over its communications with the public.

The IMDMC is a nonprofit association of 31 large and small Indiana medical device manufacturers and 17 associate members in allied industries that are significantly affected by new rules -- both official and unofficial -- that FDA adopts. Baker & Daniels, as a law firm representing the IMDMC and companies selling food, drugs and medical devices totalling over $100 billion a year, is vitally interested in the process by which FDA promulgates new rules.

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May 2, 1995

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
Room 1-23
12420 Parklawn Drive
Rockville, MD 20857

CITIZENS PETITION

On behalf of the Indiana Medical Device Manufacturers Council, Inc. ("IMDMC") and Baker & Daniels, the undersigned submits this Petition under section 553 of the Administrative Procedures Act ("APA") (5 U.S.C. § 553) to request the Commissioner of Food and Drugs to amend the regulations of the United States Food and Drug Administration ("FDA") defining the circumstances under which the agency will use the notice and comment rulemaking procedures set forth in 21 C.F.R. § 10.40.

In particular, while we support FDA's efforts to disseminate useful guidance that does not rise to the level of a rule, we request that FDA halt its practice of developing new rules without adequate public participation and announcing them through improper means such as speeches, warning letters, and draft guidance. While this problem has been growing over the last several years, the timing of this petition is motivated in part by our hope and belief that this year, to reduce the burden of unnecessary regulation, Congress will adopt statutes restricting the ability of federal agencies to promulgate new regulations. If Congress does, or even if FDA simply wishes to appear to embrace the anti-regulatory sentiment in the Congress, FDA may be tempted to expand even further its practice of announcing significant new rules without the benefit of notice and comment rulemaking.

The IMDMC is a nonprofit association of 31 large and small Indiana medical device manufacturers and 17 associate members in allied industries that are significantly affected by new rules -- both official and unofficial -- that FDA adopts. Baker & Daniels, as a law firm representing the IMDMC and companies selling food, drugs and medical devices totaling over $100

billion a year, is vitally interested in the process by which FDA promulgates new rules.

A. Actions Requested

1. Amend Rulemaking Regulation. To add back language assuring the appropriate use of rulemaking that the Commissioner deleted in 1991, petitioners request that the Commissioner amend FDA's regulation at 21 C.F.R. § 10.40(b) (first sentence) and (d) to read as follows:

> (b) Except as provided in paragraphs (d) and (e) of this section, each regulation must be the subject of a notice of proposed rulemaking published in the Federal Register.
>
> . . .
>
> (d) The provisions for notice and comment in paragraphs (b) and (c) of this section will apply to interpretive rules and rules of agency practice and procedure except as provided in paragraph (e) of this section. Paragraphs (b) and (c) of this section do not apply to general statements of policy in the form of informational notices published in the Federal Register or to matters involving agency organization.

This rulemaking process obviously could include negotiated rulemaking as described in the Negotiated Rulemaking Act of 1990, 5 U.S.C. § 561 et seq.

2. Guidance Development Procedures. While some of the guidance documents that FDA issues might not rise to the level requiring notice and comment rulemaking under 21 C.F.R. § 10.40, FDA should control the initiation, development and issuance of even these proper guidance documents by written procedures that assure the appropriate level of meaningful, public participation. Along the lines of negotiated rulemaking, this might take the form of a negotiated or consensus-based approach first to establishing the need for guidance and then to developing the guidance documents themselves. Organizations such as the Association for the Advancement of Medical Instrumentation have developed procedures that are well-suited to facilitating this process.

3. Written Controls Over Broad, Public Communications. FDA should adopt stricter, written internal controls over communications by agency officials to broad, public audiences.

FDA should design these written procedures to ensure that the agency uses notice and comment rulemaking whenever required by its regulations. The communication vehicles that have been particularly misused include warning letters, media interviews, journal articles and editorials, speeches, guidance documents, points to consider, and other such vehicles used to communicate to a general audience.[1/] The internal controls should include written procedures for the development and approval of all communications to a general audience, including a requirement that a central office such as the Office of General Counsel ("OGC") at FDA review all such broad communications before FDA releases them.

B. Statement of Grounds

1. Policy to Which Petitioners Object.

Over the last several years, FDA has repeatedly announced what amount to new legal obligations for the regulated community under the guise of mere policy statements or statutory interpretations. These new requirements have added considerably to the cost of food, drugs, biologics, and medical devices, without a corresponding benefit to the public health or welfare. Developing new rules without adequate public input leads the agency to develop inefficient regulatory schemes that are based on an inadequate understanding of both the problem and the available solutions. In addition, FDA often overestimates the true extent of the problem or concern it seeks to eliminate.

Once in a while, FDA's use of non-public processes to develop regulatory requirements injures a particular company enough to cause the company to challenge the agency in court. This happened recently when a company successfully enjoined FDA from enforcing substantive rules on human tissue recordkeeping developed without notice and comment. Biodynamics v. U.S., No. 95-919 (D. Md. April 14, 1995) (order granting preliminary injunction). But these instances involving litigation are merely the tip of an iceberg.

Indeed, the wide-spread use by FDA of guidance documents and other such vehicles to develop and communicate new rules reveals a de facto agency policy against meaningful public participation

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1/ Warning letters, although directed at an individual firm, communicate a message to a broad audience because they are watched closely by the trade press and publicized when they include significant new requirements.

in this form of rulemaking. The extent and nature of this policy can be illustrated best through examples.

a. Drugs

One area where FDA makes significant use of unofficial regulatory vehicles to announce new rules is the regulation of prescription drug promotion. In this area, the statute only provides very general guidance by, among other things, prohibiting false or misleading statements in labeling (21 U.S.C. § 352(a)), and FDA's regulations on prescription drug advertising occupy only a few pages of the Code of Federal Regulations. 21 C.F.R. Part 202. Given the vagueness of that law, FDA has used vehicles outside of notice and comment rulemaking to impose new requirements on the prescription drug industry.[2/]

In particular, FDA has used industry-wide letters to announce significant restrictions on promotion practices. In a July 1993 letter, FDA announced that the agency had adopted a policy of requiring that all direct-to-consumer advertisements be pre-cleared by FDA.[3/] This is a particularly significant requirement, since the Federal Food, Drug and Cosmetic Act ("FFDCA") explicitly states that FDA shall not require pre-clearance of advertisements except in extraordinary circumstances. The statute also states that to adopt regulations on prescription drug advertising, FDA must use the special rulemaking procedures of section 701(e) of the act. 21 U.S.C. § 352(n).

In an April, 1994 letter to the pharmaceutical industry, FDA gave guidance on a variety of issues related to promotion and advertising of drugs.[4/] Those issues included broadcast

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2/ Cooper, Marketing "Violations", 47 Food Drug L.J. 155 (1992).

3/ Letter from Janet L. Rose, Director, Division of Drug Marketing, Advertising and Communication, Office of Drug Evaluation I, FDA, to the holders of new drug applications, abbreviated new drug applications and abbreviated animal drug applications in July 1993.

4/ Letter from Janet L. Rose, Director, Division of Drug Marketing, Advertising and Communication, Office of Drug Evaluation I, FDA, to holders of new drug applications, abbreviated new drug applications, new antibiotic applications, and abbreviated new antibiotic applications in April 1994.

advertisements, requirements for comparative claims, direct-to-consumer advertising, fair balance in context and format, formulary kits as promotional labeling, wrap-around advertisements, and unsolicited requests for information. Through this guidance, and without any input from the public, FDA imposed significant new rules such as the requirement that companies retain documentation of the nature of unsolicited requests for information. Yet this issue of unsolicited requests is completely unaddressed by FDA's regulations.

To make matters worse, FDA also explained in the April, 1994 letter that it will soon release new guidance with regard to unsolicited requests for information, but did not invite any public participation in the development of that guidance. Moreover, FDA stated that while it continues to deliberate on this issue, the regulated community should adhere to FDA's statement on that subject issued in 1982, also without public input. Beyond its failure in 1994 to seek comment about an industry quite different from the one that existed in 1982, FDA devoted only a page to an issue that is quite complicated and deserving of more careful analysis. FDA would know this if it had sought public comment. For now, however, industry must risk enforcement decisions by FDA over how the agency will interpret an outdated, overly simplistic, vague statement that FDA is treating as a binding rule.

FDA also has made significant use of speeches to regulate drug promotional practices. For example, an FDA spokesperson recently gave a speech addressing the use of "help-seeking" advertisements in which the advertisement, without mentioning any particular product, describes a disease and urges the consumer to call his or her physician.[5/] In the speech, FDA announced that the agency has decided to limit help-seeking advertisements to diseases for which there are other therapies in addition to drugs.

The agency's tendency to avoid notice and comment rulemaking is evident in the comparative claim area where FDA's regulations do not spell out many of the significant requirements for such claims, except to state that the claim must be supported by substantial evidence.[6/] Rather than use the proper rulemaking

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5/ Remarks by Nancy M. Ostrove, Ph.D., Division of Drug Marketing, Advertising, and Communications, Office of Drug Evaluation I, FDA, before the Regulatory Affairs Professional Society in Chicago, Illinois on March 2, 1994.

6/ 21 C.F.R. § § 201.57(c)(3)(v) and 202.1(e)(6)(ii).

procedures, FDA simply announces the requirements for comparative claims in informal documents, and ratchets up the requirements over time. For example, in the FDA's Compliance Policy Guidance Regarding Comparative Promotional Claims drafted in July, 1982, FDA asserts that companies must support comparative claims with two or more adequate and well-controlled studies, unless 1) the company has one very large and particularly sound study or 2) the company disseminates enough information to describe a single study completely. Apparently, however, FDA has reconsidered that policy. Based on recent warning letters, one would have to conclude that the agency at the present time is not as flexible as that guidance would suggest.[7/]

FDA also uses this regulatory approach for cost-effectiveness claims. While FDA's requirements for such claims are not specified in the regulations, FDA seems to have informally adopted an almost blanket policy against them. In a speech, one agency spokesperson explained why FDA views cost-effectiveness comparisons so skeptically.[8/] That official asserted that because the term "cost-effective" does not have a specific, identifiable meaning, a claim of "cost-effective" is automatically deceptive unless the labeling amply explains the basis for the claim. The flurry of agency warning letters over the last couple of years suggests that FDA simply does not allow most cost-effectiveness comparisons.[9/] And even more recently, FDA issued draft guidance that would impose extremely rigorous requirements for making such claims, including the requirement that in most cases the claim must be supported by two adequate and well-controlled studies.[10/]

7/ E.g., FDA warning letters to Glaxo Pharmaceuticals (1/13/93); Eli Lilly & Company (7/19/94); Marion Merrell Dow (10/13/92); Roxane Laboratories (6/22/93); The Upjohn Company (11/25/92).

8/ Remarks by Louis A. Morris, Ph.D. at the Pharmaceutical Advertising Council, New York, New York, September 11, 1986.

9/ E.g., FDA warning letters to Antibody Assay Laboratories (8/16/92); Berlex Laboratories, Inc. (4/2/93); Eli Lilly and Company (7/19/94); Knoll Pharmaceutical (10/14/93).

10/ Draft Principles for the Review of Pharmacoeconomic Promotions (March 20, 1995).

b. Biologics

Like the regulation of drug promotion, FDA's regulation of biologic promotion is largely informal. FDA's regulations in 21 C.F.R. Part 601 have very little to say about the labeling of biologics. Instead, FDA uses the Advertising and Promotional Labeling Staff Procedural Guide to communicate its expectations to industry. FDA created and implemented the manual in 1993 without any public input. See 58 Fed. Reg. 42340 (August 9, 1993). Later, after receiving comments in response to a notice of availability (rather than the process required for rulemaking under 21 C.F.R. § 10.40), FDA belatedly revised the manual in 1994, but left in place many of the substantive rules. 59 Fed. Reg. 39570 (August 3, 1994).



Another example of the FDA's failure to involve the public in rulemaking is the agency's approach to developing recordkeeping requirements for "banked human tissue." In Biodynamics v. U.S., No. 95-919 (D. Md. April 14, 1995), the court issued a preliminary injunction against FDA's efforts to detain some human tissue imported by Biodynamics. FDA had ordered the tissue detained because the recordkeeping procedures for the tissue did not comply with a December, 1993 interim rule made effective without notice and comment. 58 Fed. Reg. 65514 (December 14, 1993). This "interim rule" actually was an entire new part to Title 21 of the Code of Federal Regulations comprised of eight separate regulations addressing a subject area that previously was essentially unregulated. See 21 C.F.R. Part 1270. In developing that interim rule, FDA suspended the normal notice and comment process because of what FDA characterized as an immediate need to protect the public health from the transmission of disease through transplantations. While FDA accepted comments on the interim rule after it became effective and suggested that the agency would quickly develop a revised program, the agency had not yet responded to the comments or issued a revised rule more than a year later when it ordered the detention of the Biodynamics tissue.

FDA also based its detention order on some agency Inspection Guidelines that added to the interim recordkeeping rules, but which FDA had never published or subjected to comment. The Inspection Guides required sellers of banked human tissue to document several specific types of hard-to-obtain information about the medical histories of the tissue donors. These records were supposed to include information on such subjects as the donor's lifestyle to determine whether the donor was at risk for AIDS or hepatitis. After an initial hearing, the District Court concluded that FDA unlawfully promulgated the interim rules and

Inspection Guides in violation of the APA, and ordered the tissue released.

c. Medical Devices

In the context of medical devices, a classic example of a rule announced through a speech is the so-called reference list. In July 1992, Ronald Johnson, then Director of the Office of Compliance at FDA's Center for Devices and Radiological Health, announced during the Health Industry Manufacturers Association's ("HIMA's") Second Annual Submissions Workshop, that CDRH was using the so-called reference list to determine whether medical device companies are in compliance with the Good Manufacturer Practices prior to clearance of the 510(k) submission. It was only after a significant ground swell of opposition from industry that FDA more than a year later published information about the reference list in the Federal Register. 59 Fed. Reg. 57614 (October 26, 1993).

After two organizations questioned the legality of the reference list in Citizens Petitions filed with the agency,[11/] FDA is redesigning the reference list program under a different name. As announced in an April 7, 1995 industry-wide letter, FDA soon will disseminate a compliance program guide describing a procedure for linking Good Manufacturing Practices (GMP) compliance to premarket notification clearances. Based on the FDA's letter, it appears that this new program will articulate significant new rules for when a GMP deficiency will hold up a 510(k) clearance. Remarkably, despite the many complaints lodged with FDA about the agency's process for creating the reference list, FDA made this redesigned program effective on May 1, 1995 without any substantial public input.

FDA has taken a similarly unofficial approach to regulating computer software. In the late 1980s, FDA released a couple of draft guidances on the "FDA Policy for the Regulation of Computer Products". The most recent of those draft guidances was released on November 13, 1989. That guidance identifies the circumstances under which software will constitute a medical device under the FFDCA. While FDA last year announced its intention to update that policy once again, the agency has never taken the draft designation off the document. 20 M-D-D-I Reports 20 (May 9, 1994).

11/ Citizens Petitions filed by Hyman, Phelps & McNamara (No. 94P-0323, September 2, 1994) and the Health Industry Manufacturers Association (No. 94P-0389, October 25, 1994).

The unofficial status of FDA's rules with regard to the regulation of computer software has not kept FDA from enforcing those rules. In a March 31, 1994 letter to the device industry, Kathryn Zoon of the Center for Biologics Evaluation and Research announced that software used in blood establishments is a device under the FFDCA when it is intended for use in the manufacture of blood products. The letter required blood establishment computer software manufacturers to register with FDA within sixty days of receipt of the letter and to submit a 510(k) by March 31, 1995, among other things. FDA Talk Paper 94-21 (April 13, 1994). In addition, FDA recently issued several warning letters advising companies that their software programs used in blood banks constitute medical devices.[12/] FDA did all of this without ever amending the agency's regulations. In particular, FDA has never revised its classification regulations to classify software used at blood banks as a finished medical device.

An example of regulation through industry-wide correspondence in the medical device context is FDA's adoption of a certification program for investigational and research in vitro diagnostic (IVD) devices. This new program initially was announced on October 17, 1991, through a letter to the entire medical device industry from the Director, Office of Compliance and Surveillance, CDRH. The letter describing the certification program included significant new obligations for IVD manufacturers and was initially developed without any significant input from the public. Moreover, the letter added regulatory controls that FDA had specifically considered and rejected in prior rulemaking proceedings. In that regard, using the letter to announce the new rules clearly departed from the requirements of notice and comment rulemaking under the APA.[13/] The agency has since sought to define the certification requirements in a Compliance Policy Guide, but thus far has not finalized that CPG. Even so, FDA has enforced its requirement that companies adopt

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12/ e.g., FDA warning letters to Blood Bank Computer Systems, Inc. No. SEA 94-55 (June 28, 1994), Collaborative Medical Systems, Inc. No. BOS-24-93W (April 9, 1993) and Western Star Business Systems, Inc. No. SEA 92-83 (August 17, 1992).

13/ Thompson, The Food and Drug Administration's New Rules for Investigational and Research IVDs, 4 Regulatory Affairs 305 (1992) (copy attached.)

additional controls to ensure that research and investigational IVDs are used only for those purposes.[14/]

FDA's approach to components used in orthodontic appliances is a good example of an instance in which FDA used warning letters to announce new rules. In about 1992, FDA apparently became concerned about its ability to regulate orthodontic appliances. Orthodontists manufacture orthodontic appliances on a custom made basis for individual patients. Because of the administrative burden associated with trying to regulate the activities of thousands of orthodontists, FDA instead decided to regulate the component suppliers. But the FDA's classification regulations did not (and still do not) classify the components as finished medical devices. E.g., 21 C.F.R. § 872.5410. This is in contrast to FDA's classification regulations for components such as mercury and other base metal alloys used by dentists to make fillings. E.g., 21 C.F.R. §§ 872.3700 and 872.3710. Rather than amend its classification regulations to classify resins and other materials used to make orthodontic appliances as finished medical devices, FDA chose simply to push orthodontic supply companies into filing 510(k)s.[15/]

Yet another example of FDA's preference for draft guidance over rulemaking is the agency's recently released Draft Points to Consider (PTC) for Collection of Data in Support of In-vitro Device Submissions for 510(k) Clearance (September, 1994). This draft PTC recites in very forceful terms what is expected of IVD manufacturers when submitting a premarket notification. Indeed, the PTC attempts to expand FDA's regulations in the area of labeling, and specifically with respect to claims made in package inserts, as explained in comments filed by HIMA earlier this year.

HIMA filed those comments without being invited to do so because of the concern of its members that FDA developed the document entirely without public input. Not only did FDA not follow any process remotely resembling notice and comment rulemaking, but the agency also missed an easy opportunity to gain public input at its September 22, 1994 advisory panel meeting by waiting to distribute the draft document until the meeting, thus not allowing for preparation. Even though the

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14/ E.g., FDA warning letters to American Biochemicals (W.L. 77-3, 7/20/93); Gen-Trak (94-PHI-28, 2/25/94) and Lampire Biological Laboratories (93-PHI-50, 6/1/93).

15/ E.g., FDA warning letter to Professional Positioners, Inc. No. MIN 92-131 (June 19, 1992).

document is stamped "draft", HIMA's members report that the FDA reviewers already are rigidly using the requirements outlined in the PTC to review 510(k) submissions.

FDA also has decided not to use rulemaking to identify the devices subject to the medical device tracking requirements. The tracking requirements add considerable cost to a medical device, and FDA's practice of deciding unilaterally which devices fall within the scope of the tracking requirements without the benefit of notice and comment is quite remarkable.[16/]

In each of these areas, FDA has abandoned the requirement of notice and comment rulemaking by announcing rules through informal vehicles. But in doing so, the agency confuses form with substance. In many of the instances recited above, FDA has tried to put rules in a form that the agency thought would save it the expense of notice and comment rulemaking. This form, for example, has included simply stamping draft on a document or adding language at the end of the document suggesting that the document represents only one approach to compliance, and others might be acceptable.

These forms, however, do not change the substance of what FDA does with respect to these new rules. As the U.S. District Court for the District of Columbia held recently, merely stamping a document as draft is not determinative of its nature. Washington Legal Foundation v. Kessler, Slip Op., Cause No. 94-1306 (March 9, 1995). If that were so, FDA could effectively regulate industry without ever exposing itself to judicial review. Id. On many occasions, FDA has enforced the contents of these documents, despite the draft stamp or the language suggesting that the agency is open to alternatives. Indeed, FDA's actions demonstrate that FDA believes the new rules in fact to be binding requirements despite their packaging.

2. Source of the Problem

The problem of FDA announcing significant new rules through improper means is not a new one and stems from the FDA's basic desire to conserve its resources. However, the problem has become considerably worse since 1991 when the agency amended its regulations to no longer require itself to undertake notice and comment rulemaking for interpretive rules. 56 Fed. Reg. 13757 (April 4, 1991). Before that date, FDA's own regulations

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16/ Thompson, Keeping Track of Medical Devices, 11 Food, Drug, Cosmetic and Medical Device L. Digest 24 (1994) (copy attached.)

required it to utilize notice and comment rulemaking for substantive and interpretive rules and rules of agency practice and procedure. Now that FDA regulations only require notice and comment rulemaking for substantive rules, not only do some officials within FDA erroneously conclude that a given rule is interpretive rather than substantive (and thus fail to utilize notice and comment rulemaking when required by the APA), but also the public misses out on the opportunity to comment on interpretive rules.

Concurrently with the agency's decision to relax its own regulations with regard to notice and comment rulemaking, the agency also decentralized its organizational structure to give certain offices within FDA greater autonomy. In Commissioner Kessler's own words, one of FDA's principal goals in 1991 was to "empower" all FDA managers.[17] According to Dr. Kessler, "it is only when Center Directors and their managers feel they have the authority to act that they can fairly be held accountable."[18]

In the context of product reviews and approvals, Dr. Kessler's efforts to empower FDA managers have resulted in the decision-making authority being pushed to lower levels. For example, in the Office of Device Evaluation at the Center for Devices and Radiological Health, the authority to sign most kinds of decisions on 510(k)s has been pushed to lower levels within the office. ODE Memorandum No. K94-2 (June 3, 1994). While this streamlining of the approval process has provided some welcomed relief to device manufacturers facing significant delays in obtaining approvals, it also has resulted in new rules being developed and applied in the approval process without the benefit of notice and comment rulemaking. Empowerment is a good thing, but it needs to be accompanied by clear, predictable and properly established standards to guide the conduct of the empowered managers.

This decentralized structure also is evident in the agency's largely unwritten and fluid policy regarding the issuance of guidance. See Staff Manual Guides, Chapters 1200 and 1400. Any unit within the FDA may develop guidance for its own purposes. And before guidance is released to the public, a high level manager may or may not have even signed off on it. In the case

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17/ Remarks of Commissioner David Kessler to the Drug Info Association (June 17, 1991).

18/ Remarks of Commissioner David Kessler to the Annual Educational Conference of the Food and Drug Law Institute, Washington, D.C. (December 11, 1990).

of the Office of Device Evaluation, for example, any level from the individual reviewer on up can develop guidance. There exists only an informal understanding that a group within ODE should not release a guidance until at least a division director has accepted it. The extent of public participation through advisory panel input or distribution to specific industry groups is largely left to the discretion of the group developing the guidance.

These guidances have the laudable goal of increasing consistency among reviewers. But while the agency says that they are living documents that describe only one acceptable approach among perhaps many, in practice the industry finds that reviewers often treat these guidances as specific, inflexible legal standards. Thus, since FDA has no written procedures controlling how guidances are developed, approved, and implemented, and since some of these guidances become at least de facto standards, FDA in effect produces some very important rules with very little public input.

An example of Dr. Kessler's empowerment initiative in the context of the FDA field force is contained in the procedures for warning letters. Regulatory Procedures Manual, Chapter 8-10 (5/23/91). Under the RPM, district offices can send warning letters in most cases without oversight from FDA headquarters.[19] Section 8-10-40. This practice in effect allows district offices to make independent evaluations regarding whether a requirement contained in a warning letter represents a new substantive rule requiring notice and comment rulemaking.

This decentralization of the organizational structure at FDA has allowed many of the offices within the agency to independently adopt new rules and policies and effectively to impose these rules and policies on the public without ever having the benefit of public comment. Greater oversight of the issuance of warning letters, guidance and other such documents by some group well-versed in the procedural requirements in 21 C.F.R. part 10 therefore is needed to prevent this from continuing.[20]

19/ The few instances where center concurrence is necessary for a warning letter to issue are specifically listed in section 8-10-45 of the RPM.

20/ Compounding our concern is the agency's apparent intention to relax its rulemaking process by making advisory opinions, including guidelines, no longer binding on the agency. FDA proposed this change in 1992, and has not yet published its (continued...)

While the volume of product approval decisions and associated guidance makes it inefficient and unreasonably burdensome for a group outside of ODE to oversee that process, the OGC or some other suitable group could assist in the training of reviewers to educate them with regard to identifying new rules that require notice and comment rulemaking.

3. Legal and Policy Bases for Our Objections

The actions requested would both bring FDA policies and practices into compliance with the requirements of the APA, and also assure the benefits of greater public participation in the rulemaking process.

The APA requires federal agencies to observe the notice and comment requirements whenever an agency seeks to adopt a substantive rule. 5 U.S.C. § 553. A "rule" is an agency's statement of general or particular applicability and future effect designed to implement, interpret or prescribe law or policy. 5 U.S.C. § 551(4).

All of the examples recited above constitute rules in that they represent statements of applicability, with future effect, designed to implement their respective portions of the FFDCA. In the case of the medical device tracking regulation, for example, the FDA's list of devices falling within section 519(e)(1) clearly meets that description. FDA's regulatory activity with regard to the promotion of prescription drugs is based on essentially three statutory sections -- section 201(n) on fair balance, section 502(a) on false or misleading labeling and section 502(n) on prescription drug advertisements. Similarly the FDA software policy is simply an interpretation of section 201(h) defining a device.

A rule is "substantive" if it creates rights, imposes obligations, or effects a change in existing law. Yesler Terrace Community Council v. Cisneros, 37 F.3d 442 (9th Cir., 1994). In addition, a substantive rule narrowly limits an agency's administrative discretion. State of Alaska v. U.S. Department of

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final intentions. 57 Fed. Reg. 47314 (Oct. 15, 1992) If FDA takes this step, the agency essentially could impose new rules through a variety of informal means while at the same time leaving itself the flexibility to change these rules at its whim. Binding advisory opinions are a very efficient regulatory tool that FDA should preserve.

Transportation, 868 F.2d 441, 445-447 (D.C. Cir. 1989); Community Nutrition Institute v. Young, 818 F.2d 943 (D.C. Cir. 1987).

Thus, to determine whether a rule is substantive, courts must look at a variety of factors. Those factors include whether the rule is binding in character (with special attention paid to the language of the rule), the amount of discretion accorded the agency, and the agency's own characterization of the rule. Benten v. Kessler, 799 F.Supp. 281, 288-289 (E.D. N.Y. 1992); Bellarno International Limited v. Food and Drug Administration, 678 F.Supp. 410 (E.D. N.Y. 1988). Agency guidances which use words such as "shall" and "will" are routinely found to be legislative or substantive in character. E.g., National Treasury Employees Union v. Reagan, 685 F.Supp. 1346, 1356-1357 (E.D. La. 1988); See also, Bellarno, 678 F.Supp. at 415. Moreover, while the agency's characterization of the regulation is important, it is not conclusive. Phillips Petroleum Co. v. Johnson, 22 F.3d 616 (5th Cir. 1994); Chamber of Commerce v. OSHA, 636 F.2d 464 (D.C. Cir. 1980); National Senior Citizens Law Center, Inc. v. Legal Services Corp., 581 F.Supp. 1362 (D. D.C. 1984), aff'd, 751 F.2d 1391. It is well-settled that exceptions to the notice-and-comment rulemaking requirement of the APA are to be narrowly construed. Wells v. Schweiker, 536 F.Supp. 1314 (E.D. La. 1982).

These principles, when applied to the examples described above, clearly indicate that the rules announced by FDA in many cases are substantive, and should have undergone notice and comment rulemaking. An examination of the documents in which these rules were announced demonstrates FDA's penchant for using dictatorial language such as "shall" and "will", rather than merely providing advice. In the case of the reference list, FDA itself has stated that it routinely uses the list to delay determinations of substantial equivalence under section 510(k).[21/]

Indeed, the binding nature of these various rules can be seen most clearly in FDA's enforcement activity. As already noted, FDA has made generous use of warning letters for comparative prescription drug promotions,[22/] drug cost-effectiveness claims,[23/] computer software for bloodbanks,[24/] and

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21/ Reference List: Letter to the Device Industry from the Center for Devices and Radiological Health, dated January 21, 1993.

22/ See supra, note 7.

23/ See supra, note 9.

research/investigational IVDs.[25] Those enforcement activities demonstrate that the forcefulness of the language of these rules was no accident. In fact, agency observers have published numerous articles reciting examples of FDA's failures to follow notice and comment rulemaking, but for the sake of brevity further examples will not be repeated here.[26]

Even in many circumstances where the APA does not require a rule or policy statement to undergo notice and comment rulemaking (for example, interpretative rules), the benefits of following such a process outweigh the costs. Those benefits of notice and comment rulemaking are well-known. Public participation invariably leads to more sensible rules. Rules cannot be developed in a vacuum, and the insights and wisdom offered by consumers, academics and those upon whom FDA will impose the rules can often lead to more effective and efficient regulatory approaches. Since both healthcare technology and the structure of the healthcare industry are changing at an incredibly rapid rate, FDA by itself simply cannot be expected to keep abreast of those changes. Moreover, the rulemaking process itself results in greater buy-in and compliance by the regulated community as the agency develops a consensus approach. The regulations take

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24/(...continued)
24/ See supra, note 12.

25/ See supra, note 14.

26/ Thompson, Keeping Track of Medical Devices, 11 Food, Drug, Cosmetic and Medical Device L. Digest 24 (1994); Scientists Call FDA Approval of Gene Altered Foods a Sham PR Newswire, Nov. 3, 1994; Note, Benten v. Kessler: The Time for Uniformity in the Application of Section 553 of the Administrative Procedure Act Has Come, 7 Admin. L.J. Am. U. 345 (1993); Alternatives to "Jelly Bean" Health Claim Rule Offered, Food Labelling News CRC Press, Feb. 18, 1993; Pilot, Reform the Product Approval Process Before We All Go Out of Business, Biomedical Market Newsletter, Feb. 1, 1993; Anthony, Interpretive Rules, Policy Statements, Guidances, Manuals, and the Like -- Should Federal Agencies Use Them to Bind the Public?, 41 Duke L.J. 1311 (1992); Cooper, Marketing "Violations", 47 Food Drug L.J. 155 (1992); Strauss, Comment: The Rulemaking Continuum, 41 Duke L.J. 1463 (1992); Thompson, The Food and Drug Administration's New Rules for Investigational and Research IVDs, 4 Regulatory Affairs 305 (1992); Leflar, Public Accountability and Medical Device Regulations, 2 Harv. J. Law and Tec 1 (1989); Holmes, Paradise Postponed: Suspensions of Agency Rules, 65 N.C.L. Rev. 645 (1987).

on an air of legitimacy if the public had an opportunity to help fashion those requirements. In addition, the process of notice and comment itself helps to publicize the requirements, thus educating the regulated community with respect to what is required of them. These benefits, while hard to measure precisely, certainly outweigh the cost of utilizing the procedure outlined in 21 C.F.R. § 10.40.

4. Proposed Solution

The action requested will serve both to bring FDA into compliance with the APA, and to increase the public's participation in the development of rules at FDA to everyone's benefit. As explained above, using notice and comment rulemaking in more circumstances than required by the APA will gain significant benefits for interpretive rules and statements of agency practice and procedure.

The proposed solution also avoids the risk that agency officials will incorrectly decide that a rule is interpretive rather than substantive, and fail to use notice and comment rulemaking when legally required. Agency officials have proven to be too often unable to make those determinations reliably, and as a consequence have adopted new substantive rules through improper means. By requiring notice and comment rulemaking for all rules, FDA would avoid asking its officials to make those difficult and fine distinctions and thus reduce the risk that FDA will mistakenly fail to use the required public process. Because agency officials have a built-in incentive to use rulemaking sparingly to save agency resources, we think there is no other practical and effective solution that will prevent violations of the APA.

The language that we propose adding to 21 C.F.R. § 10.40(b) and (d) is identical to the language that FDA deleted in 1991. 56 Fed. Reg. 13757 (April 4, 1991). As the agency noted at the time, that language requires notice and comment rulemaking in circumstances where the APA does not. When FDA deleted the language, the agency argued that there was no reason to bind itself to following more process than the APA required, and that FDA could always exercise its discretion to utilize notice and comment rulemaking in certain circumstances even when the APA does not. Experience shows, however, that since 1991, FDA has not succeeded in exercising that discretion appropriately, and thus the language should be added back.

To make sure that FDA in fact observes the notice and comment requirements, the various offices within FDA should not be solely responsible for deciding when their pronouncements fall

into the rulemaking realm. We thus request greater control by an office such as OGC over industry-wide communications from FDA to the public. This oversight obviously requires agency resources, but the trade-off in terms of more reliable communications that do not impose significant new requirements at the unbounded discretion of a particular office is well worth those resources. A group like OGC, trained in the requirements of the APA and the FDA's regulations, would be able to decide more objectively and reliably when an announcement constitutes a rule or statement of agency policy requiring notice and comment rulemaking. And in the case of product approvals, rather than reviewing the myriad of communications from FDA, OGC would be able to train the reviewers to spot those rules and statements of agency policy.

As with many of the processes regulated under the Good Manufacturing Practice regulations, FDA could ensure greater quality in its communications to the public if it controlled those communications through a set of unified and consolidated written procedures. In developing those procedures, FDA could borrow procedures from voluntary standard-setting organizations that have developed very sophisticated and effective models for standard setting activities. These procedures could be used as a part of notice and comment rulemaking as allowed by the Negotiated Rulemaking Act of 1990, and also could be utilized in the process for initiating, developing and issuing guidance. This kind of consensus-building works best when FDA invites the public into the process as a partner to participate fully, rather than simply requesting specific, discrete information from the public, as the agency has a tendency to do.

We emphasize that this Petition is directed at broad, public communications from FDA, and not at the communications between the agency and individual companies. In fact, we would like to compliment the Center for Drug Evaluation and Research (CDER) on its willingness to educate and counsel individual companies. Unlike many other federal agencies, CDER often provides written opinion letters to companies with respect to specific factual circumstances. These opinion letters provide useful guidance to the companies, and obviously are not the kind of industry-wide communication that should undergo the processes we describe above.

While the last four years have demonstrated that many of FDA's practices need to be changed, we are especially motivated to file this Petition out of our concern that the current rulemaking reform being debated in Congress, if ultimately adopted into legislation, will tempt the agency to rely even further on improper mechanisms for adopting new rules. Even if Congress does not adopt the reforms, FDA might seek ways to

appear in step with the anti-regulatory sentiment in Congress. In anticipation of that and because of the present de facto policy disfavoring notice and comment rulemaking, we request that FDA reconsider its policy for rulemaking, and adopt the safeguards outlined above.

C. Environmental Impact

The requested action falls within the categorical exclusion from environmental impact statements under 21 C.F.R. § 25.24(a)(8).

D. Economic Impact

Not applicable.

E. Certification

The undersigned certifies that, to the best knowledge and belief of the undersigned, this Petition includes all information and views on which the Petition relies, and that it includes representative data and information known to the Petitioners which are unfavorable to the Petition.

Respectfully submitted,

BAKER & DANIELS,
on behalf of itself and the
Indiana Medical Device
Manufacturers Council, Inc.

By: _____
Bradley Merrill Thompson

BMT/mtm

Attachment 2

THE HUMAN COSTS OF REGULATION: THE CASE OF MEDICAL DEVICES AND THE FDA

David C. Murray

THIS IS A PRE-PUBLICATION DRAFT, SUBJECT TO REVISION AND CHANGE

September 7, 1995

The Competitiveness Center of Hudson Institute

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The Human Costs of Regulation: The Case of Medical Devices and the FDA

by David C. Murray

Medical technology has advanced at an incredible pace over the last fifty years. Physicians and scientists have harvested the fruits of explosive growth in electronics, computing and material sciences by applying revolutionary advancements in these technologies to medical science. These developments have fed upon one another, creating an environment of synergy and rapid innovation.

American consumers have been the ultimate beneficiaries of these technological breakthroughs. Treatments that we take for granted today did not exist only a few short years ago. Thirty years ago, patients suffering from kidney failure had little hope,[1] but today nearly 500,000 Americans benefit from kidney dialysis, and artificial kidneys are now on the horizon.[2] Until only ten years ago, Americans whose hearts spontaneously started to race or stop without warning became just another statistic of sudden cardiac death, but today a defibrillator can be implanted inside the patient's body to save her life. When the heart stops beating normally, the defibrillator sends an electronic shock to the heart, bringing it back into a normal rhythm. Such advancements have benefited literally millions of Americans over the past decades and generated confidence that millions more will live longer and better lives in the decades ahead.

While most of these innovations have been developed in America by American physicians and scientists, American consumers are no longer the first to benefit from these often life-saving and life-enhancing products. All too frequently, new medical devices are approved for use in Europe, Japan, and Canada years before they are approved for use in the United States by the Food and Drug Administration (FDA). The

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[1]Susan Bartlett Foote, *Managing the Medical Arms Race*, pages 98-103.
[2]"Artificial Kidneys May Soon Be Reality," *Medical Materials Update*, 3, no. 3.

delay in introducing these new technologies in America has real consequences for American consumers; consequences that can be quantified in losses in the quality of life, and sometimes even of life itself, for thousands of Americans each year. While proponents of the FDA system argue that these delays are the price that must be paid for a system that ensures safety, there is very little evidence to support this view. Almost all of the medical devices that have encountered serious post-market difficulties have been approved by the FDA. The evidence presented in this paper indicates that in certain instances, the FDA approval system is actually costing lives.

This basic yet vital fact is often obscured in debates over the safety and efficacy of medical technology. Rather, the public and the press have been well sensitized to the dangers of prematurely approving a medical device or drug. While premature approval is certainly a risk, minimizing this risk comes at great cost; it maximizes the risk that the entry of safe and effective new technologies will be delayed, with attendant costs in human lives. Conversely, the absence of all regulation would minimize the risk of delaying the entry of new technologies but would maximize the risk of an unsafe or ineffective product reaching the market. Clearly, neither of these extremes is desirable as public policy -- the risks of one must be balanced against the risks of the other.

To date, however, the risks and costs of delayed entry of medical technologies have fallen on deaf ears, while the costs associated with the very small percentage of unsafe medical devices that have been approved for use by the FDA grab the limelight. Part of this is simply the nature of the phenomena. When a device fails and people are hurt or killed, they are easily identifiable and they, their families, or their lawyers are more than willing to talk about it in front of the news cameras. People who die because a device is not available due to a regulatory backlog, however, are much more difficult to identify. They simply die -- no news coverage, no lawsuits, no investigation. In short, we never hear about it. In the final analysis, though, a human life is a human life. Just because the people who die from the absence of a device that should have been available

are more difficult to identify, does not meant that they should count less than the victims of a defective device when policymakers weigh the costs and benefits of our current policies governing the introduction of new medical technologies.

To bring the magnitude of these human costs to light, this study examines the human costs associated with the delayed entry to the U.S. market of several medical technologies. To do this, the study looks at when a device was approved in Europe, either by an individual country or by receiving the CE mark from the European Community, and when it was approved by the FDA. The difference between these two approval dates is the "regulatory lag" associated with the device. For each device, the study examines the comparative advantages of the new device with its predecessor, with a particular emphasis on improvements in mortality and morbidity. The number of lives that the new device would save per year, relative to the old device or alternative treatments, is then multiplied by the regulatory lag to achieve an estimate of the number of American lives that would have been saved had the new device been approved by the FDA at the same time that it was approved abroad.

For instance, if device Y was approved in Europe in June 1990 and approved in the US in June 1992, the regulatory lag is two years. Suppose device Y has superior capabilities to its predecessor such that operative mortality associated with the device is reduced from 5 percent to 1 percent. Suppose also that 100,000 of these procedures are done per year in the US. The estimated human cost of the regulatory lag would be: regulatory lag (2 years) x percent change in mortality (.04) x number of procedures per year (100,000) = estimated number of lives that would have been saved (8,000 lives). These numbers are, of course, statistical estimates based on the results of the clinical trials conducted for approval of the device. In fact, the actual number of people whose lives would have been saved by the newer devices could be higher or lower than the estimates presented in this report. The estimates presented, however, are based on solid

clinical medical evidence that has appeared in refereed medical journals, which builds confidence that they are reliable.

Note from the beginning that this study is not inclusive of all devices, it is only a baseline from which we can begin to understand the magnitude of the problem. Because it is not a random sample the results cannot be extrapolated to all medical devices, but the overall track record shows that the FDA and the Europeans have erred at about the same rate in pre-maturely approving devices. By focusing on the delayed entry of new technologies, the costs of regulatory delay can be explored. However, there are certainly other medical devices that have life-saving or life-enhancing capabilities that have been introduced more rapidly abroad than in the United States. This estimate, then, is only the bare minimum number of people who have suffered substantial adverse effects from the delayed entry of new medical device technologies into mainstream American medicine. Before examining individual devices, however, it will be useful to review the regulatory regimes utilized by the FDA and the European Community.

Differing Regulatory Regimes

The FDA first received specific authority to regulate medical devices in 1976 when Congress amended the Food, Drug and Cosmetic Act specifically for this purpose. The FDA classified medical devices based on the risk that they could potentially pose to the patient. Low risk devices, such as tongue depressors, reside in Class I. Intermediate risk devices such as X-ray machines are in Class II. High risk devices, such as pacemakers, implantable defibrillators, and coronary stents reside in Class III, the most heavily regulated class of all medical devices.

Before a medical device can reach the market in the United States, the FDA must approve the manufacturer's application for Pre-Market Approval (PMA) or pre-market notification (510(k) application). A device which is "substantially equivalent" to a device that was on the market before the FDA received express authority to regulate the industry

in 1976 need only obtain affirmation from the FDA that the device is equivalent and that the pre-market notification application has been accepted. Nearly 98 percent of all devices come to market through this pre-market notification procedure. Devices in Class I and Class II take this route to market.

Before the Safe Medical Devices Act of 1990, manufacturers needed to give 90 days notice before marketing their products. Unless a manufacturer was notified by the FDA to the contrary, it could go ahead and market its device upon the expiration of 90 days. The 1990 amendments, however, changed the law so that manufacturers could only market their devices if the FDA specifically informed them that the pre-market notification had been approved. While the FDA was supposed to continue to process these applications in 90 days or less, the amount of time it actually took to process these devices exploded from 78 days in 1990 to 184 days in 1994.[3] Drawing out the pre-market notification process has had a serious impact on the ability of small firms to bring their products to market resulting in less innovation and a lower quality of care for consumers.[4]

The other route to market in the U.S. is through the Pre-Market Approval process, which is utilized for Class III devices. This process has come to increasingly resemble the Pre-Market Approval process used for pharmaceuticals. Like drugs, Class III devices must undergo large scale clinical trials, often conducted over a number of years. Before the clinical trials can begin, the manufacturer must apply for an investigational device exemption (IDE) which allows the manufacturer to test the device using an approved clinical plan. Once the preliminary results from the clinical trial are in, the manufacturer must go back to the FDA to obtain permission to expand the trial to include other hospitals and to increase the number of patients involved. Once the clinical trials are completed, the manufacturer must assemble the clinical and technical data and submit an application to the FDA for approval. The FDA then evaluates the application, which can

[3]Pierce, page 3.

[4]See Thomas J. Duesterberg, David J. Weinschrott, David C. Murray, *Health Care Reform, Regulation and Innovation in the Medical Devices Industry*, Indianapolis, IN: Hudson Institute, 1994.

involve subsequent requests for more information and may take anywhere from several months to several years.

By contrast, in the European Community (EC), medical devices are approved by private, government-licensed organizations known as "notified bodies." These organizations are licensed by member nations of the EC to evaluate devices before they enter the market, to inspect manufacturers' facilities, and ensure that manufacturers' quality assurance plans comply with the guidelines set out by the EC. The governments of the member states ensure that the "notified bodies" maintain their independence from the manufacturers that hire them and that they meet the technical qualifications set out by the EC.[5]

The second fundamental difference between the U.S. and European systems relates to the philosophy governing quality assurance. The American system relies on highly detailed case-by-case review of technical and/or clinical data to determine a device's safety and effectiveness -- in essence, its quality. The Europeans, however, use a quality systems approach to quality assurance. Each manufacturer is required to establish and aggressively support an internal quality assurance system that governs all phases of the device's development from design through manufacture. As discussed below, the EC has outlined rigorous standards for quality systems which each manufacturer must adapt to its own situation. When a device is under evaluation in the EC, in many cases it is the system itself that is as much a target of scrutiny as the specific device.

To be marketed in the EC, all medical devices must meet certain "essential requirements." Above all else, the benefits of the device must outweigh the risks associated with using it. The devices must be designed to mitigate risk to the patient and where appropriate, measures need to be taken to warn or protect the patient from any residual risk. The device must achieve the level of performance that the manufacturer intends in its design specifications. There are also specific requirements governing the

[5]See Council Directive 93/42/EEC, *Official Journal of the European Communities*, 36 L 169 (7.12.1993).

design and construction of devices, including rules for their physical, chemical and biological properties and protections against unnecessary exposure to radiation, infection, and electrical risks.[6]

Like the FDA, the European Community has grouped medical devices into various classes, based upon their risk to the patient. Lowest risk devices are in Class I and highest risk are in Class III, with intermediate risk devices in Class IIa and Class IIb. Generally, non-invasive devices are in Class I unless they are designed to store or channel blood or other body liquids or tissues.[7] Invasive devices are generally in Class IIa or Class IIb, unless they come into contact with the central nervous system, central circulatory system, or heart, in which case they are in Class III.[8]

For devices in Class I, no pre-market approval is required. The manufacturer certifies that the device is in conformance with the technical standards and requirements for the device laid out by the European Community.[9] The manufacturer must establish a system to review post-market experience with the device and to notify the national authorities if a recall is necessary.[10]

For devices in Class III, a notified body must certify that the manufacturer is in conformance with the European Community's technical regulations governing the design, manufacture and labeling of these devices. To begin with, the notified body must audit the manufacturer's quality system. The quality system must meet a series of rigorous requirements including the quality objectives of the manufacturer; clear identification of who is responsible for quality control; procedures for monitoring and verifying the

[6] *Official Journal* (7.12.93), Annex 1, pages 13-8.
[7] *Official Journal* (7.12.93), pages 37-8. Non-invasive devices that come into contact with injured skin are in Class I if used solely as a mechanical barrier, Class IIb if designed for wounds that have breached the dermis or in IIa for all other purposes.
[8] *Official Journal* (7.12.93), pages 37-40.
[9] The documents certifying conformance with EC standards must be available for inspection by the national authorities until at least five years after the product was last manufactured. They are also required to make any necessary corrections to the device based on that experience. In the event of any malfunction or deterioration of performance that might have led to the death or serious deterioration in health of the patient, the manufacturer most notify the appropriate agency in the national governments.
[10] *Official Journal* (7.12.93), pages 32-3.

design of the products; technical and clinical data that demonstrate that the performance of the device meets its design specifications; a draft of the label; specification of the procedures used for sterilization, purchasing, and product identification among others; an inspection of the manufacturer's facilities and relevant supplier's facilities; and specific tests to be done during manufacturing to test the quality of the product.

In addition, the notified body must examine and certify that the product has been designed according to the technical specifications set out by the Community and examine the manufacturer's design dossier which demonstrates that the product's design meets these specifications. Any changes to the design plan or quality system must also be approved by the notified body.

To ensure that quality assurance is maintained, the notified body must conduct periodic inspections, including surprise inspections of the manufacturing facilities. All documents pertaining to these matters must be made available to the national government for five years after the device was last manufactured. Once the notified body certifies that the manufacturer is in conformance with EC standards, the manufacturer may affix the European Community's seal of approval, the CE mark, and place the device on the market. The manufacturer must then notify the national governments that the device has been placed on the market.

For devices in Class IIa and Class IIb, the manufacturer must take the same steps as for Class I devices, as well as several other measures to prove conformance with EC production quality assurance standards. The manufacturer's quality assurance system must be audited, just as for Class III devices; however, the notified body does not need to examine the manufacturer's design dossier. Essentially, the difference between Class I and Class II approval is that Class II requires a notified body to sign off on the quality assurance system while Class I leaves this to the manufacturer.[11]

[11] *Official Journal* (7.12.93), pages 7, 15-35.

The FDA and EC medical device pre-market approval systems are radically different and these differences have implications for the efficiency with which medical devices are evaluated. The real question is whether the growing lags in approval times embodied in the FDA system have made consumers safer.

There is very little evidence to support the view that these lags have added to the safety of Americans. In response to congressional interrogatories on the subject, FDA cited only one device that had been pre-maturely approved in individual European countries but was not approved for use in the US.[12] This device, the Bjork Shiley 70 degree heart valve was approved in Europe over fifteen years ago, long before the Community wide regulations were in place and when device regulation by individual European countries was only in its infancy. Thus, this experience is not directly comparable to the devices examined below as the regulatory systems used in Europe changed markedly in the interim.

Responding to a similar line of questioning, the FDA recently asserted the medical value that its 510(k) process has added to American medical products. Some of the improvements cited were enhanced sensitivity of latex condoms, reductions in minor burns to MRI patients from hot cables, and shielding electric wheelchairs from electromagnetic interference.

Other improvements involved editing labeling and advertising assertions. For instance, a company was planning to market specialized sunglasses to professional race car drivers and planned to advertise them using the endorsement of a celebrity. The FDA disallowed certain statements, such as "Your eyes are saved from the strain and not fatigued so easily."[13]

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[12]Subcommittee on Agriculture, Rural Development, Food and Drug Administration and Related Agencies, Committee on Appropriations, *Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations for 1996, Part 6*, Washington, DC, Government Printing Office, 1995, page 478.

[13]Subcommittee on Approp., page 609.

While these improvements are certainly laudable, they need to be balanced against the human costs of the FDA's approval system. The devices presented below indicate that there are substantial human costs associated with the FDA system. Rather than protecting public safety, in some cases, the FDA's system for approving medical devices actually endangers lives.

Gianturco-Roubin Coronary Stents

The development of coronary stents has revolutionized the treatment of certain heart conditions related to a severe blockage in or collapse of a coronary artery, the vessel that carries blood to the heart muscle. A stent is basically a wire mesh tube. The stent is placed over an uninflated balloon on the tip of a long guide wire and inserted into the body through a major blood vessel and snaked through the body's blood vessels into a coronary artery. Next, the stent is anchored inside a coronary artery by inflating the balloon. The balloon is then deflated, leaving the stent in place to hold the artery open and facilitate the flow of blood to the heart muscle.[14] Over a few weeks, the lining of the artery will grow over the stent, anchoring it permanently in place.

Blockages of a coronary artery can be treated using several interventional techniques, including angioplasty. During this procedure, an angioplasty balloon is inserted into the coronary artery and the balloon is expanded next to the blockage, compressing the blockage into the artery wall, allowing blood to flow freely through the artery.

Unfortunately, angioplasty has two major problems. First, the coronary artery may collapse during the angioplasty procedure, preventing the flow of blood to the heart muscle. This occurs in 2-4 percent of the 400,000 angioplasties done in the U.S. each year. Unless the flow of blood is restored, the patient will suffer a heart attack. Before the development of stents, the flow of blood to the heart was restored in about half of all

[14]"New Device for Heart Surgery," *FDA Consumer*, (September 1993), page 4.

patients by performing an emergency coronary artery bypass graft (CABG) surgery.[15] This operation was quite risky, resulting in the death of approximately 15 percent of these patients.

The coronary stent, however, became an alternative method of treatment for most of these patients. In fact, at hospitals that evaluated the stent during clinical trials, only eight percent of the patients suffering from abrupt closure of the artery were required to have the bypass surgery. Of those that did require the bypass surgery, only 5 percent died. At the time the clinical studies were done, the late 1980s and early 1990s, there were about 350,000 angioplasties done per year in the U.S. Based on these numbers, it is estimated that roughly 1,300 Americans died each year from abrupt closure before the stent was available. Had the stent been approved for use at that time, it is estimated that only 70 Americans would have died per year from abrupt closure, resulting in roughly 1230 lives being saved per year.[16]

Given the importance of this technological breakthrough, one would assume that the application for approval of the stent would have been handled expeditiously by the FDA. Sadly for the thousands of Americans who died and could have benefited from the stent, this was not the case. It took nine months for the device's developers to get the go-ahead from the FDA to begin preliminary clinical trials (Phase I).[17] These trials took another year. The manufacturer then conducted Phase II trials for nine months and based upon the results of these trials, requested immediate permission to begin the final Phase III trials. The FDA rejected this request. The manufacturer appealed and again requested permission to begin Phase III trials. After three more months, the FDA said no. In the

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[15]During this procedure, a non-essential artery is removed from another part of the body and attached to the heart. Blood is then redirected through the artery, bypassing the original coronary artery.

[16]Extrapolated from clinical trial statistics of Gianturco-Roubin Flex-Stent Coronary Stent, reported to the FDA Advisory Panel, May 11, 1992.

[17]In Phase I, a clinical trial is conducted with a relatively small number of patients, generally at a single hospital . In phase II, the number of patients is expanded and a few more hospitals may be included. In Phase III, the clinical trials are generally expanded to multiple hospitals and the number of patients participating also increases.

mean time, the manufacturer began a second set of Phase II trials. The manufacturer appealed again and after another three months, FDA finally gave the go ahead for the Phase III trials to begin. Seven months later the first segment of the Phase III trial was completed and the manufacturer requested permission to expand the Phase III trial. After another seven months, FDA allowed the Phase III to be expanded and this trial was completed after another 15 months. Four months later, the FDA's advisory panel of medical experts recommended approval of the device, but the FDA did not issue the order granting approval for another 12 months. At last, six and a half years after the initial application to begin the clinical trials, the device was approved for use in the U.S. on May 28, 1993.[18]

Obtaining approval in Europe was quite another matter. The device was first approved in Belgium in June 1992 after only a few months of review. Several other European countries quickly followed suit. On the face of it, there appears to be only an eleven month lag between the European and FDA approval dates, but the whole approval process in Belgium took only a few months, compared with two years for the formal review of the data by the FDA and four and half years in clinical trials.

It could be argued that the European approval process was a "free rider" on the clinical trials that the FDA mandated, thus making this comparison unfair. The Europeans did use much of the clinical data generated for the FDA approval process, but the Europeans have a streamlined process for facilitating clinical trials, with the go ahead generally granted in under 60 days. It is unlikely that it would have taken nine months just to get the clinical trials under way as it did with the FDA or that the manufacturer would have encountered such numerous delays in expanding the clinical trials. Indeed,

[18]Food and Drug Administration, "Cook Inc., Premarket Approval of Gianturco-Roubin Flex-Stent Coronary Stent," *Federal Register*, 58 (July 22, 1993), page 39217.

regulatory flexibility in designing and conducting clinical trials is the primary reasons given by industry for moving clinical trials to Europe.[19]

Given the absolute minimum delay of 11 months in approval between Belgium and the U.S., and the estimated loss of 1230 lives per year, the minimum human cost of delay is approximately 1128 lives. This estimate, however, does not include the delays associated with FDA's oversight of the clinical trials. Taking into account the delays in the design and oversight of the clinical trials imposed by the FDA increases the human costs substantially. Given the complexity of the situation, it is worthwhile creating a range of estimates for the human cost of the regulatory delay. In the table below, the lags in clinical trials are the time in excess of 60 days that it took the manufacturer to obtain the FDA's permission to proceed to the phase in question. The table estimates the human costs of delay by placing responsibility for various percentages of the delay in clinical trials on the FDA. FDA responsibility for the 11 month lag between European and FDA approval is estimated at 100 percent for all scenarios.

Estimated Lives Lost Due to Regulatory Delay

Regulatory Phase	Lag	Percent of Lag Attributable to the FDA			
		25%	50%	75%	100%
Investigational Device Application	7 months	182	365	547	729
Begin Phase III trials	5 months	130	260	391	521
Expand phase III trials	5 months	130	260	391	521

[19]The Wilkerson Group, *Forces Reshaping the Performance and Contribution of the US Medical Device Industry*, Washington, DC: Health Industry Manufacturers Association, 1995, pages 93-5.

Clinical Subtotal	17 months	443	885	1328	1771
Approval Lag	11 months	1128	1128	1128	1128
Total	**27 months**	**1571**	**2013**	**2456**	**2899**

It seems reasonable to estimate that between 1571 and 2899 lives were lost in the U.S. due to the regulatory lags imposed by the FDA for this device. It is readily evident that delay does have a heavy price.

Implantable Cardioverter-Defibrillators

As discussed above, implantable defibrillators have saved the lives of tens of thousands of Americans, many of whom would only have survived a short time had they not received the implant.[20] Implantable defibrillators were first approved or use in the U.S. in 1986, being first brought to market by CPI, then a subsidiary of Eli Lilly and Company.[21] The original defibrillators were so large that they could not be implanted in the chest; instead they were placed inside the patient's abdomen. To connect the defibrillator to the patient's heart, a thoracotomy needed to be performed, which involves cracking the patient's sternum and opening the chest. A wire or lead from the defibrillator was then embedded into the chest and grafted onto the heart. Needless to say, this was quite a traumatic procedure for the patient and resulted in substantial operative mortality. Although the early defibrillators certainly saved many, many more lives than they claimed, they were only able to deliver one type of energy shock to the patient's heart.

[20]This has been widely documented in the medical literature. For example, see M. Mirowski, PR Reid, RA Winkle, et al "Mortality in patients with implanted automatic defibrillators, *Annals of Internal Medicine*, 98 (1983), pages 585-8.

[21]In 1995, CPI and Lilly's other device subsidiaries were spun off into the Guidant Corporation.

The high energy shock that these devices delivered was effective in some patients, but not all.

A second generation of implantable defibrillators were approved for use in Europe in 1988 and in the U.S. in 1991. These devices could deliver both high and low energy shocks to the patient's heart and could be programmed by the physician to maximize effectiveness.

The third generation of implantable defibrillators were approved for use in Europe in 1991 and in the U.S. in 1993, and were multiprogrammable. The physician could tailor the type of shock that the defibrillator would deliver to best the meet the patient's needs, even after the device had been implanted, through the use of an electronic wand. The defibrillator also had an internal memory that kept a record of the number times it had discharged and a few key statistics concerning the nature of the shock it had delivered. This information was also accessible to the physician through the use of the wand. The defibrillator could also be used to pace the heart's beat. Recent advancements in pacing technology were incorporated to allow the device to correct for both slow and rapid beating problems.[22]

Third generation defibrillators could be attached to the heart though two types of leads, epicardial or endocardial. Epicardial leads were grafted onto the heart muscle through the use of screw-in or stab-tab electrodes. Use of this type of lead required a thoracotomy or open chest procedure. Endocardial leads, on the other hand, were threaded through the patients blood vessels to the heart. Because these leads reside inside the blood vessels, there is no reason to open the chest. Endocardial leads were not originally approved for use with third generation defibrillators in the U.S., but became available in December 1993. Endocardial leads were first widely available in Europe in late 1991, two years before they were widely available in the U.S.

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[22]Sanjeev Saksena, et al., "Third and Fourth Generation Implantable Cardioverter Defibrillators: Current Status and Future Development," *Journal of Interventional Cardiology*, 7 no. 5 (1994), pages 427-430.

The clinical evidence in favor of endocardial leads over epicardial leads is extremely strong. A clinical study carried out at 125 participating hospital centers demonstrated that 4.2 percent of patients receiving the epicardial leads died within 30 days following surgery, while only 0.8 percent of patients receiving the endocardial leads died over the same period.[23] Two years after surgery, 87.6 percent of the patients receiving endocardial leads were alive, while only 81.9 percent of patients with epicardial leads were still alive.[24] The medical characteristics of patients in both groups were similar. Other studies have also demonstrated the superiority of endocardial leads, demonstrating a differential in survival rates of about four percent.[25]

The fourth generation of implantable defibrillators are much smaller than the previous three and can be implanted in the chest, under the pectoral muscle, much like a conventional pacemaker. This greatly reduces the length of the leads required and results in a smaller incision. These devices can send out a more efficient type of energy wave which allows the use of endocardial leads in nearly all patients.[26] This new biphasic wave achieves the same results as monophasic waves, but at substantially lower energy levels and with fewer electrodes. The gains in efficiency allows near universal use of endocardial leads.[27] Again, because of this enhancement in efficiency, far less testing of

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[23]Sanjeev Saksena, MD, FACC, "Clinical Outcome of Patients With Malignant Ventricular Tachyarrythmias and a Multiprogrammable Implantable Cardioverter-Defibrillator Implanted with or Without Thoracotomy: An International Multicenter Study," *Journal of the American College of Cardiology*, 23 no. 7 (June 1994), pages 1521-30. These results were statistically significant at the .001 level.

[24]These results were also statistically significant at the .001 level, but when those who died in the thirty days following surgery were eliminated from the analysis, the survival rates at 2 years were similar.

[25]See also, "James M. Kleman, et. al., "Nonthoracotomy Versus Thoracotomy Implantable Defibrillators," Circulation, 90 no. 6 (December 1994), pages 2833-2842.

[26]See Joerg Neuzner, "Clinical Experience with a New Cardioverter Defibrillator Capable of Biphasic Waveform Pulse and Enhanced Data Storage: Results of a Prospective Multicenter Study," *PACE*, 17 (July 1994), pages 1243-1255. In this trial, endocardial leads were successfully implanted in 98% of patients.

[27]Saksena, "Third and Fourth," page 431.

the device is required while the patient is on the operating table. This leads to a reduction in the time the patient is in surgery and should decrease several other complications.[28]

Operative mortality with this fourth generation device again fell, this time to less than 0.5 percent.[29] The smaller device is also said to be much more comfortable for the patient than the bulkier devices previously implanted in the abdomen. Fourth generation defibrillators were first approved for use in Europe in October 1993 and in the U.S. in March 1995.[30]

Lead systems have also continued to advance. The latest version requires the placement of only one lead to the heart, while previous systems used two or three leads. Needless to say, this simplifies the surgical insertion of the lead. These leads were introduced in Europe in 1994, but have not yet been approved for use in the U.S.

Over the last several years, European consumers have had earlier access to the latest model of implantable defibrillators than American consumers. In fact, American consumers were one full product cycle behind their European counterparts for most of the past five years. Given the improvements in patient survival for each generation of the device, this is hardly a trivial issue. In the early 1990s, it is estimated that roughly 13,200 Americans received defibrillators each year, reaching 20,000 by the mid 1990s.

Because of the regulatory lags outlined above, we can estimate that 1206 Americans died who, statistics indicate, would not have, had the same generation device available in Europe been available in the U.S. 1056 of these deaths are associated with the two-year regulatory lag in approving endocardial leads, while the remaining 150 deaths are associated with the 18 month regulatory lag in the approval of fourth generation

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[28]Andrea Natale, "Preliminary Experience With a Hybrid Nonthoracotomy Defibrillating System That Includes a Biphasic Device: Comparison With a Standard Monophasic Device Using the Same Lead System." *Journal of the American College of Cardiology*, 24 no. 2 (August 1994), pages 406-12.
[29] Munger et. al, *Journal of the American College of Cardiology*, 147A, page 736.
[30]Food and Drug Administration, "Cardiac Pacemakers, Inc., Premarket Approval of VENTAK P2 AICD System." *Federal Register*, 60 (April 21, 1995), page 19948.

defibrillators. Once again, the price of inefficient regulation carried a heavy human cost for American consumers.[31]

Omnicarbon Heart Valve

Designers of the Omnicarbon heart valve attempted to do what no-one else had done before, mate what they perceived as a superior structural design, the monoleaflet design, with a superior housing material, pyrolitic carbon.

In the evolution of heart valves that used metal housings, the monoleaflet design came to be favored over the bileaflet design because it caused fewer complications such as strokes and internal bleeding. This led the designers of the Omnicarbon valve to conclude that, housing materials being equal, the monoleaflet design was superior to the bileaflet design. Metal monoleaflet valves continue to be manufactured in substantial numbers today.

The development of pyrolitic carbon, a ceramic material, gave the bileaflet design a new lease on life. Bileaflet valves made from pyrolitic carbon did not suffer from the problems that metal bileaflet valves encountered. In fact, pyrolitic carbon rehabilitated the image of the bileaflet design to such an extent that some in the industry perceive it to be superior to the monoleaflet design. Pyrolitic carbon bileaflet valves are also commonly used today.[32]

The Omnicarbon's design is based on a metal monoleaflet valve, the Omniscience, which is manufactured by the same company that makes the Omnicarbon valve. The Omniscience received FDA approval in 1985. In fact, the Omnicarbon is identical to the

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[31]This number is arrived at by taking the patient population affected, multiplying by the difference in mortality rates and then multiplying by the length of the regulatory lag. For example, for non-thoracotomy leads, 13,200 patients were potentially affected each year and the difference in mortality rates was 4 percent. The regulatory lag for the leads was two years. Thus we arrive at 1056 lives (13,200 x .04 x 2). For the 4th generation defibrillators, there is a 0.5 percent difference in mortality, 20,000 procedures done per year, and the regulatory lag was one year. Thus 150 = 20,000 x .005 x 1.5

[32]For an excellent discussion of the history of valve development see, F. Javier Teijeira and Adel A. Mikhail, "Cardiac Valve Replacement With Mechanical Prostheses: Current Status and Trends," in *Advances in Cardiovascular Engineering*, edited by N.H.C. Hwang et. al., Plenum Press, New York, 1992.

Omniscience except that the housing of the Omnicarbon is made out of pyrolitic carbon rather than metal. Since the structural design of the Omnicarbon is the same as the Omniscience, and pyrolitic carbon was not a new material, the designers believed that they would be able to obtain FDA approval by merely filing a supplement to their already approved Omniscience valve. The FDA initially agreed, but later insisted that a full Pre-Market Approval application be submitted for the Omnicarbon, and the manufacturers did so in 1986.

Over the next two years, there were many rounds of communication between the FDA and the manufacturer in the form of requests for additional information and clarification. In 1989, over objections from the FDA, an FDA advisory panel was convened to review the pre-market approval application. The panel recommended that the valve not be approved because the agency claimed that the clinical results from the five European centers used could not be verified. The leading surgeons from these centers were available for questioning, however, at the panel meeting.

While the FDA did not approve the device for use in the U.S., it did grant the manufacturer permission to export the device, beginning in 1987.[33] Since that time, the device has been exported to Europe, Japan, and Canada. Because this device came on the market before the European Community issued directives regulating medical devices, it was approved on a country-by-country basis. In response to the new European Community Directives, the Omnicarbon received approval from the European Community in June 1995, after only four months of review.

Clinically, the Omnicarbon valve appears to have performed quite well. The complication rate associated with the device for thromboembolic (blood clotting) and internal bleeding are less than half that of the bileaflet carbon valves.[34] Currently,

[33]FDA need only issue an "export certificate" for a device to be exported. It does not need to be approved for use in the US nor does the export certificate establish safety and efficacy.

[34]For instance, see Yoshio Misawa, et. al. *The Journal of Thoracic and Cardiovascular Surgery*, 105 no. 1 (January 1993), pages 168-172. See also, Marti Peter et al., "The Omnicarbon tilting disc heart valve prosthesis: A clinical and Doppler echocardiographic follow-up," *Journal of Thoracic and Cardiovascular*

approximately 400,000 Americans have mechanical heart valves, and about four percent of them, 16,000 Americans, experience either a thromboembolic or bleeding complication each year.[35] The results of these complications can be catastrophic, including stroke, cerebral hemorrhaging, and even death.

If the clinical results achieved in Europe are accurate, up to 8,000 Americans could have been spared severe complications associated with currently available mechanical heart valves every year.[36] Naturally, this assumes that the Omnicarbon captured one hundred percent of the U.S. market, which is unlikely for any number of reasons. It is reasonable then, to forecast a range of values for the number of lives that could have been saved, dependent on the share of the market that the Omnicarbon captured. This is set out in Table ##=

Market Penetration of Omnicarbon Valve (%)	Number of Patients Averting Serious Complications per Year
10	800
25	2000
50	4000
75	6000
100	8000

Surgery, 106 no.4 (October 1993), pages 599-608. Prospective clinical studies comparing two different valves are quite rare. Instead a polled meta-analysis of the data from several studies published in peer-reviewed journals and presented at major conferences is frequently used as a substitute. While comparisons between studies is fraught with difficulties due to variations in demographics of patients, among other things, the weight of evidence in this case is quite strong. By polling several studies, over 4,100 patient-years of data can be obtained for the Omnicarbon valve and similar methods can obtain over 14,000 patient years of data for other mechanical heart valves.

[35]Although there is some statistical variation from study to study, owing in part to the demographics of the study population, the studies seem to cluster around 4 percent. For instance, see LS Czer, A. Chaux and JM Matloff, et al., "Ten Year Experience with the St. Jude Medical valve for primary valve replacement," *Journal of Thoracic and Cardiovascular Surgery*, 100 (1990), pages 44-55.

[36]This estimate is based on the following calculation: number of serious complications in the US per year (16,000) x relative reduction in serious complications using the Omnicarbon technology (.5) = 8,000.

Left Ventricular Assist Device

About 2,300 Americans receive heart transplants every year. Unfortunately, there are more people who need hearts than there are hearts available. The American Heart Association estimates that each year, about 15,000 Americans under the age of 55 could benefit from a heart transplant, and about 40,000 Americans 65 and under could benefit from a heart transplant. Currently, there are over 3,000 Americans on the active waiting list for a heart.[37] In 1994, 723 Americans died while on the waiting list for a heart.[38]Because of improvements in transplant procedures and technologies and a growing number of clinicians who are capable of performing the procedures, the number of patients eligible for transplant continues to rise. A study conducted in 1994 projected that the number of people who die while on the waiting list could grow to 1,440 within two years.[39]

	1988	1989	1990	1991	1992	1993	1994
Heart Transplants	1675	1705	2106	2126	2172	2298	2340
Deaths on the Waiting List	493	523	617	781	779	762	723

[40]

The disparity between the number of hearts needed for transplant and the number of hearts available for organ donors is staggering, as table ### demonstrates. This has led to an increase in mortality among those on the waiting list.[41] It seems unlikely that the number of organ donors will rise to meet the demand for hearts anytime soon, if ever.

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[37]*Heart and Stroke Facts: 1995 Statistical Supplement,* American Heart Association, page 21.
[38]United Network for Organ Sharing, "Reported Deaths on the Waiting List, by Organ, 1988-1994, "based on data submitted as of July 31, 1995.
[39]LW Stevenson, et. al., "The Impending Crisis Awaiting Transplantation, modeling a solution based on selection," Circulation, (January 1994), page 452.
[40]United Network for Organ Sharing, "Number of US Transplants," based on UNOS Scientific Registry data as of July 31, 1995.
[41]LW Stevenson, et. al., "The Impending Crisis Awaiting Transplantation," *Circulation*, 1994

Rather than relying on the generosity of the deceased, the other course is to use a mechanical device that can aid the heart until a suitable donor can be found or ultimately, to use a mechanical device in lieu of a heart transplant.[42]

Left Ventricular Assist Devices (LVADs) are designed to do the "heavy lifting" for diseased hearts. These devices take over the function of the left ventricle, which pumps oxygenated blood from the heart to the rest of the body. The devices are inserted into the patient's chest and abdomen and come in a few varieties.

Early versions of the device were designed solely as a "bridge" to keep patients alive in the hospital while they waited for a suitable heart to become available. They were powered by air and were attached to a large console mounted on wheels that the patient could push in front of her while she walked through the hospital. The device could be detached from the external console for a short period of time which enabled the patient to "roam" freely without the encumbrance of the console.[43]

Clinical studies of the device have been very favorable. In one early trial, 15 of the 18 patients implanted with the device lived to receive a heart transplant. Four patients died shortly after transplant from complications associated with the failure of other vital organs such as the liver and kidneys; they died because these organs were so deteriorated from poor circulation. In other words, the LVAD was not responsible for their deaths. To correct this problem, the rules of the clinical trial were amended to allow implantation of the LVAD before irreversible organ damage had occurred. Of the 12 patients implanted after the change in protocol, eleven were still alive at the time the study went to press (mean follow-up of 12.6 months). Patients who have the LVAD can participate in physical therapy and rehabilitative exercises strengthening their bodies, which increases

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[42]Howard R. Levin and Jonathan M. Chen, "Potential of Left Ventricular Assist Devices as Outpatient Therapy While Awaiting Transplantation," *The Annals of Thoracic Surgery*, 58 n5 (November 1, 1994), pages 1515-19.

[43]Laura A. Seche, "The Thermo Cardiosystems implantable left ventricular assist device as a bridge to cardiac transplantation," *Heart & Lung*, (March 1, 1992) pages 112-4.

the chances that eventual heart transplants will be successful.[44] In a similar study, 16 of 19 patients were successfully supported until a heart was received.[45] Other studies have reported similar results.[46]

The device was first marketed in Europe in the late 1980s and was approved for use in the US on September 30,1994 (the last day in FDA's 1994 fiscal year).[47] The data on waiting list deaths demonstrates that a left ventricular assist device is needed. A total of 3,662 people died while waiting for a heart from 1990 to 1994. If the LVAD had been approved by the FDA at the same time that it was approved in Europe, most of these patients could have had access to the device as it would have been available on a commercial basis rather than an investigational basis. This would have resulted in the dissemination of the device to most transplant centers rather than the select few where clinical trials were being conducted. Needless to say, the LVAD model that is currently approved does not "save" lives in and of itself, but it does lengthen life and improve the quality of life until a heart can be found.[48] Clinical results indicate that most patients can be supported until a suitable transplant is found, which can be considered a "life-saving" technology, as two-year survival rates for heart transplant recipients now exceed 77 percent.[49] Thus, the unavailability of the Left Ventricular Assist Devices on a commercial basis in the United States from 1989-1994 can be presumed to have had substantial human costs.

Pedicle Screw

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[44]O.H. Frazier, et. al., "Successful Bridge to Heart Transplantation with a New Left Ventricular Assist Device," *Journal of Heart and Lung Transplantation*, 11 n3 p1 (May 1, 1992), pages 530 - 537.

[45]Patrick M. McCarthy and Karen B. James, "Implantable Left Ventricular Assist Device: Approaching an Alternative for End-Stage Heart Failure," *Circulation*, 90 n5 p2 (November 1, 1994), pages 83-6.

[46]See Levin, cited above, see also O.H. Frazier et al. "Multicenter Clinical Evaluation of the HeartMate 100 IP Left Ventricular Assist Device," *Annals of Thoracic Surgery*, (June 1, 1992) pages 1080-90.

[47]need Federal Register citation

[48]Newer, all-electric versions of the device are currently undergoing clinical trials in the US as a bridge to transplantation and it is hoped that the device will also be available investigationally as an alternative to transplantation within the next year.

[49]Patrick M. McCarthy, "Implantable Left Ventricular Assist Device: Approaching an Alternative for End-Stage Heart Failure," *Circulation*, 90 n5 p2 (November 1, 1994), page II-83.

While the devices examined above demonstrate the dangers of regulatory lags in product approval, the pedicle screw demonstrates the human costs of the perverse incentives established by the current regulatory regime when going around the system is a more effective remedy than working within it.

The pedicle screw has been instrumental in easing the pain and speeding the recovery of American patients suffering from spine injuries, diseases and deformities for nearly 30 years. Primary uses of the pedicle screw involve stabilizing the spine after spinal injury and correcting spinal curvature. Spine injuries can be life-threatening, but most often they affect the quality of life of the patient by interfering with the patient's ability to carry out everyday functions, such as walking, reaching and sitting.[50]

Spine surgeons agree that pedicle screws are useful in selected patients for many conditions, such as spondylolisthesis and scoliosis, which require bone fusion surgery to immobilize the spine. The bone fusion takes several months to become affixed, but use of the pedicle screw allows healing to occur more rapidly and reliably than previous technologies.

One of the reasons that the pedicle screw is so effective is that it is an internal fixation device. Prior to the development of internal technology, doctors were forced to use external methods that caused considerable pain to back patients, and took a comparatively long time to heal. For example, after surgery to correct severe back problems, patients were frequently placed in full or partial body casts for at least six months; to immobilize the patient to promote healing, doctors would attach the skull and hips to a metal frame outside of the body.[51] These characteristics of external procedures resulted in great discomfort to the patient, and made it impossible to lead a normal life while healing.

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[50]Statement of Charles E. Johnston, II, M.D., before the Oversight and Investigations Subcommittee Commerce Committee, United States House of Representatives, March 30, 1995.

[51]Johnston

The advent of internal techniques has vastly improved the quality of life for back patients. When internal devices were first developed, doctors relied on wires and hooks to affix rods or plates to the vertebrae in the spine, including attaching hooks to adjacent healthy vertebrae.[52] Now doctors pass a pair of bone screws through the pedicles, or sturdy side pillars of the vertebrae, and fit the screws into vertical plates or connect the screw to rods, thereby involving only the specific vertebrae necessary to form a short fusion.[53] Implanting the pedicle screws allows greater correction of deformity and more rigid fixation than the wire and hook apparatuses because the pedicle screw is more stable and stronger than the wire and hook alternative.[54] Benefits of the pedicle screw include fifty per cent shorter healing times,[55] lower cost, and easier treatment, as compared with external procedures.[56] In fact, the hospital stay time associated with scoliosis surgery has been cut in half by using internal devices, and patients receiving pedicle screw implants can quickly return to an active lifestyle because body casts are not needed when pedicle screws are implanted.[57]

Despite the widespread acceptance and well documented advantages of the pedicle screw, the FDA classified it as a Class III device based on a determination that no substantially equivalent device existed before the 1976 Device Amendments. Although

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52 North American Spine Society Position Statement Pedicle Screw Fixation Devices, page 1, October 1993.

53 NASS Position Statement page 1.

54 NASS Position Statement page 1.

55 Transcript of Proceedings, Department of Health and Human Services, Public Health Services, Food Drug Administration, Orthopedic and Rehabilitation Devices Advisory Committee Panel Meeting, page 27, July 22, 1994.

56 Johnston

57 Transcript of Proceedings, Department of Health and Human Services, Public Health Services, Food Drug Administration, Orthopedic and Rehabilitation Devices Advisory Committee Panel Meeting, page 31, July 22, 1994.

the identical device was approved by the FDA a decade ago for other uses as a bone screw, most uses in the pedicle of the spine have still not been approved. Thus, most pedicle fixation is considered an off-label use, which means using an approved device for an unapproved indication.[58]

Yet, prior to the 1976 Medical Device Amendments, pedicle screw usage was recognized as a standard procedure for spinal fusion.[59] In the early 1980s', pedicle screw manufacturers received Investigational Device Exemptions to perform clinical tests to demonstrate the pedicle screw's safety and effectiveness. Then, in the mid-1980's, pedicle screw manufacturers unsuccessfully petitioned the FDA for 510(k) clearance so that they could promote and market the bone screw for use in the pedicle. The FDA denied the 510(k) for pedicle screws, finding that no substantially equivalent product existed prior to the enactment of the 1976 Device Amendments. However, 510(k) clearance was obtained for several other uses of the bone screw.

Ironically, in 1995 one manufacturer finally was able to prove to the FDA that pedicle screws had been on the market and commercially available before 1976, as the manufacturers had always contended, resulting in a new FDA finding that the pedicle screws were substantially equivalent to a pre-1976 device after all. This was only after the FDA in August 1993 assembled an Orthopedic and Rehabilitation Devices Advisory Committee to discuss off-label usage of the screw and plan a retrospective clinical study to be conducted by the FDA Collective Spine Organization Study Group to analyze the safety and effectiveness of the screw for two indications, thoracolumbar fractures and degenerative spondylolisthesis.

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58 Department of Health & Human Services. Update on the Regulatory Status of Pedicle Screws, February 17, 1994.

59 Reduction of Severe Spondylolisthesis in Children, *Southern Medical Journal*, P.R. Harrington, MD and H.S. Tullos, MD, January 1969.

Upon examining the results of the study, in July 1994 the FDA Advisory Panel unanimously recommended that FDA reclassify the pedicle screw from Class III to Class II for degenerative spondylolisthesis and fractures. Acceptance of the Panel's recommendation to reclassify would allow the pedicle screw to be approved under section 510(k), without clinical trials. In January 1995, the FDA cleared a variety of manufacturers' pedicle screws for one type of spondylolisthesis.[60] Although the FDA has cleared marketing of pedicle screws for one type of spondylolisthesis, the FDA has not otherwise acted on the Advisory Panel's advice and the screw remains an unapproved Class III device for most uses in the pedicle.

Aside from FDA's limited approval of the pedicle screw for one use, FDA's error in determining that it was not a pre-amendment device forces manufacturers to perform an end-run around the system. The medical community continues to use the screws in the pedicles for a wide ranges of uses not approved yet by the FDA, leading to widespread off-label use of the screw.

In August 1993, before the FDA had approved any use of the bone screw in the pedicle it issued a Warning Letter to manufacturers The letter required that the manufacturers stop promoting pedicle use of the bone screw, and to cease supplying devices to programs which provide hands-on training. The Warning Letter is a typical FDA prohibition of marketing a device for off-label usage. However, while FDA disallows marketing of devices for unapproved uses, doctors are permitted to use the devices for nonindicated uses. Permitting off-label use of devices is a facet of FDA's policy of allowing a doctor to use his own judgment and discretion when treating his own patients, because the doctor is in the best position to determine what is best for his

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[60] Sofamor Danek Group received approval in early 1995. Several other manufacturers received clearance shortly thereafter.

patient. The doctor is not required to get approval for off-label usage, but can be subject to medical malpractice actions for his decision to use the product.

FDA's Warning Letter disallowing marketing, and especially education, regarding the pedicle screw is inconsistent with its policy of allowing off-label uses to encourage doctor autonomy. The education seminars held by the manufacturers of the pedicle screws before the FDA prohibited them often included hands-on training to ensure that surgeons become skillful at implanting the device. Prohibition of training while still allowing the off-label uses has the obvious effect of halting the dissemination of scientific information that would enable doctors to improve their techniques and make informed, educated judgments about which procedures to use. The net result of these conflicting FDA policies defies all logic. Doctors are allowed to freely use devices as their judgment dictates, yet manufacturers are not permitted to show them the best way, or tell them about the most recent scientific studies and the safest techniques.

Roughly 70,000 Americans receive pedicle screws annually. For the past two years, no doctor implanting the pedicle screw has received hands-on training from manufacturers. Doctors can read the studies detailing the benefits to patients in widely accepted medical journals, but the FDA prohibits them from being instructed in the proper way to do the procedure. The result has been a flood of lawsuits against the manufacturers of pedicle screws even though the screws have rarely failed. The lawsuits allege that the treatment received did not cure the patient's back pain or made it worse. Documented studies show that proper placement of the pedicle screw in appropriate patients does not increase back pain.

In addition to the human costs outlined above, there are also substantial economic costs associated with regulatory delay. Such delays are often cited by manufacturers as

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[61]The Effect of Pedicle Screw/Plate Fixation on Lumbar/Lumbosacral Autogonous Bone Graft Fusions in Patients With Degenerative Disc Disease, George W. Wood, Robert J. Boyd, Thomas A. Carothers, Frederick L. Mansfield, Glenn R. Rechtine, Michael J. Rozen and Chester E. Sutterlin, Spine, Volume 20, Number 7 April 1, 1995.

grounds for moving manufacturing plants and even research and development facilities to more hospitable locations abroad.[62] When these plants move, Americans lose high paying jobs.[63] Regulatory delays have the most severe impact on development stage companies who do not have sales from other products to sustain themselves while the device is under review by the FDA. Because these companies are dependent on venture capital to survive in the pre-marketing period, these companies need to begin achieving positive returns for their investors as soon as possible. To the extent that regulatory delays lengthen the pay-back period they make investment in the device industry less attractive, ultimately starving development stage device companies of the cash that they need to sustain themselves until FDA approval is obtained.[64] Indeed, many venture capitalists will not commit money unless the company has a plan to introduce the product in Europe while the FDA approval process drags on. Thus, investors have already mastered what the press and public have not, that regulatory delays add needless costs and drive new technologies overseas.

Who is to Blame?

A multitude of reform plans for the FDA have been put forward in recent months by various interested parties and academic organizations, some of which have found their way into the proposals before Congress. These proposals run the entire spectrum in the breadth and depth of FDA activities that would be reformed. For instance, the white paper put forward by the American Association of Advertising Agencies (AAAA) deals almost exclusively with FDA's regulation of pharmacoeconomic information and advertising for medical products.[65] On the other hand, the National Medical Device Coalition has put out an in-depth critique of FDA's Center for Devices and Radiologic Health (CDRH) with

[62]The Wilkerson Group, pages 94-5.
[63]Duesterberg, et al. pages 124-7.
[64]The Wilkerson Group, pages 134-7.
[65]See "Legislative Proposal To Reform FDA Marketing Regulation," American Association of Advertising Agencies, Inc., Washington, DC, May 1995

recommended changes covering a host of issues, including taking CDRH out of FDA and setting it up as an independent agency in the Public Health Service.[66]

The Progress and Freedom Foundation has recently released an interim white paper detailing a new approval system for devices and drugs that borrows heavily from the system used in the European Community that relies heavily on private labs.[67] The Health Industry Manufacturers Association (HIMA) has advocated exempting Class I medical devices from the pre-market notification process and allowing the FDA to contract out parts of the pre-market approval process while retaining the final authority to sign off on the approval.[68] The National Electrical Manufacturers Association has outlined a proposal that would prohibit the FDA from establishing performance standards for Class II medical devices and would rely instead on consensus standards developed by panels of experts and would streamline post market surveillance.[69] The Competitive Enterprise Institute (CEI) has even called for abolishing the FDA's veto power on medical products by setting up a scheme whereby such products could be brought to market without any type of approval process at all so long as this was made to clear to physicians and users.[70]

Enhancing medical innovation while protecting public safety should be the primary goal of any FDA reform plan as the price of delaying the entry of medical technologies into the market is high. Before laying out a reform plan, it is instructive to ask why things have deteriorated so badly at the FDA over the past few years. Was it a

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[66]*A Blueprint for Reform of the FDA's Center for Devices and Radiological Health (CDRH),* The National Medical Device Coalition, Washington, DC, Spring 1995.

[67]Thomas M. Lenard, Ralph A. Epstein, Robert D. Tollison, W. Kip Viscusi, William M. Wardell, *The Future of Medical Innovation: A New Approach for Bringing Medical Products to Market,* The Progress and Freedom Foundation, Washington, DC, June 9, 1995.

[68]"Summary of Draft HIMA Legislation on FDA Reform," Health Industry Manufacturers Association, Washington, DC, distributed Spring 1995.

[69]"Reinventing the Regulation of Medical Devices II: Towards A Public-Private Partnership for Device Regulation," National Electrical Manufacturers Association, (June 1995), pages 5-7.

[70]Sam Kazman, "The Food and Drug Administration: A Modest Proposal," Competitive Enterprise Institute, Washington, DC, January 6, 1995.

lack of resources? Growing demands? Changing priorities within the agency and government? Fundamental flaws within the approval system?

A Real Cornucopia of Resources

In 1988, FDA had a budget of $482 million and a staff of 6,869 people.[71] At that time, FDA approved 46 applications for Pre-Market Approval of new medical devices. By 1994, its budget had grown to $877 million and the staff had ballooned to 8,539,[72] but only 26 PMAs were approved. For 1996, FDA is requesting $884 million in appropriations and $142 million in special industry user fees to pay for a staff of 9,592.[73]. Legislation passed in 1992 gave the agency authority to collect these user fees from pharmaceutical companies to bolster FDA's resources for evaluating new drug applications.[74]

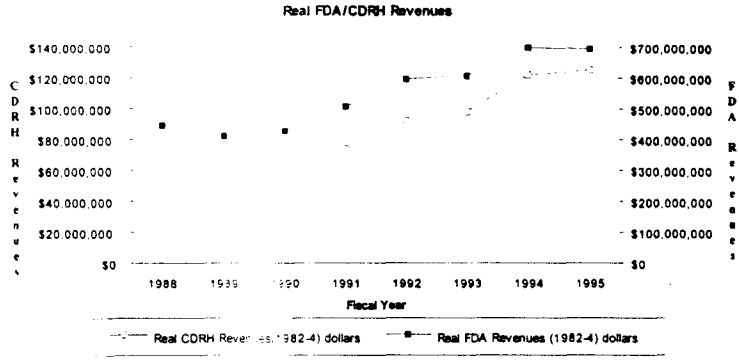
The section of the FDA that evaluates medical device applications for approval, the Center for Devices and Radiological Health (CDRH), has also benefited from Congress' largesse to the agency. In 1990, CDRH received $85 million, but this figure had grown to $167 million by 1995. For 1996, the agency is requesting permission to collect $23 million in user fees from the industry,[75] in addition to its appropriation of $175 million.[76] In return for this tax on industry, the FDA is "committing" to meet a 180 day evaluation deadline for PMAs 60 percent of the time, even though the original 1976 device law

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[71]Food and Drug Administration, *PMS Blue Book*, Fiscal Year 1988, page 11.
[72]Food and Drug Administration, *PMS Blue Book*, Fiscal Year 1994, page 11.
[73]United States House of Representatives, Committee on Appropriations, Subcommittee on Agriculture, Rural Development, Food and Drug Administration, and Related Agencies, ***Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations for 1996, Part 6,*** Government Printing Office, Washington, DC, page 594.
[74]David A. Kessler, Statement before the Subcommittee on ?Agriculture, Rural Development, Food and Drug Administration, and Related Agencies, Committee on Appropriations, US House of Representatives, (March 28, 1995), pages 3, 14.
[75]Kessler, pages 15-6. Legislation to allow the FDA to collect user fees from medical device makers died in the 103rd Congress. The prospects for passage in the 104th Congress are uncertain at best.
[76]*Agriculture, Rural Development, Food and Drug Administration and Related Agencies Appropriations for 1996, Part 6,* page 526.

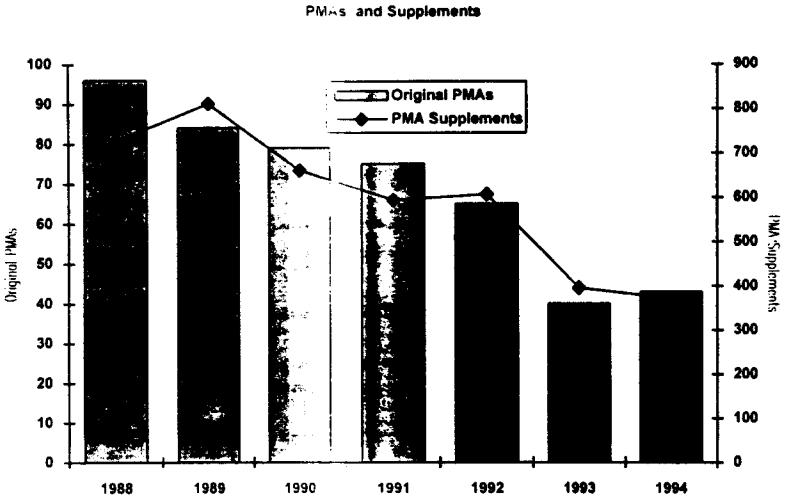
compelled the agency to meet the same deadline 100 percent of the time without charging user fees.

The agency's deterioration in performance while receiving more resources is alarming enough, but the picture looks even worse when FDA's resources are adjusted for inflation. In constant dollars, the FDA received $446 million in 1988 and $695 million in 1995, a 65 percent increase in real purchasing power. CDRH also posted impressive gains in purchasing power, increasing 56 percent when adjusted for inflation over the same period.



As resources have grown over the last five years at the FDA and CDRH, the number of applications for Pre-Market approval for new medical devices has decreased substantially. As figure ## shows, the number of original PMA applications declined from 96 in 1988 to 43 in 1994. The number of supplemental PMAs, requests to market an improved version of the original device or involving a change in the manufacturing process, also declined over the same period, falling from 727 to 372. Thus, the number of PMAs that the CDRH processed declined as real resources increased. Based on these

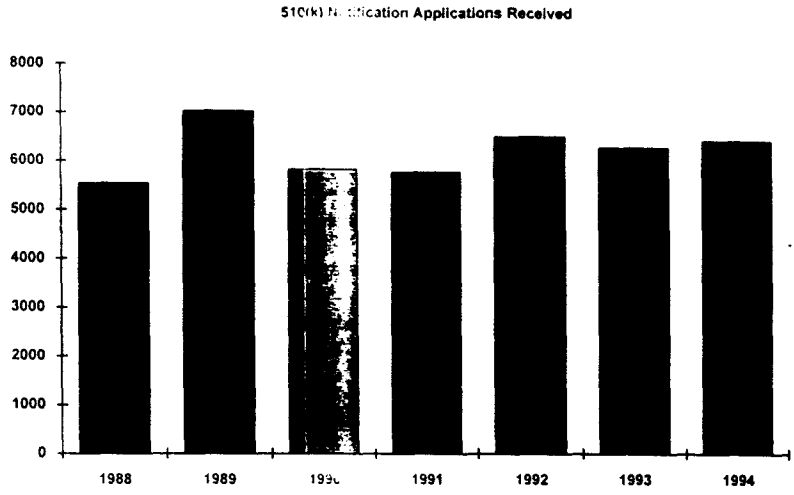
numbers, it is safe to conclude that the deterioration in FDA's performance over the last half decade cannot be attributed to a lack of resources.



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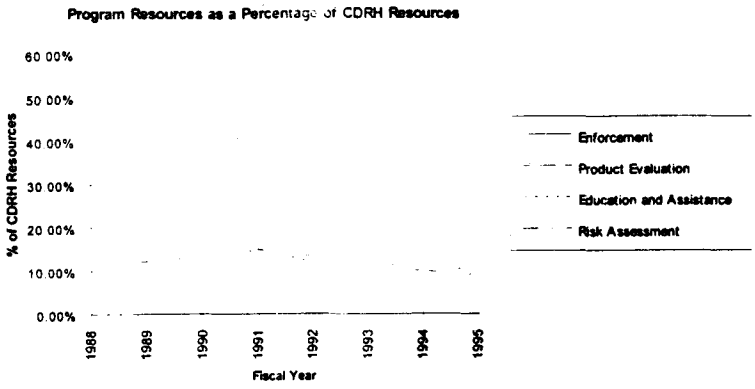
The number of 510(k) applications received has not followed any clear trend bouncing between 5,500 and 7,000 from year to year as Figure ### shows.

[77]Data taken from Food and Drug Administration, *Office of Device Evaluation Report*, Fiscal Year 1993, and *Agriculture, Rural Development, Food and Drug Administration and Related Agencies Appropriations for 1996, Part 6*, pages 636-7.



It is instructive to look at how the Center for Devices and Radiologic Health has spent the money appropriated to it over the past several years. CDRH has consistently spent a plurality of its money, and in some cases the majority, on enforcement of its regulations. No-one disputes the need for enforcement, but growing lags in approval times might indicate that CDRH's spending priorities should be re-evaluated. CDRH spends about the same percentage of its resources on evaluation as it did in the late 1980s, when review times were far shorter than today. The constancy of the allocation of resources between program areas within the CDRH in the face of growing delays in product approvals belies FDA's stated commitment to evaluating devices more quickly. Rather than reallocate resources, FDA has instead asked for permission to tax the industry to bolster its budget. To add insult to injury, only 81 of the 109 employees to be hired with the user fee moneys will be evaluating device applications; the other 28 will be added to the ranks of the FDA's enforcement program.[78]

[78]Jeffrey Pierce, "Truth Serum for the FDA," *Issues and Answers*, (March 30, 1995), page 4.



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Prescribing Animosity and Censorship

To say that the FDA's current Commissioner, Dr. David Kessler, has received substantial criticism and praise for his performance at the head of the FDA is an understatement. Dr. Kessler has positioned himself as the consumer's champion, launching crackdowns against a variety of industries including tobacco, dietary supplements, and food processors.[80] In perhaps one of the most critical pieces written about Dr. Kessler's self-styled crusade to protect consumers, *Forbes* asked bluntly, "But who will protect us from Kessler?".[81]

Witnesses before Congress have suggested that the FDA has veered from its central duties while focusing instead on punishing companies for violating technicalities

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[79]Data for FY 1988-93 taken from each fiscal year's *PMS Blue Book*, Department of Health and Human Services. Food and Drug Administration, Public Health Service, Washington, DC. Data for FDA resources generally appears on page 11, while data for CDRH generally appears on page 127 or 137. Data for FY1994 and 1995 taken from Department of Health and Human Services, *Justifications of Estimates for Appropriations Committees*, Food and Drug Administration, Fiscal Year 1996, Volume XII, p77.
[80]James Bovard, "Double-Crossing to Safety," *The American Spectator*, (January 1995), pages 24-9.
[81]Peter Brimelow and Leslie Spencer, "Just Call Me 'Doc'," *Forbes*, 152 no. 12 (November 22, 1993), page 4.

in the law that do not impact the safety or effectiveness of the product. Perhaps the most often cited example is the FDA's "reference list." Companies that have been cited for violations in Good Manufacturing Practices regulations are placed on the list, meaning that the company cannot receive approval to market any new products, even if the violations had nothing to do with the sites or processes that would manufacture the new product. This list was developed without the benefit of public notice and comment rulemaking and the finer details surrounding its use remain somewhat hazy.[82] The Reinventing Government initiative announced this spring has targeted the reference list for reform by restricting the denial of approval to violations that could reasonably be expected to impact the production of the device under review.[83] Medical device trade groups have called for the outright abolition of the list.[84]

Several physicians have noted that FDA has taken a more interventionist role in the practice of American medicine. As one physician noted, "The FDA never received a legislative mandate to police or even direct the practice of medicine, but that is exactly what it does."[85] FDA has taken it upon itself to encourage physicians to obtain individual investigational device exemptions when they wish to test out an experimental use of a device or to use multiple devices that have been approved for use individually, but have not been approved for use together. Essentially, FDA is arguing that physicians need the FDA's permission to carry out an experimental treatment, thus substituting the FDA's expertise for that of the physician, to say nothing of the desires of the patient. Obtaining such individual exemptions, is at best, a cumbersome process for the physician. As three

[82]Alan Magazine, President, Health Industry Manufacturer's Association, Prepared Statement for testimony on Food and Drug Administration FY 96 Appropriations, Subcommittee on Agriculture, Rural development, FDA, and Related Agencies, house Committee on Appropriations, (April 3, 19950, pages 2-3.
[83]Bill Clinton, Al Gore, *Reinventing Drug & Medical Device Regulations*, Washington, DC, National Performance Review, April 1995.
[84]Magazine, page 4. See also, Medical Device Manufacturers Association, "Preliminary Comments to the April 1995 National Performance Review Report on Drug and Medical Device Regulations,"(April 6, 1995), page ???.
Medical Device Manufacturers Association
[85]See "Statement of Neil Kahanovitz, M.D." before the Subcommittee on Oversight and Investigations, House Committee on Commerce, (March 30, 1995).

physicians writing in response to an FDA letter note, "Physicians should have the right to mix and match when it is to the patient's benefit and when alternative, approved systems are not available."[86]

The FDA has also been actively regulating the distribution of medical information between manufacturers and clinicians as the pedicle screw discussion illustrates. After a drug or device is approved for a given medical condition, clinicians often realize that it can be used to treat other medical conditions. Using a device as a therapy for these conditions is considered an "off-label" use, because it is being used for a purpose other than that stated on the label of the product. In fact, most cancer therapies are technically off-label because they use a combination of treatments (radiation, chemotherapy, drugs) that have not been specifically approved for use together.[87] It has been estimated that roughly 90 percent of the drugs used in pediatrics are technically off-label.[88] Opponents of the practice argue that this denies critical medical information to clinicians and ultimately impacts the quality of care for patients.[89]

The FDA is empowered to regulate and approve the labeling of medical products under the Food, Drug and Cosmetic Act; this is not in dispute. Recently, however, FDA has expanded the definition of "label" to include statements about the efficacy of off-label therapies in medical text books, peer-reviewed journal articles, proceedings of medical conferences, etc. While the FDA claims that it is empowered by statute to do so, a close reading of the statute belies this argument. The act defines a "label" as "a display of written, printed, or graphic mater *upon the immediate container of any article*;"[90] and "labeling" as "all labels and other written, printed, or graphic matter (1) upon any article

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[86]James D. Maloney, MD, FACC, Dirar S. Khoury, PhD, Weixi Zhu, MD, Carlos Rizo-Patron, MD, "The Art and Science of Mixing and Matching," *Journal of the American College of Cardiology*, 24 no. 2 (August 1994), page 415.

[87]Get cite from Jeff Pierce

[88]Andrew Skolnick, "Pro-Free Enterprise Group Challenges FDA's Authority To Regulate Drug Companies' Speech," *JAMA*, 271 no. 5 (February 2, 1994), pages 332-5.

[89]See WLF petition

[90] Emphasis added. See §201(k) of the Food, Drug and Cosmetic Act as amended or 21 USC 321(k).

or any of its containers or wrappers, or (2) accompanying such article."[91] Nowhere in the legislation does the definition of "label" or "labeling" include the distribution of journal articles or other scientific literature by third parties.

The Washington Legal Foundation (WLF) has filed suit against the FDA in federal court on grounds that the FDA's behavior violates the freedom of speech under the First Amendment. The FDA requested that the case be dismissed, but the court has ordered the case to proceed to trial.[92] Rep. Ron Wyden (D-OR) has introduced legislation that would specifically exclude the distribution of peer-reviewed scientific literature at scientific meetings from the labeling regulations so long as the distribution of those materials was not required as a condition of financial support for development of the materials or the meeting.[93]

Whatever the outcome of the WLF case or the Wyden legislation, it is safe to conclude that the actions undertaken by the FDA's management in recent years have aggravated the relationship between the agency and the regulated community. The use of the reference list, by definition, can draw out the approval process, even for companies whose violations do not pertain to the product being considered for approval. Taken to the extreme, the pressure on physicians to obtain investigational device exemptions could act to deny patients the highest quality of care otherwise available to them by substituting the FDA's judgment for that of the attending physician, who is more familiar with the case at hand. The censorship issue does not in and of itself delay the approval of new treatments, although it certainly could ultimately prevent patients from receiving the most appropriate care for their conditions. Taken together, the FDA's actions amount to a

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[91]See §201(m) of the Food, Drug and Cosmetic Act as amended or 21 USC 321(m).
[92]Washington Legal Foundation v. David A. Kessler, et.al, United States District Court for the District of Columbia, Civil Action No. 94-1306(RCL), (March 9, 1995).
[93]Rep. Ron Wyden, Section 7, "HR 1742," 104th Congress, 1st Session, (as introduced June 6, 1995). The bill has been referred to the Health and Environment Subcommittee of the House committee on Commerce. No hearings have been held to date.

pattern of oversight and intervention that contribute significantly to delays in the introduction of new medical treatments in the United States.

A System Ripe for Reform

The FDA's approval process seems as clogged and diseased as the coronary arteries of some of the patients that the agency seeks to protect. Although the agency could certainly use the bureaucratic equivalent of angioplasty or even a stent or two, the long-term solution is to allow the flow of commerce to bypass the agency entirely.

In the final analysis, the FDA has a monopoly over the approval of medical devices in the U.S. Both economic theory and bureaucratic tradition would predict that such an administrative monopoly would underperform and overcharge for its products, in this case approval of new devices. It should not be surprising, then, that the approval process for devices has slowed to a crawl while the agency consumes ever more public resources. The prescription to end these destructive practices is as old as economics itself, simple competition.

The advantages of the European system are manifested in the private nature of the pre-market evaluation process. Notified bodies, while regulated by the national government and EC regulations, compete against one another for clients. Firms that do a quality job in a timely manner will prosper while those that are careless or inefficient will be forced out of the market. Note also that the market has the ability to respond to changes in the overall demand for pre-market evaluation services. As demand grows, firms will expand their capabilities to take up the new business and/or new firms will enter the market. Because these are private firms, the amount of resources available to them is not subject to the whims of elected officials, bureaucratic politics or the fiscal predicament of the nation's government. Rather, the resources available to these firms approximates the demand for their services, ensuring that delays do not grow long during periods of high demand or that an oversized bureaucracy remains in times of low demand.

It is tempting to speculate that the notified bodies could lose their objectivity and cave into pressure from the companies whose applications they are evaluating. While a cause for concern, there are several factors that mitigate against this in practice. First, the notified bodies are licensed by the national governments. If they become co-opted by a manufacturer they can lose their license and be put out of business. This is a life or death risk that few companies would wish to take. Second, notified bodies are exposed to civil liability. If they commit a tort by being careless or by deliberately biasing their evaluation, they are subject to civil suit and potentially enormous penalties. Third, the companies that manufacture these devices are exposed to civil liability. They certainly have no desire to be sued and potentially forced into bankruptcy because their device was unsafe. Fourth, devices that are unsafe or that are not efficacious will not sell well. It is to a manufacturer's advantage to do everything possible to optimize the safety and effectiveness of the product to maximize long term competitiveness. While regulatory theorists might argue that companies might take too much risk or be too hasty in bringing products to market, the European experience seems to demonstrate that private regulators sucha sthe notifed boides are as capable at keeping dangerous products off the market as the FDA.

The reliance on quality systems has both advantages and disadvantages. The primary advantage is that standards for quality systems are much easier to harmonize among different nations than national standards of safety and efficacy for individual devices. By harmonizing requirements for quality assurance systems, the EC has made it possible for a manufacturer to obtain approval for its device in all the nations of the European Community with a single approval.

The International Organization for Standardization has been the international leader in harmonizing standards including quality assurance systems.[94] By relying on the

[94]The International Organization for Standardization is headquartered in Geneva and is composed of the national standard setting agencies of each member's government. The American National Standards Institute (ANSI) is the American member.

International Organization for Standardization's ISO 9001 guidelines, the members of the European Community have been able to standardize their regulation of quality assurance systems for medical devices. Before the ISO 9001 regulations were applied to medical devices, individual member states were beginning to adopt disparate national regulatory standards that threatened the free flow of devices in the common market.[95]

The primary disadvantage of the standardized quality assurance approach is the burden it places on the small firms. In the U.S., where quality systems are not yet required, a great deal of innovation is done by very small firms. These firms spend a very high percentage of their revenues on research and development and the additional cost of a quality system may be too much for them to bear. These systems are heavy on documentation and oversight, which is less of a problem for a large manufacturer, but is a tremendous burden to a three person firm struggling to bring its product to market.

The FDA recently proposed design controls that would bring American manufacturers into conformance with the ISO 9001 guidelines, but would not affect the FDA's other requirements for approval. The FDA estimates that these regulations would cost small manufacturers an average of $19,300 per year, which could be a burden for very small development stage companies. The cost to larger manufacturers is not clear because many, if not most, have voluntarily instituted similar programs.[96]

The real cost of the additional regulations, however, is that they may prevent new devices from being developed. The failure to develop a new device at all is perhaps the ultimate example of the regulatory delay of the introduction of new technologies and has all of the human costs described above. The paramount question, then, is whether the advantages in the efficiency of pre-market evaluation can be obtained without maximizing the risk that new technologies will not be developed at all because of the burden of design controls on highly innovative small firms?

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[95]See the preamble of 93/42 EEC, *Official Journal* (7.12.93), page 1.
[96]*Federal Register*, 58 no. 224 (November 23, 1993), pages 61952-61986.

An Agenda for Reform

In an increasingly global industry, harmonization of approval and inspection processes is a long term imperative. The U.S. and EC systems are radically different in philosophy and practice. The holy grail of reforming the FDA regulatory regime should be to harmonize the regime with foreign regulatory regimes in such a way that medical innovation is optimized to produce safe and effective medical products.

To accomplish this, this paper proposes fundamental change in the pre-market approval process for American medical devices based on the conclusion from the analysis above that the current FDA system incurs substantial human costs. While critics might note that the devices considered were not a simple random sample of all medical devices approved by the FDA, the overall track record of the two system builds confidence that these conclusions are justified. The fact that the FDA could not produce a single example of a device approved in Europe that was not approved in the US in the last 10 years speaks volumes on the relative safety of the two systems. In any event, the devices examined above do have real human costs associated with their delayed entry into the US market, indicating that at the very least, there is room for improvement in the American device approval system.

First, and foremost, the FDA's monopoly on the Pre-Market Approval of medical devices should be terminated. The FDA should, instead, become one of many competing groups that could approve medical devices. Private firms, licensed by the federal government, would be permitted to evaluate and approve all classes of medical devices if the firms met the technical and professional requirements established by the government.

Unfortunately, the FDA seems to be the natural agency to establish these regulations and to license the firms. Given that the FDA would be competing against these firms, there are obvious incentives for the FDA to craft the regulations in such a manner as to keep firms out of the market or to impose burdensome requirements upon

them. To mitigate this problem, five safeguards should be adopted. First, require the Center for Devices and Radiologic Health of the FDA to meet and operate under the same regulations as the private firms. Second, relocate CDRH out of the FDA and set it up as an independent agency within the Public Health Service (the branch of government that contains the FDA itself). Third, establish legislative deadlines or "hammers" for promulgation of the new regulations. Fourth, the FDA should operate under strict Congressional oversight while developing these regulations. Fifth, all regulations should be enacted through notice and comment rulemaking, allowing full participation by the regulated community in developing these regulations.

The EC system relies heavily on quality systems, both philosophically and practically. In order to adopt a more European system for device approvals, the manufacturers of American medical devices would need to adopt their own quality systems. Many large American companies have already done so to ease the approval of their devices in the EC. The costs of such systems are much more easily borne by large manufacturing concerns than the small start-up companies engaged primarily in research and development. Rather than impose a one size fits all mandate, it would be more appropriate to exempt firms that do not manufacture or market the device or its components from the quality system requirement. The Europeans follow this approach. This would preserve the well-spring of innovation in the American industry, the small firm, while ensuring that devices do pass through an orderly set of internal systematic quality controls before ever nearing the market.

The approval process itself would change for different classes of devices. Devices currently classified as Class I by the FDA, low risk devices substantially equivalent to those on the market before 1976, would no longer need to receive affirmation from the FDA before they could be marketed. Instead, manufacturers would declare self-conformance with the technical guidelines governing that class of devices 90 days before marketing the device. This would be true pre-market notification. In addition, many of the

devices that are currently in Class I would be exempted from this requirement. The National Performance Review was on the right track when it suggested exempting an additional 125 categories of devices from the pre-market notification requirements.[97] The FDA should be mandated to conduct a systematic review of all devices within Class I to determine if other categories of devices should also be exempted from this requirement.

Devices in Class II, intermediate risk devices substantially equivalent to those on the market before 1976, would be evaluated under a scheme similar to the EC regulations for Class IIa and Class IIb devices. Either the FDA or a notified body would evaluate the manufacturer's application for approval. Just as is done in the EC, all relevant technical and clinical data would be reviewed and the manufacturer's quality system would be audited. A design dossier for the device would not be required. Inspections of the manufacture's facility and relevant suppliers would also be conducted. Either the FDA or a notified body could issue final approval for the device to be marketed.

Under current American law, the FDA has the authority to set performance standards for Class II devices, although it has not done so. On the other hand, the EC uses consensus standards developed by committees of government agencies, scientists, industry experts, and other professional associations. These standards represent the minimum performance requirements that new devices must meet. Rather than being difficult to amend as most government regulations are apt to be, consensus standards can evolve as technology evolves, ensuring that consumers continue to receive state-of-the-art technology. Because this is done by private working groups, it is off-budget, eliminating the problem of government budget constraints in promulgating and revisiting standards. Rather than waiting for the FDA to get around to issuing performance standards, consensus standards should become the norm.[98]

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[97]Clinton, page 4.

[98]For an excellent discussion of consensus standards see, "Reinventing the Regulation of Medical Devices II: Towards A Public-Private Partnership for Device Regulation," National Electrical Manufacturers Association, (June 1995), pages 5-7.

Devices in Class III, high risk devices and devices not substantially equivalent to devices on the market before 19[illegible],[99] would be evaluated under a scheme similar to that utilized by the EC. Notified bodies would have the authority to issue final approval for the device without concurrence from the FDA. This is likely to be highly controversial, but sound policy. As the above discussion demonstrates, the delays in the entry of new medical technologies in the United States imposed by the current regulatory regime for Class III medical devices have substantial human costs.

The rules for approving clinical trials must also be reformed. In Europe, clinical trials may begin after 90 days unless the agency specifically notifies the manufacturer not to begin the trials. In the U.S., it can take years to gain permission to begin clinical trials. The American system should be reformed to allow the trials to go ahead unless the FDA specifically orders the manufacturer not to proceed and identifies specific reasons why the trial should not go forward. In such a case, the FDA would be required to meet with the applicant in a timely fashion and work with the applicant to resolve the issue.

Overall, the EC system has provided as much protection to consumers as the FDA's regulatory system. There have been devices marketed in Europe that have turned out to be unsafe, but most of these have also been approved in the US. As noted above, the FDA could only cite one example, the Bjork Shiley 70 degree heart valve, of a defective device that was approved in Europe and not in the US. On balance, there does not seem to be much evidence that FDA system contributes much in consumer protection beyond that offered by the EC system, while imposing substantial delays on the introduction of new medical technologies. While it may take some time for Americans to get used to the idea, a largely privatized approval system would protect the public from unsafe devices as well as the FDA currently does. Over the long term, Americans would probably accept the new arrangement. After all, people in Europe, who rely on

[99]Technically, non-substantially equivalent devices can be reclassified into a lower category if they are not high risk, but this rarely occurs in practice.

government for cradle to grave protection from a variety of social and economic ills, have accepted the private approval of medical devices.

Moreover, reforming the device approval process is more than just an academic philosophical debate: it has very real implications for the quality of health care in the United States. Regulatory delay costs America high-paying jobs and threaten one of its most innovative industries. The real losers under the current system, however, are the patients who are denied access to the latest medical devices and may ultimately pay with their lives. Just as FDA needs to realize that inaction has costs and consequences, so does Congress. Putting off FDA reform for another year may be safe and effective politics, but it saddles Americans with the current system and all of its human costs for another year.

Attachment 3

FDL Issue 95-02: IHS Regulatory Products, Inc.
Search Date: Wed Jul 26, 1995

ERICAN BIOCHEMICALS INC.

od and Drug Administration
Los Angeles District
1521 West Pico Boulevard
Los Angeles, California 90015-2486
Telephone: (213) 252-7583

July 20, 1993

WARNING LETTER
WL: 77-3

Certified Mail
Return Receipt Requested

Simon C. Khoury, President
American Biochemicals, Inc.
11180 Roselle Street
San Diego, CA 92121

Dear Mr. Koury:

During an inspection of your medical device manufacturing facility, conducted between April 13 and 14, 1993, our investigators documented serious violations of applicable medical device regulations, causing your in vitro diagnostic oducts to be adulterated and misbranded within the meaning of the Federal d, Drug, and Cosmetic Act ("Act").

The inspection revealed there is no assurance that the methods used in or the facilities and controls used for the manufacture, packing, or storage of in vitro diagnostic products are in conformance with the Good Manufacturing Practice for Medical Device regulation (Title 21 of the Code of Federal Regulations, Part 820). The violations cause your products to be adulterated within the meaning of Section 501(h) of the Act. Among the violations are the following:

1. Failure to establish device master records for each device manufactured, packaged, and/or labeled.

2. Failure to prepare and maintain device history records.

It was also determined during the inspection that labels for your firm's products fail to include control numbers which make it possible to determine the complete manufacturing history of each products. Control numbers are required for in vitro diagnostic products by 21 CFR part 809.

The inspection also revealed that your in vitro diagnostic products (e.g., goat anti-human IgG FC fragment and thyroglobulin) are misbranded under Section 502(o) of the Act, in that premarket notification information was not provided to the Food and Drug Administration as required by Section 510(k) of the Act, nd the devices were not found to be substantially equivalent to predicated ices. Moreover, because the devices have not been determined to be ostantially equivalent, they are adulterated under Section 501(f)(1)(B) of the

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Act, in that as Class III devices they do not have in effect approved applications for premarket approval pursuant to Section 515(a) of the Act, or approved applications for investigational device exemption under Section 520(g).

Finally, the inspection disclosed that your firm has not submitted device establishment registration to FDA, nor device listing information, required by 21 CFR part 807. Your in vitro diagnostic products are therefore further misbranded under Section, 502(o) of the Act.

We note that labels for each of your in vitro products bears a statement that they are intended for "research use only". It was determined, however, that your firm does not assure the products are limited only to research use.

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence with each requirement of the Good Manufacturing Practice regulation. Until these violation are corrected, Federal agencies will be informed that FDA recommends against the award of contracts for affected products.

You should take prompt action to correct these deviations. Failure to do so may result in regulatory action without further notice. These actions include, but are not limited to seizure, injunction, and/or civil penalties.

You should notify this office in writing, within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step taken to prevent the recurrance of similar violations. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your reply should be addressed to:

Thomas L. Sawyer
Director, Compliance Branch
U.S. Food and Drug Administration
1521 W. Pico Blvd.
Los Angeles, CA 90015

Sincerely,

Elaine C. Messa
District Director

cc: California State Department of Public Health
Food and Drug Branch
714 "P" Street, Room 440
Sacramento, CA 95814

Attachment 4

FDA

TALK PAPER

FOOD AND DRUG ADMINISTRATION
U.S. Department of Health and Human Services
Public Health Service 5600 Fishers Lane Rockville, Maryland 20857

FDA Talk Papers are prepared by the Press Office to guide FDA personnel in responding with consistency and accuracy to questions from the public on subjects of current interest. Talk Papers are subject to change as more information becomes available. Talk Papers are not intended for general distribution outside FDA, but all information in them is public, and full texts are releasable upon request.

T95-22
May 23, 1995

Sharon Snider
(301) 443-3285

TELECTRONICS AGREES TO CORRECT MANUFACTURING PROBLEMS

Telectronics Pacing Systems has agreed to stop distributing in the United States all pacemakers and pacemaker leads made at its facilities in Englewood, Colo., and Miami Lakes, Fla., while it corrects manufacturing problems.

In a consent decree signed by Telectronics (also called TPLC, Inc.) and its president, and filed in federal court, the firm agreed to bring its facilities into compliance with regulations governing current good manufacturing practice (GMP).

The firm's manufacturing deficiencies have caused numerous problems that may have affected the safety or quality of its products.

Recent inspections by FDA have shown that Telectronics did not have an adequate program in place to identify and solve manufacturing problems. The firm had not followed proper testing and inspection procedures, had not adequately investigated device failures before and after products were distributed, and had not properly reviewed and investigated complaints.

-More-

T98-22, Teletronics Agrees to Correct Problems

Many of these same problems were identified by FDA in previous inspections of the firm during 1993 and 1994, but Telectronics did not implement necessary corrections.

Telectronics has now agreed to correct the GMP deficiencies at its facilities and have those corrections certified by an outside consultant. The company will then demonstrate to FDA's satisfaction that corrective action has been taken. Outside audit inspections will be conducted at each facility at least twice a year for three years to ensure that the facilities continue to meet the GMP regulations.

In addition, because of similar GMP problems detected during inspections in 1993 and 1994 at its facilities in Australia and France, products from those facilities will continue to be denied entry for sale in the United States.

Last fall, certain Telectronics pacemaker atrial "J" lead wires were reported to fracture in some patients after they were implanted. Telectronics alerted doctors, and patients who had the device implanted, to this problem. The unused leads were recalled by the firm.

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Attachment 5

REMARKS

by

DAVID A. KESSLER, M.D.
COMMISSIONER OF FOOD AND DRUGS

Good morning.

I'm fully aware that the past couple of years have seen a crisis of confidence about the Food and Drug Administration. Some people have been saying that the FDA simply cannot do the job it is supposed to do.

I am here this morning to dispel those rumors.

Any rumors you may have heard about the death of the FDA have been greatly exaggerated.

Since joining the FDA, I have emphasized management and enforcement. In my view, strong management is essential if the FDA is to regain its reputation as an organization that makes decisions -- and then acts on them.

There is no substitute for decisiveness in all aspects of FDA's work.

Likewise, strong enforcement provides the best means I know to restore FDA's most precious commodity: credibility.

But management and enforcement are only tools.

This morning, I'd like to discuss two results I hope to achieve through the use of these tools. They are central to the Agency's public health mission. And, because of my professional training, they also have great importance to me personally.

First, the information on products must be factual, and it must tell the whole story.

Second, our creative energies must be focused on speeding up product development and review. Let me speak about each goal in turn.

Clear and accurate labeling is a fundamental premise of the Federal Food, Drug and Cosmetic Act -- and of the 1962 Kefauver-Harris amendments as well. The recent FDA actions concerning the food label were designed to restore clear and accurate labeling, so that American consumers can make informed choices about the food they purchase and consume.

If there is one resounding message from our recent actions, it was that Americans care very deeply about not being misled -- especially those who rely on product labels to make decisions that affect their health.

No one should underestimate the depth of their feeling. The American people -- and health care professionals -- have no stomach for the feeling that they are being deliberately misled.

Concerning food labeling, there are some who have argued that the FDA should provide clearer guidance about what it expects on the label.

I agree with those observers.

And yet -- there is a fundamental repositioning that needs to take place in the industry.

I would urge certain segments of the industry to shift their thinking on labeling. Unfortunately, it's as if some firms are asking themselves, "How long can I get away with misleading information on my label?"

A more appropriate question, in my view, is this: "How can I use accurate information, clearly presented, as a competitive advantage?"

When it comes to product labeling and promotion, I have two expectations: the information must be factual, and it must contain the whole truth.

Recent experience shows that the kernel of truth in a half truth is sometimes the worst half.

The importance I attach to accurate information has obvious ramifications for the advertising and promotion of prescription drug products.

Last week, I had the opportunity to testify before Representative Weiss, Chairman of the House Government Operations Subcommittee on Human Resources and Intergovernmental Relations.

My message was stark and clear:

- First, the use of unapproved drugs and devices must stop.

  For example, using liquid silicone for injection is illegal. Its use by physicians to remove wrinkles has not been approved. This practice must stop.

- Second, the promotion of unapproved products -- including unapproved uses -- is also illegal, and subject to regulatory action.

Selected promotional practices have, to be blunt, gotten out of hand.

The current situation requires action.

We have seen the frank promotion of collagen injections for unapproved uses. Ultimately the firm in question agreed to cease these illegal promotions. But in my view such promotions may have become an unfortunate sign of the times.

Please do not misunderstand my message. What I am saying is that the FDA needs to take a closer look at the various promotional activities of the pharmaceutical and medical device industries. We want to make sure that promotional activities are appropriate, that they provide clear and accurate information.

You have my word that we will go about this task in a way that legitimate, responsible pharmaceutical firms will have no difficulty accepting.

We do not seek to interfere with innovations in the way legitimate information about new products is conveyed. I am acutely aware that the FDA has a responsibility to foster the availability of useful and accurate information.

But -- when action is called for -- I can assure you that the FDA will not hesitate to act.

Let me take a few minutes to explain why I believe there is a problem -- and what the FDA intends to do about it.

When a former star athlete appears on national television and discusses his arthritic knees, that is his business.

However, when the same former star, under sponsorship of a pharmaceutical firm, extols the virtues of a particular drug, his endorsements fall within the jurisdiction of the FDA.

When the drug is not unique, but one of many in its class, and when the former star has not been taking any medication for his arthritis, it is misleading to suggest that the product is a uniquely effective wonder drug.

It is more than misleading. In essence, the star's television appearance constitutes an advertisement -- it is promotional.

To the extent that it is promotional and fails to disclose side effects and contraindications or to include a so-called "brief summary," it also lacks fair balance.

Consider another example: the promotion of Retin-A to prevent wrinkling. The only approved use of this product is for acne vulgaris. Promotion of any other use of Retin-A is by definition an unapproved use and is, therefore, contrary to law.

These examples illustrate the three principal requirements of drug advertisements and promotions:

-- that they be true and not misleading,

-- that they provide "fair balance,"

-- and that they do not promote unapproved uses.

The sheer volume of prescription drug promotional activities concerns me.

Over the past two decades, for example, resources devoted to industry-sponsored symposia have increased exponentially. According to the Congressional Research Service, sixteen companies sponsored 34 thousand symposia during 1988 -- at a cost exceeding 85 million dollars.

Comparable figures for 1974 showed that the same firms had sponsored seven thousand symposia, spending some six million in 1988 dollars.

In 1988, these 16 firms spent more than 13 times what they spent -- in constant dollars -- 14 years earlier.

Perhaps even more significant, conventional methods of drug promotion -- print advertising and written materials -- are being supplemented by non-traditional promotional techniques that rely heavily on researchers and medical experts.

There may be nothing inherently wrong with new techniques, such as special supplements to professional journals and satellite symposia. But the FDA is seeing several drawbacks in their current, "real world" application.

First, the new promotional techniques are beginning to blur the distinction between promotion and legitimate scientific exchange. If left unchecked, this trend could eventually dilute the quality of scientific discourse.

Second, these practices can mislead the medical community and, ultimately, the public.

Third, the inappropriate use of promotional tactics can give unscrupulous firms an unfair market advantage.

When it comes to questionable promotion of prescription drug products, I'm not sure who's kidding whom.

There is no place in pharmaceutical advertising and promotion for misleading statements and half truths.

That is why FDA is paying increased attention to the advertising and promotion of prescription drugs. We are beefing up the Division of Drug Marketing, Advertising, and Communications by more than doubling the number of employees in the Division.

The significance of these changes should not be lost on anyone.

I have asked Ann Witt, the new acting director of this division, to pay special attention to one particular concern: promotion in the guise of scientific exchange.

Beefing up enforcement, adding new resources, however, is not enough. It is simply not acceptable for the FDA to declare unilaterally, when we have concerns, that -- in effect -- "we won't permit that kind of promotion."

We must also provide guidance on what is acceptable. Moreover, we should find ways to involve affected parties in the dialogue.

We are working to achieve both of these goals.

For traditional advertising and promotion, there is a reasonably clear sense of what is acceptable.

But for the newer promotional tools, it has become more difficult to judge where scientific exchange ends -- and promotion, sometimes illegal promotion, begins.

To remedy the current situation, FDA is hard at work on a policy that will suggest ways of drawing the line -- often a fine line indeed -- between scientific exchange and promotion.

We are in the final stages of preparing a draft policy. Before adopting a final policy, however, we will seek the advice of industry, consumers, and the medical community.

We intend to have the final guidance in place by the end of the year -- this year!

I would urge all members of the pharmaceutical industry to take a long and hard look at their promotional practices. I do not expect companies to wait until this guidance becomes final to put their advertising and promotional houses in order.

The current excesses must stop.

Although our draft policy is not quite ready for public discussion, I would like to suggest the broad directions that any such policy is likely to include.

I expect that such a policy would take into account several factors that the FDA will consider in determining whether drug products have been illegally promoted.

- The first characteristic is independence. This is very important.

  I would expect that "independence" under such a policy would mean that the sponsor of a symposium would not be able to exert control, implied or expressed, over the content of the program.

- A second factor is objectivity. Sponsors should provide funds to organizations, such as professional societies, that are known for their objectivity.

  The programs should involve independent scientists. The goal is presentations that are objective and not promotional in tone.

- A third, related, factor is balance. The concept of "balance" would apply to the statements or presentations in aggregate.

  It would involve diverse views about a drug, or a class of drugs, or of ways to treat a disease. "Balance" would suggest that a variety of legitimate medical opinion be represented.

- A likely fourth factor would be scientific rigor. This connotes reliable data. It suggests an appropriate research paradigm that shows no bias concerning a drug -- and does not rely on anecdotal evidence.

Presumably, this policy will describe how the FDA can deem a company-sponsored educational activity to be promotional.

There is, however, one important caveat.

FDA can never anticipate every possible promotional scheme -- nor can we be reasonably expected to do so.

I would suggest that it would be prudent for industry to watch FDA's stance on the promotion of all products.

You should not confuse me with Pollyanna, or with Voltaire's Dr. Pangloss, who always contended that ours was the best of all possible worlds. What we are attempting is not easy, and it will not occur overnight.

What I'm trying to achieve in regulating the promotion of prescription drug products is simple: the FDA must ensure that information about drug products tells the whole story.

And I hope that FDA will also be able to make these changes permanent -- so that, when other priorities come along, the flow of accurate information about drug products will not be interrupted.

That's one priority: accurate and complete information about FDA-regulated products.

Now, I'd like to shift gears and describe the second overall priority -- finding ways to manage the product review process so that safe and effective products reach the market promptly.

The truth is that FDA's approach toward drug development has, within the last few years, undergone a sea change. Instead of waiting for completed marketing applications, many review divisions have begun to involve their scientists at an earlier stage in the review process.

The intensity of their efforts is noticeable.

They are working more closely with the drug sponsors and FDA's sister agencies, such as the National Institute for Allergy and Infectious Diseases and the National Cancer Institute. The relationship between FDA and NIH has never been stronger.

The FDA Division of Anti-Viral Drug Products has become intensely involved in all phases of drug development. FDA scientists are helping advance the process all the way from discussions of concepts through protocol design, from early review of data to discussions of post-marketing studies.

Anyone who has had contact with them cannot fail to notice that the division's reviewers are physicians and scientists who are filled with a special spirit. They are energetic, assertive and determined to make a difference -- and more often than not, they succeed.

For many life-threatening diseases, the FDA now permits the therapeutic use of drugs to occur at the same time as clinical studies. And much of this transformation is being codified to become a permanent part of FDA's response to life-threatening diseases.

We need to make sure the same sense of urgency characterizes our approach to Alzheimer's disease.

We agree that Alzheimer's is serious and devastating. And we understand that it is sometimes appropriate to allow patients to accept greater risks with respect to safety -- given reasonable assurances of efficacy.

There is no doubt that the FDA has made progress. Dr. Peck and his colleagues face a task of enormous magnitude -- and I commend them for their systematic and competent approach to getting the job done.

Dr. Peck and his team have my unqualified support.

FDA has accomplished much in becoming more compassionate and flexible in reviewing new products. In the new drug area overall, some very positive trends have emerged. I fully expect them to continue -- and to accelerate.

During the first five months of 1991, the Center for Drug Evaluation and Research approved nine new molecular entities, an approval rate that is distinctly unusual for the first half of the year.

Barring unforeseen obstacles, there is good reason to believe the approvals of new molecular entities in 1991 will significantly exceed those of most previous years.

Nevertheless, much work remains.

I recognize that the new flexibility, the new attitudes, have not quite penetrated everywhere. Change never takes hold instantaneously in a large, diverse, professional organization.

That is why we must continue to drive change in the way we review new drug products, new biologicals, new medical devices.

Let me focus on three areas which, in my view, require attention.

First, it is clear to me that FDA needs a greater degree of consistency in what it requires of drug sponsors. There is simply not enough consistency among the various drug review divisions.

One project already underway should help remedy this situation: the pilot program for computer assisted new drug applications. FDA must move that project along and standardize the process, so that drug firms will have the benefit of more consistent procedures across the board.

We are also looking at ways to use advisory committees more uniformly. I am hopeful that an improved advisory committee process will improve the consistency of FDA's interactions with industry.

Second, the agency needs to empower capable scientists and reviewers -- at all levels -- to make decisions. A couple of weeks ago we announced that from now on the Director of the Division of Oncologic Drugs will be authorized to sign off on new cancer drugs.

No one should underestimate the importance of this change.

But everyone should recognize that we cannot take review layers out -- until we put capability in. And by capability I do not mean scientific capability. The FDA has plenty of that.

I mean management capability.

We need to find better ways to support our first-line scientists and drug reviewers.

We must provide them with clearer guidance on what kinds of issues they should routinely handle and when -- and how -- they should pass on complex matters to those higher in command.

We need to avail ourselves of the expertise of supervisors without the delays that accompany additional layering. And we need to get the whole job done within a prescribed time frame.

Third, I believe that -- to the extent possible -- FDA needs to give industry a better sense of our projected timetables for product review.

This means better tracking and coordination systems within FDA, so that we can predict with a greater degree of accuracy when a given review will be complete.

If FDA can become more reliable at forecasting, industry will be able to plan more efficiently for the manufacture, production and "launching" of its new products.

Those are three goals -- admittedly ambitious goals -- for the drug review process.

I'd like to add an endnote. Senator Hatch has eloquently discussed the problems with generic drugs. Let me comment on where we are in restoring the generic drug review process.

Drs. Peck and Williams -- and their colleagues -- have done much to reestablish the credibility of the nation's generic drug program.

However, the dramatic reduction in generic drug approvals -- from around 800 per year to less than 100 last year -- concerns us all.

I believe that the management changes now in place are beginning to take hold. We anticipate that by next year the new Office of Generic Drugs can attain the full production rate suggested by the Kibbe review panel -- somewhere between 20 and 25 ANDA approvals per month.

Dr. Peck's staff is currently preparing a management plan to ensure that this forecast is accurate.

That's the news from Rockville, as Garrison Keillor might say, concerning drug promotion and advertising -- and the review of new drug products.

Let me close with a couple of stories I've heard in the past two weeks. Both concern the perceptions of highly placed executives in the pharmaceutical industry.

One of them told me of a recent experience in his office. A subordinate of this executive walked in and complained, "Those guys at the FDA just told me they didn't like the way we had presented the summary of safety data."

"What are you complaining about?" the senior executive quickly responded. "We sent that summary in just two months ago."

Another senior manager in the pharmaceutical industry told me of a call he had recently received from the FDA.

The FDA's call had set off a mild panic -- but not of the sort you might expect. The FDA official had called simply to report that, within 12 months, the agency would complete its review of an NDA submitted by the firm.

This had never happened before.

Apparently the company didn't know what to do. Its manufacturing plans for the drug were not ready.

In essence, the firm had to scurry around to catch up with the FDA.

I hope -- and I expect -- that the pharmaceutical industry will begin to witness more and more of these episodes in the months and years ahead.

One last anecdote: last week, a reporter asked me about the nicest thing that had happened to me during my first six months at the FDA.

Without hesitation, I answered that it is the people of the FDA, coming up to me in hallways, shaking my hand in elevators. They tell me that the agency is alive again. They say they have pride in the FDA.

They report that they are happy to be doing the job they signed on for: protecting and promoting the public health.

Thank you.

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