



HEALTH INDUSTRY MANUFACTURERS ASSOCIATION

SUSAN K. ZAGAME

VICE PRESIDENT TECHNOLOGY AND REGULATORY AFFAIRS

1000 17th Street, N.W. Suite 400
Washington, D.C. 20036-3814

May 19, 1999

Docket Management Branch
(HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 99N-0386: Talking With Stakeholders About FDA Modernization; Notice of Meetings and Teleconference

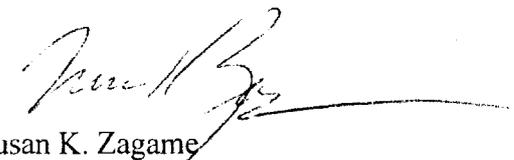
Dear Sir or Madame:

Attached is a copy of written comments submitted to Docket No. 99N-0386 in connection with the series of stakeholders meetings held on April 28, 1999.

Please let us know if you have any questions.

Thank you.

Sincerely,



Susan K. Zagame

Attachment

99N-0386

World Leaders in Health Care Innovation
200 B STREET, N.W. SUITE 400
WASHINGTON, D.C. 20005-3814
TEL: 783-8700 FAX: (202) 783-8750
WWW.HIMA.ORG

C30

“TALKING WITH STAKEHOLDERS ABOUT FDA MODERNIZATION”

Written Comments Submitted in Connection with April 28, 1999 FDA Stakeholders' Meetings

Submitted by Susan K. Zagame
Vice President
Technology and Regulatory Affairs
Health Industry Manufacturers Association

Docket No. 99N-0386

These comments are submitted by the Health Industry Manufacturers Association (HIMA) in connection with public meetings and an interactive satellite teleconference entitled “Talking With Stakeholders About FDA Modernization” held on April 28, 1999. HIMA is a Washington, D.C.-based trade association and the largest medical technology association in the world. HIMA represents more than 800 manufacturers of medical devices, diagnostic products, and medical information systems. HIMA’s members manufacture nearly 90 percent of the \$62 billion of health care technology products purchased annually in the United States, and more than 50 percent of the \$147 billion purchased annually around the world.

Introduction

HIMA applauds the Food and Drug Administration (FDA)—especially the Center for Devices and Radiological Health (CDRH)—for its considerable efforts in implementing the Food and Drug Administration Modernization Act of 1997 (FDAMA). We further recognize the achievements resulting from the agency’s reengineering and management initiatives. Review times for medical devices have decreased since the peak year of Fiscal Year (FY) 1994, collaboration has increased measurably, progress has been made to improve the inspections process, and many of the conditions that led to the enactment of FDAMA have ameliorated if not abated.

However, the challenges for the agency—and consequently, for industry in its dealings with the agency—have not diminished. FDA is charged with implementing a complex and demanding statute. It wields enormous economic power over a substantial portion of the marketplace. Public expectations of the agency’s ability to provide the most technologically advanced products, risk-free, and immediately—can be unrealistic. And the agency is under constant scrutiny by the Congress, the public, and we, the stakeholders.

Such challenges require optimal levels of communication, cooperation, consultation, and collaboration. We support the agency’s ongoing attention to seek improvements in these areas and welcome the opportunity to provide suggestions.

Our comments are organized as follows: **I. Overall General Recommendations:** HIMA's answers to the specific questions together with comments at previous stakeholders' meetings, contain similar themes. These can be distilled into several overall general recommendations. **II. Ongoing General Concerns:** HIMA's priority concerns of a more general nature than the specific issues posed by FDA include development times, review times, and issues involving the Center for Biologics Evaluation and Research. **III. Responses to FDA's Specific Questions.**

I. Overall General Recommendations

Faced with shrinking resources, increased statutory obligations and public expectations, we recommend that the agency (1) devote its resources to core statutory obligations, (2) focus its resources on highest risk and new technology products, (3) maximize the tools of FDAMA, (4) continue to seek improvements through reengineering and other management initiatives, (4) leverage resources from both the public and private sectors, (5) cease activities that are not essential to carrying out the law, and (6) seek additional funding from Congress for device reviews.

HIMA supports additional funding for the agency devoted to device review and other activities. Attached is a copy of HIMA's testimony on FDA's fiscal year 2000 budget submitted to the House Committee on Appropriations' Subcommittee on Agriculture, Rural Development, FDA, and Related Agencies and the Senate Committee on Appropriations' Subcommittee on Agriculture, Rural Development, and Related Agencies (Attachment I).

II. Ongoing General Concerns

Development Times

One of the general concerns of the medical device industry is development time—the time it takes to produce the data and other information required by FDA to meet the threshold level of evidence necessary for the review to begin. This issue is tied to Section 205 of FDAMA that requires FDA to consider the “least burdensome” appropriate means to demonstrate device effectiveness or substantial equivalence to predicate devices with differing technological characteristics. The least burdensome concept does not reduce the scientific standard for effectiveness; this concept is intended to carry out Congress' longstanding purpose included in the “Medical Device Amendments of 1976” to avoid over-regulation of devices. It is also tied to President Clinton's statement upon signing FDAMA that the law would “ease the regulatory burden on industries” Furthermore, the overall goal of speeding beneficial technology to patients is one that is greatly affected by the length of time it takes to meet FDA's threshold review requirements.

HIMA chairs an industry-wide “Least Burdensome Industry Task Force” that has submitted a proposal to the agency on recommended approaches for how this concept should be implemented by FDA. A copy of that proposal is attached to these comments (Attachment II). We urge the agency to carefully consider that proposal and request a meeting to exchange ideas concerning “least burdensome.”

Review Times

Review times remain an issue of primary concern to medical device manufacturers. According to information submitted by FDA to Congress,¹ only 64% of 510(k)s and 51% of PMAs were reviewed within statutory time frames in FY 1997. Despite the fact that FY 1998 data appears to show improvements, we believe that FDA's goal should be to complete nearly all submissions within the review time frames established by law.

We are becoming increasingly concerned with what appears to be a redefinition of the review time frames mandated by statute. For 510(k)s, the law requires the Secretary to "review the report. . . and make a determination . . . not later than 90 days after receiving the report." (Federal Food, Drug, and Cosmetic Act (FFD&C Act) § 513(n)) For PMAs, the statute requires that "As promptly as possible, but in no event later than one hundred and eighty days after the receipt of an application . . . (or unless . . . an additional period as agreed upon . . .), the Secretary . . . shall . . . issue an order approving the application . . . or deny approval of the application . . ."

In the FDA Plan for Statutory Compliance (the "Plan") and in its budget justification documents (see footnote 1), FDA appears to be redefining its statutory obligation to be one of "completing first actions" or "percentage of first actions" within statutory time frames. In the Plan, the agency states that its FY 1999 goal is to review 50% of PMAs within 180 days (compared with 65% in FY 1997) but indicates that the goal is stated in terms of "percentage of first actions within time frames."

In comparison, the budget justification documents state that the FY 1999 estimate is for 70% of PMA First Actions [to occur] Within 180 Days. It is confusing for industry to be able to determine whether the goal is 50% or 70% or what the differences are between the two documents. Attached are copies of the relevant pages of the two documents (Attachment III).

An additional concern we have is the potentially misleading way in which the agency portrays the "overdue" applications. In the Plan, the agency defines "overdue" applications as "those whose review period exceeded the time frames and were under active review at the end of the fiscal year." This excludes all those applications that are pending but which are not "under active review" because the agency has put them "on hold" due to questions about the application, requirements for the applicant to produce additional data, or some other obligation imposed on the applicant. While it may be technically accurate to define overdue applications in this manner, at the very least it is misleading in that it does not give stakeholders a true picture of the number of applications that are pending with the agency and the obstacles that may be delaying marketing. We urge the agency to at least list the number of applications pending at the end of the year (i.e., those that are still active but "on hold") in all such documents.

However the numbers are articulated by the agency, it is clear that the agency believes time frames will increase unless user fees are enacted this year—an unlikely event. This is of grave

¹ See, Department of Health and Human Services Fiscal Year 2000 Food and Drug Administration "Justification of Estimates for Appropriations Committees and Performance Plan."

concern to the medical device industry and one that we urge the agency to address in accordance with Section 406 (b)(2)(E) and (F) of FDAMA. Those sections require the agency to establish mechanisms by July 1, 1999, for eliminating backlogs and for meeting statutory time frames for submissions. The agency indicated in the Plan that it intended to "reevaluate where it stands in relation to this objective" in the spring of 1999 and that it planned to make information on this objective "easily available to Congress, the public, regulated industry and other stakeholders." We do not know of any actions taken by FDA in accordance with these statements.

The Center for Biologics Evaluation and Research (CBER)

While the majority of devices are regulated by CDRH, there are a number of devices that are regulated by CBER. The device provisions of FDAMA also apply to these devices. Not surprisingly, industry's ongoing concerns with device reviews conducted by CBER do not differ significantly from those expressed earlier in this document with regard to CDRH. Product review times top the list of issues for both Centers. However, medical devices are not CBER's primary focus. Consequently, until very recently, little attention has been paid to the medical device industry's concerns over the increasing product review backlog at CBER.

Changes are in progress. CBER has held several meetings to gain a better understanding of the concerns of the device industry. As a result of these interactions with industry, CBER is now focusing on improving its device review activities through the development of a CBER Device Action Plan. The plan, which is greatly needed and long overdue, is intended "to facilitate the implementation of the device provisions of FDAMA and to assure consistency of policy and procedures between CBER and CDRH." This is a laudable goal and we look forward to learning more about the specifics of the plan.

Any plan is only as good as the input provided to develop it. We remind CBER of the necessity to communicate, collaborate and consult with stakeholders in the development of the device action plan. It will be a challenge for CBER to involve industry as a partner in the development of a device action plan. Part of that challenge will require CBER to think beyond its traditional ways of doing business and allow its stakeholders both in the medical device industry and the blood banking community to help set realistic, science-based goals for its device-related functions.

Although long product review times remain an issue of primary concern, manufacturers also note an apparent disconnect between what CBER wants in product submissions and what manufacturers think CBER wants in product submissions. After waiting six months to receive the initial round of questions on a submission, on average it takes a manufacturer three to six months to respond to CBER's queries. CBER cites poor product submissions for these delays. We believe part of the problem is lack of clear guidance on submission requirements. CBER and the industry must work together to develop guidance documents that clearly define what is expected of both parties.

CBER should also ensure that its reviewers are adequately trained on and make appropriate use of the "least burdensome" concept discussed earlier. Often, CBER requests extensive studies when other less burdensome studies could demonstrate device safety and effectiveness. This discourages manufacturers who often then develop and market products that could improve the

safety of the nations' blood supply outside of the U.S. We recommend that CBER participate in any discussions between CDRH and industry on "least burdensome."

Any good plan includes some way to measure progress. Traditionally industry has measured FDA progress by monitoring product review times. Complete, timely data on CBER device review times is generally not available. CBER should publish its review times metrics on a regular basis to provide both the Agency and industry a yardstick to gauge the progress made.

III. Responses to Specific Questions for April 28, 1998 Stakeholders' Meeting

In the *Federal Register* announcement of the meeting, FDA asked for specific input on five questions. HIMA's responses follows:

Question #1: What actions do you propose the agency take to expand FDA's capability to incorporate state-of-the-art science into its risk-based decision-making?

One of the issues this question raises, as a general matter, is the need for FDA to be vigilant in ensuring that it is incorporating the appropriate level of science in its decision-making processes. For instance, the regulatory requirements for PMA approval set a "reasonable assurance" of safety and effectiveness standard—not an "absolute assurance." FDA must ensure that whatever quantum of science it applies to its decision-making must be within the regulatory construct of the law. Scientifically-based conclusions must represent a balance between risks to public health and benefits to public health.

In addition, as a government agency, there will always be financial constraints on FDA's ability to hire leading experts. The agency will seldom be able to compete with the resources of academia or industry. However, the key to incorporating state-of-the-art science into the FDA decision-making process lies in the ability of reviewers to understand data, interpret results, and ask *appropriate* questions. FDA should focus on developing these skills for its review staff.

Specific actions that address this question are as follows:

Leverage Industry Resources—Company tutorials, vendor days, cosponsored educational workshops, etc.

HIMA proposes that FDA take advantage of industry resources to expand its own scientific base of knowledge. Industry is willing to bring scientific experts into FDA to provide state-of-the-art information to staff. Vendor days have been a very successful mechanism to provide "hands-on" exposure to actual devices and demonstrations from industry. We recommend they be continued. Cosponsored educational workshops are another vehicle for dissemination of scientific information. HIMA is working with the agency to develop a "Cooperative Research and Development Agreement" (CRADA) to fund such workshops.

Outside Experts—Government Agencies, Academia, the Private Sector, Scientific Advisory Panels

In this age of budgetary restraint, FDA should recognize that it is impractical to have adequate resources to hire leading experts in all the disciplines that are required for the wide variety of FDA-regulated products and should develop a strategy that identifies outside resources to support internal needs. FDA should continue to strengthen its use of and relationships with its sister governmental agencies such as the National Institutes of Health. The agency should also use the expertise resident in its own scientific advisory panels. Consulting contracts with academia and private sector scientists are additional ways to meet this need.

In order for the agency to have greater access to private sector resources, we suggest reviewing the current conflict-of-interest policy to determine whether it can be amended to allow more flexibility in the hiring of outside experts. We believe there may be many situations where experts with some degree of conflict-of-interest may still be acceptable provided there is full disclosure.

We understand that there have been instances where FDA has declined to meet with industry experts when similar expertise is available within FDA or its sister agencies. Since outside experts can bring additional and up-to-date views and information to the discussion, we recommend such a policy be discontinued.

Continuing Education for Staff

We recommend that FDA require staff physicians to participate in Continuing Medical Education—preferably in the areas of expertise they are required to use in their positions. Members of industry report instances where medical officers within FDA are not familiar with current medical procedures and practices. The lack of up-to-date medical knowledge causes delays in the review process. Similarly, FDA should at least encourage, if not require, its scientists to keep current in their field by taking advantage of seminars and other educational opportunities.

Optimal Collaboration Meetings

The need for knowledge about state-of-the-art science often arises during the course of the FDAMA meetings for (1) determining the type of scientific evidence required to show device effectiveness and (2) agreeing on the investigational plan. Both industry and the agency can optimize these meetings by ensuring that scientific experts, statisticians, and other necessary experts are present and fully prepared to discuss the scientific issues.

FDA's Own Excellent Scientists

HIMA supports increased funding for the agency targeted to device reviews. If FDA receives such an increase, some portion should be devoted to hiring reviewers with excellent scientific backgrounds. The decisions of current (and future) reviewers and other staff involved in the review process should be respected and not “second-guessed” by staff who may become involved in the process at a later point. Industry reports incidents when this has happened, causing unnecessary disruption and delay. The agency should give deference to the decisions of its scientists and not allow another scientist's subsequent view or opinion regarding an aspect of the process to prevail unless there is a clear public health or safety issue.

Standards for High Risk Devices

Many scientific experts, including FDA's own, are substantially involved in developing standards for medical devices, or portions thereof, as part of national and international consensus committees. Scientific issues associated with such standards are debated and discussed in an atmosphere not governed by a single company's product. Such standards and industry's declarations of conformance thereto are effective surrogates for FDA's independent scientific review. We recommend, therefore, that both industry and the agency increase their participation in standards-setting bodies and that FDA continue to recognize such standards and defer to them in the application process. We further recommend that the focus be on standards-setting activities involving high risk devices since that is the area of greatest potential return for both the agency and industry.

Question #2: What actions to you propose to facilitate the exchange and integration of scientific information to better enable FDA to meet its public health responsibilities throughout a product's lifecycle?

This question first asks for ways to improve FDA's access to scientific information. This was addressed in the previous question. The second part of this question deals with FDA's public health responsibilities through a product's lifecycle. This part of the question raises again the need for FDA to focus on the principles of risk assessment embodied in the regulatory scheme and to train its staff to ask appropriate questions related to risk assessment.

Optimal Use of Staff College and Staff Training

FDA has existing mechanisms in place to facilitate the exchange and integration of scientific information. Those include its staff college and training programs. We recommend that the agency, if it has not already done so, adopt private sector approaches to these mechanisms. They include "Train the Trainer" programs—where one person is trained to return to the workplace and conduct training for the rest of the staff; dissemination of the learning—persons trained return to the workplace and communicate orally, in writing, or via e-mail the main points of the training; diversification of attendance—all levels of staff are sent to training or rotated through—not just senior staff. In addition, we recommend that FDA ask industry to provide scientific experts with practical, relevant experience to participate in training programs.

PMA Annual Reports

Companies with approved PMAs are required to submit annual reports to FDA that contain information about a product throughout its history. 21 CFR §814.84 requires companies to identify certain changes to devices, a summary and bibliography of both published and unpublished reports about the device, including data from any clinical investigations or nonclinical laboratory studies involving the device or related devices. FDA can request copies of such reports.

The annual report provides an excellent mechanism for providing information about a device throughout its lifecycle. We recommend that FDA review how these reports are being used to gather the types of information envisioned by this question.

Question 3: What actions do you propose for educating the public about the concept of balancing risks against benefits in public health decision-making?

Increasingly, consumers are becoming better educated about their own health and personal medical problems. The availability of Internet resources results in patients having more information than their physicians. This creates a demand in the marketplace for additional information by both the consumer and the physician—a demand that will largely be met by the marketplace, not a government agency like FDA. There is no magic bullet that will fully educate the public about how to balance risks and benefits.

Some consumers do believe that products should be completely risk-free. FDA can play a useful role in educating the public generally about the risks and benefits of its regulated products. In addition, FDA has an important role to play in responding to specific allegations of harmful products or materials used in products. It is critical for FDA to determine which of these allegations are legitimate and which are not. FDA must engage in solid risk assessment reviews, make determination about the safety of its regulated products, and ensure that the public is well informed about its decisions.

FDA Web Site

FDA could provide general guidelines for consumers on its web site addressing the concept. A list of questions for consumers to ask may be appropriate. FDA may wish to use its web site to describe, in laymen's terms, the nature of its own responsibilities to balance risk and benefit and how difficult that is at times and that no product is completely risk-free. FDA could provide Internet links to other sites that may contain more specific information about a particular condition, disease, or product. Links could be provided to professional societies, patient groups, as well as individual companies.

Question 4: Because the agency must allocate its limited resources to achieve the greatest impact, what actions do you propose to enable FDA and its product centers to focus resources on areas of greatest risk to the public health?

Continuous FDAMA implementation and reengineering

FDA should continue to implement the tools of FDAMA and its own reengineering initiatives in order to free up resources to use on higher risk devices. This includes taking a critical look at ways to (1) increase exemptions from 510(k), (2) expand recognized standards and increase their use by industry, (3) streamline the reclassification process especially for well-understood medical devices, (4) make optimal use of early collaboration meetings, and (5) harmonize regulatory requirements.

We further recommend that the agency continue to look for management improvements. We applaud FDA Commissioner Jane Henney's recent announcement to reorganize and streamline the Office of the Commissioner.

Industry/Agency Training, Education, Communication

In order to maximize the tools of FDAMA and to create the most efficient systems possible, FDA staff must be adequately trained in their application. In addition, industry must be

adequately educated on FDAMA and reengineering tools as well as the agency's expectations. We applaud the agency's excellent Internet site and its commitment to the publication of guidance documents.

Elimination of Unnecessary or Redundant Functions

FDA should closely examine all of its functions and determine which are not essential to carrying out its core statutory obligations. For instance, scientific research is not FDA's primary role. Consequently, the agency should not attempt to maintain a scientific research infrastructure. Scientific research is the goal of other government agencies, not FDA. FDA should rid itself of all but absolutely necessary functions mandated by law.

Continuation of Inspection Initiatives

HIMA has participated in several successful initiatives to improve the FDA inspection process. Attached is a copy of the presentation addressing these issues given by Nancy Singer, Special Counsel for HIMA, at the Stakeholders Meeting hosted by the Office of Regulatory Affairs in Atlanta, Georgia (Attachment IV).

With regard to the statutory mandate to conduct inspections biennially for manufacturers of Class II and Class III devices, we note that in the Plan, the agency hinted that it might take a look at determining what type of statutory flexibility might be desirable in this area. We believe that the agency should have the discretion to determine the frequency of inspections based on risk and recommend consideration of a statutory amendment to this effect.

Question #5: Because the agency wants to assure that its stakeholders are aware of and participate in its modernization activities, what additional actions do you propose for enhancing communication processes that allow for ongoing feedback and/or evaluation of our modernization efforts?

Need for true consultation, not just comments

As we pointed out at the August 18, 1998 stakeholders' meeting, the statute uses the term "consultation" in connection with FDA's 406(b) obligation. This means more than just listening to or reading comments. If Congress had intended the FDA only to seek public comments, it could have done so. *Webster's* dictionary defines consultation as "meeting to discuss, decide, or plan." Discussion, decision-making, and planning all involve brainstorming, a give-and-take exchange of ideas, dialogue. These meetings do not allow for that kind of activity. We urge the agency to engage in consultation with its stakeholders that may be more meaningful and productive than the type of "consultation" exemplified by these meetings.

No or little feedback from agency on previous comments from industry

HIMA has commented extensively on the regulations, notices, and guidance documents published by the agency to implement FDAMA. In some cases, it appears that our comments have not been acknowledged. While we do not expect all of our comments to be adopted, we do believe that, especially on key issues, the process would benefit from a true dialogue with industry and other interested parties.

Agency and Industry Focus on Important Issues

We have tried unsuccessfully to establish a working dialogue with the agency on several key initiatives such as the “least burdensome” concept. We fail to understand how such an important concept would not benefit from the synergy of a joint working group. Several successful precedents include agency-industry working groups on the Product Development Protocol (the working group received a Vice President Gore “Hammer Award”) and “When to File a 510(k) for a Modification.” These should serve as models for similar activities that should have been undertaken to help develop FDAMA implementation documents. We urge the agency to support and encourage future agency-industry working groups. We believe such groups are particularly useful for difficult and complex issues and issues with the most resource-saving potential.

HIMA Questionnaire

HIMA is in the process of obtaining feedback from its member companies on their experiences with FDAMA. We intend to share the results of the questionnaire with the agency and will consider polling our members on a periodic basis on the same issues.

Conclusion

In conclusion, we thank the agency for this opportunity to provide our ideas and comments. We congratulate the agency on its progress to date in implementing FDAMA. However, we also believe more needs to be done to achieve the promise of FDAMA and stand ready to work with the agency to hasten the day when that promise becomes a reality. Thank you.

ATTACHMENT I

HEALTH INDUSTRY MANUFACTURERS ASSOCIATION

FISCAL YEAR 2000 APPROPRIATIONS TESTIMONY

ON THE

FOOD AND DRUG ADMINISTRATION

SUBMITTED FOR THE RECORD

**SUBCOMMITTEE ON
AGRICULTURE, RURAL DEVELOPMENT, FDA AND RELATED AGENCIES**

HOUSE COMMITTEE ON APPROPRIATIONS

MARCH 18, 1999

Summary

This testimony is submitted on behalf of the Health Industry Manufacturers Association (HIMA) and the more than 800 manufacturers we represent. HIMA is the largest medical technology trade association in the world. Our members manufacture nearly 90 percent of the \$58 billion of health care technology products purchased annually in the United States and more than 50 percent of the \$137 billion purchased annually around the world. We welcome the opportunity to comment on issues surrounding FDA's funding for the next fiscal year.

This year marks a departure from the position HIMA has taken on funding for FDA for the past few years. This year, we believe there should be an increase in funding for the Center for Devices and Radiological Health (CDRH) that is specifically targeted to the following activities:

- Premarket review process
- Activities associated with mutual recognition agreements and international harmonization, and
- The Sentinel Reporting System

With regard to additional recommendations for increased funding contained in the President's FY 2000 budget and FDA's budget accountability, our position is as follows:

- Congress should (1) ensure the optimal design of the Adverse Event Reporting System and (2) direct the agency to invite participation by interested parties in its design.
- Congress should direct the agency to invite participation by interested parties in the design of the Sentinel Reporting System.
- Congress should continue to press for greater budget accountability from FDA.
- We remain opposed to user fees and believe Congress should provide sufficient funds to enable the agency to review device applications within the time frames mandated by law.

Basis for Increased Funding for Devices

In the past, we have supported level funding for CDRH. However, this year, there are several factors that convince us that, unless CDRH receives additional funds for the premarket review process, review times could increase thus depriving patients access to beneficial medical technology. Moreover, we believe FDA needs to invest resources now in initiatives that will ultimately result in a harmonized worldwide regulatory system. We do not wish to see a return to the circumstances of several years ago when products were regularly available to people outside the United States years before American citizens could benefit from them.

Among the reasons for our support of a targeted increase in funding is that FDA itself has announced loudly and clearly that it cannot carry out its statutory obligations without additional resources. Moreover, the agency has taken on new responsibilities—notably in the tobacco and food safety

areas—without full funding. The Food and Drug Administration Modernization Act of 1997 (FDAMA) has been implemented without any additional funding.

At the Food and Drug Law Institute's annual educational conference in December of 1998, FDA's Associate Commissioner for Strategic Management, Linda Suydam, estimated that the agency is \$165 million short of what it actually needs to do its job. She stated that "The agency has been effected by ...new programs, which were not fully funded and flat-lined budgets which did not allow for the cost of inflation on personnel and procurement dollars. These numbers clearly illustrate that there's less money to do our core responsibilities." Those core responsibilities include device reviews, she stated.

In the "FDA Compliance Plan" required by FDAMA and its budget justification documents, the agency projects that its review times for fiscal year 1999 will increase from fiscal years 1997 and 1998. In the plan, the agency cites insufficient funds as well as the increased complexity of medical technology for the longer review times. This is an alarming statement and one that is completely counter to the underlying goal of FDAMA to create efficiencies that help speed beneficial technology to patients.

We strongly believe that FDA should have the resources to meet its statutory time frames. This means the completion of *final actions* for PreMarket Approval Applications (PMAs) within 180 days and 510(k)s within 90 days. The agency has been expressing its review goals in terms of completion of *first actions* within the statutory time frames. The "Compliance Plan" mandated by FDAMA required the agency to tell Congress how it was going to meet all of its obligations under the Federal Food, Drug, and Cosmetic Act--including the obligation to *complete* reviews within established limits. We believe the agency should let Congress know exactly what resources are needed in order to meet the statutory time frames set forth in the law. We support a funding plan that will ultimately result in full compliance with the law's time limits.

Streamlining the Regulatory Process

Although we support increased funding targeted to device reviews, we believe that the need for increased funds should diminish in future years. Through full implementation of FDAMA, continued reengineering, effective execution of mutual recognition agreements, and aggressive international harmonization activities, FDA should be moving steadily toward a regulatory system that will be more efficient, faster, and less costly. This system should reduce unnecessary governmental procedures, eliminate regulatory redundancy, provide a uniform framework for protecting and promoting public health worldwide, and recognize and adapt to the realities of the global economy.

FDAMA mechanisms that, when fully implemented, will reduce regulatory burden include adoption and use of national and international standards, reliance on the declaration of conformity to standards, exemptions from 510(k), and adoption of a sentinel reporting system. In addition, FDAMA's requirement that FDA consider the "least burdensome" appropriate means of demonstrating effectiveness has yet to be fully defined and incorporated into standard operating procedure. This should, over time, together with the new collaboration requirements of FDAMA, result in a net savings of resources although more time may be spent at the beginning of the premarket approval process while the parties come to a meeting of the minds on the blueprint for device approval.

Similarly, the agency has a variety of reengineering initiatives in the early stages of implementation that have the potential to ripen into substantial resource savings tools. Examples include the special and abbreviated 510(k)s, guidance on when to file a PMA modification, and the product development protocol. Congress should direct the agency to aggressively and fully implement the tools of FDAMA and the agency's own reengineering mechanisms.

Global Harmonization

While the above initiatives concern the current processes for device review, FDA should not discount the potential savings to be realized from ongoing and future mutual recognition agreements and international harmonization activities. The need for federal funds will be reduced as devices approved offshore in accordance with harmonized requirements will not need to be re-reviewed by FDA.

This past year, the United States and the European Union entered into a Mutual Recognition Agreement (MRA). This agreement authorizes its signatories to review and approve devices based on the requirements of the other parties to the agreement, thus providing a forum for one-stop shopping for manufacturers. The agency is in the midst of determining the level of resources to be devoted to a confidence-building period required by the MRA. Through this activity, U.S. and European officials will learn about each other's requirements for regulating medical devices. This type of learning among nations is an important building block to a new global system that will reduce unnecessary, time-consuming, and costly regulatory redundancy. Investing the time and resources now to build a foundation of trust and respect will contribute enormously to the long-term goal of harmonizing regulatory requirements with Europe and provide valuable lessons for other global harmonization initiatives.

Ultimately, the forces of the global marketplace will drive nations of the world to recognize the economic value and efficiencies of a unitary worldwide regulatory system. Such a system will reduce if not eliminate duplicative reviews and inspections, with the added benefit of standardizing public health protection for patients throughout the world. The United States does not have a monopoly on what is the best approach to protecting and promoting the public health. In fact, there is some evidence to suggest that the European device approval process is faster and more efficient than our system with no demonstrable loss of product safety or quality. Aggressive and full participation by FDA in discussions with nations on a common sense approach to regulatory requirements worldwide will hasten the day when international harmonization becomes a reality. And, while we recognize that this type of activity costs money in the short term, in the long term, it should reduce the financial burden to U.S. taxpayers as other nations share responsibilities formerly performed exclusively by FDA.

The President's FY 2000 Budget

We note that the President's FY 2000 budget requests an increase of \$26 million for the device program--\$7 million in user fees for premarket reviews and \$19 million for improved inspections, MRA implementation, compliance activities, the Sentinel Surveillance System, and adverse event reporting.

HIMA opposes user fees for the medical device industry and believes Congress should provide sufficient funds to the agency to enable it to review applications within the time frames mandated by law. This core statutory obligation is essential to ensuring patient access to the benefits of medical technology.

With regard to inspections, we applaud the agency's recent efforts to streamline the inspection process. The industry has worked with the agency in a "grass-roots" initiative to bring common sense changes to key aspects of the inspection process.¹ We believe that there are additional efficiencies that can be realized through continued agency-industry discussions. At the FDAMA-mandated stakeholders meeting of August 18, 1998, we suggested that the agency take into account inspections conducted by internationally recognized organizations in executing a risk-based inspection strategy. We continue to believe that ISO (International Standards Organization) certification should provide some level of assurance to FDA that good manufacturing practices are being followed.

In addition, we note that the agency itself has questioned the biennial inspection requirement in the statute for certain manufacturers.² We support giving FDA the flexibility to exercise its own discretion in determining the frequency of reviews necessary to assure safety, based on the risk presented. Other types of flexibility may also be desirable.

The Sentinel Surveillance System--designed to replace reporting of adverse events by device user facilities (hospitals, nursing homes, etc.)--is one that holds great promise for improving the ability to collect meaningful information about device-user interaction. We believe it also has the potential to eliminate medical device reports from manufacturers. We support increased funds devoted to this system. However, we believe that it is important for the system to be well designed and provide optimal benefits for the provider, the agency, and the manufacturer. We recommend that the agency participate in a tripartite working group to engage in discussions as to how such a system can best meet the needs of the various interested parties.

The agency's proposal for increased funds for the Adverse Event Reporting System (AERS)--totaling \$15.3 million agency-wide--raises questions about whether such an expensive system will produce the intended results. We know little about the system and simply urge Congress to ensure that (1) there is a real need for this system and (2) its benefits will justify its costs. We believe that the system could benefit from an open airing of the agency's plans early in the design stages. Such an airing would enable industry and other interested parties to provide valuable observations and comments to help ensure that taxpayer dollars are being spent wisely.

¹ One pending change that we strongly support is an agency proposal to "credit" time spent by field personnel in educational and outreach activities that promote voluntary compliance by the industry rather than focusing solely on actual inspection time as a performance measure.

² In the FDAMA-mandated "FDA Plan for Statutory Compliance" published in the *Federal Register* on November 21, 1998, the agency said, in a section on inspections, "Because all public and private sector organizations in the future will be subject to the same resource-constrained environment, FDA may have to consider that even a highly collaborative inspectional network may not be adequate to completely meet existing statutory inspection requirements. A strategic reassessment may be in order to determine the kinds of statutory flexibility that would be desirable to preserve the comprehensive consumer protection intent of the FD&C Act, and at the same time, allow FDA to address the most critical health and safety priorities."

On a process-related matter, we strongly support this Subcommittee's efforts to seek greater accountability from the agency on the allocation and use of taxpayer dollars appropriated by Congress. The submission of detailed operating plans from the agency to this subcommittee is key to ensuring appropriate execution of the laws of the land. We are grateful for your initiative in this area and urge the continuation of this important process.

Conclusion

In conclusion, we support a funding increase for FDA for FY 2000 that is specifically targeted to device review functions, MRA confidence building, international harmonization activities, and the Sentinel Surveillance System. We ask Congress to ensure that such funds are not diverted to other agency activities. We believe this increase will help the agency meet its statutory obligations, advance the long range harmonization goal, and provide the means whereby the agency can achieve its FDAMA-mandated mission to "promote the public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner." We further believe the Congress should encourage the agency to continue to seek improvements in the inspection process--including consideration of legislation to enable the agency to exercise discretion in the frequency of inspections. We urge Congress to help open the agency to input and ideas from interested parties on key initiatives such as the Sentinel Surveillance System and the Adverse Event Reporting System. We oppose user fees for the medical device industry. Finally, we support this subcommittee's continued efforts to seek greater budget accountability from FDA.

Thank you for the opportunity to present our views.

ATTACHMENT II



JAMES S. BENSON

EXECUTIVE VICE PRESIDENT, TECHNOLOGY AND REGULATORY AFFAIRS

March 11, 1999

Susan Alpert, M.D., Ph.D.
Director, Office of Device Evaluation
Center for Devices and Radiological Health
U.S. Food and Drug Administration (HFZ-400)
9200 Corporate Blvd.
Rockville, MD 20850

Dear Dr. Alpert:

In response to your letter of February 18, 1999 requesting input on how the agency could implement "least burdensome," our Industry Task Force submits the attached "Least Burdensome Proposal." As we agreed at the January 4, 1999 meeting, the Health Industry Manufacturers Association (HIMA) established an industry task force consisting of representatives from HIMA, the Medical Device Manufacturers Association, the Association of Medical Diagnostics Manufacturers, Medical Alley, Massachusetts Medical Device Industry Council, National Electrical Manufacturers Association, and the Cook Group (a roster of members is attached).

The attached document represents the collaborative effort of this group. The Task Force believes this document to be a "first step" and would like to meet with you to discuss the proposal in detail and to answer any questions you may have regarding it.

The proposal consists of several sections including a chart describing a hierarchy of increasing burdensomeness, a list of least burdensome general principles followed by examples intended to illustrate these general principles.

We are looking forward to working with you as you develop guidance on implementation of least burdensome and appreciate the opportunity to provide this industry proposal.

Sincerely,

A handwritten signature in black ink that reads "Jim Benson". The signature is fluid and cursive, with the first and last names clearly legible.

James S. Benson

jt/ts

World Leaders in Health Care Innovation

1200 G STREET, N.W. SUITE 400

WASHINGTON, D.C. 20005-3614

(202) 763-6700 FAX (202) 763-6750

<http://www.himainet.com>



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

February 18, 1999

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

J. Benson

*Janet
hand copy*

Dear Association/Industry Representative:

Thank you for your participation in the January 4, 1999 meeting with FDA on Section 205 of FDAMA concerning the meaning and implementation of the language regarding least burdensome development of products for the marketplace. We found that meeting to be very useful in identifying the concerns of the regulated industry as we continue to move forward on FDAMA implementation.

At the close of the meeting we discussed the processes that might be used to convey to FDA review staff and the industry what these words mean and how one can address the preparation and review of submissions to ensure that Congressional intent is being carried out in this area. There was general agreement at our meeting that a Level 1 Guidance with publication of a draft and an opportunity for comment before preparation of a final guidance would provide both a mechanism for communication of these issues as well as an opportunity for all of the interested parties to have input concerning the interpretation and processes which are put in place to address this issue. The format options for such a guidance, including question lists, flow charts and text, were also discussed.

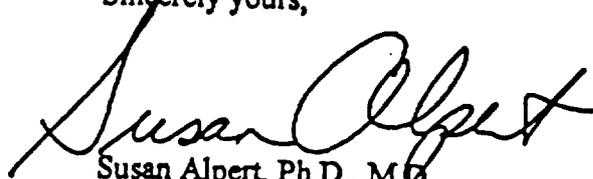
The Health Industry Manufacturers Association (HIMA) through the Executive Vice President, Technology and Regulatory Affairs, James Benson, volunteered to explore the possibility of convening a working group to develop a straw person proposal for consideration by FDA as a basis for this guidance. In recent communication Mr. Benson informed FDA that initial contact to other interested parties is being made and that HIMA expects the working group to convene shortly.

In order to meet the announced need for complete guidance that will be available to sponsors, reviewers and the public, FDA is hoping to publish an initial draft document for public comment in April. This time frame is being driven by a need, even today, for the Office of Device Evaluation to work with sponsors who expect FDA to consider the least burdensome pathway for their product to reach the marketplace. In addition to considering the information we have already received, the Agency would like to provide you and your constituents another opportunity to convey to us in writing any new or additional issues or points that you believe have not been expressed to date and that will advance the process. Such communications should reach us by March 12, 1999 in order to provide input as we develop the draft guidance. If the HIMA convened working group or other interested parties are only able to provide their input subsequent to mid-March, we will consider that input in development of the final guidance. I want to assure you that the Agency will remain open to input from all interested parties as we move forward, and that the publication of the draft guidance will provide an additional opportunity for industry and user groups as well as individual sponsors and consumers to comment on next steps.

As you are aware, at the January 4 meeting it was suggested that the guidance be developed by a joint Agency-industry-user working group. While such working groups may be a useful mechanism for policy development, the Center has determined that the time and resource commitment necessary to proceed via that mechanism at this time will be less efficient than building upon the extensive information and varied opinions that have already been expressed on this issue.

Thank you again for your help on this issue, and I look forward to hearing from you in the near future.

Sincerely yours,

A handwritten signature in cursive script that reads "Susan Alpert". The signature is written in black ink and is positioned above the printed name and title.

Susan Alpert, Ph.D., M.D.
Director
Division of Device Evaluation
Center for Devices and
Radiological Health

LEAST BURDENSOME TASK FORCE

Representing the Association of Medical Diagnostics Manufacturers (AMDM):

Ms. Patricia B. Shrader
Becton Dickinson Microbiology Systems

Representing the Cook Group:

Neal Fearnot Ph.D.
MED Institute, Incorporated

Representing the Health Industry Manufacturers Association (HIMA):

Mr. Dean Bruhn-Ding
Daig Corporation

Mr. Andrew M. Green
Novoste Corporation

Dan Jolivette M.D.
Orquest, Inc.

Mr. Michael C. Morton
Sulzer CarboMedics, Inc.

Mr. Robert O'Holla
Johnson & Johnson

Mr. William J. Pignato
Bayer Diagnostics

Mr. Jonas A. Runquist
St. Jude Medical, Inc.

Ms. Cheryl Shea
CryoGen, Inc.

Charles H. Swanson Ph.D.
Medtronic, Inc. Pacing Business

Representing the Health Industry Manufacturers Association (HIMA) cont. :

Ms. Marlene Valenti
*Cordis, a Johnson & Johnson
Company*

Ms. Pamela J. Weagraff
MediSpectra, Inc.

Ted M. Wendt Ph.D.
Zimmer, Inc.

Representing the Massachusetts Medical Device Industry Council:

Mr. Bruce A. Beauchemin
Boston Scientific Corporation

Representing Medical Alley:

Lisa Heine
EMPI, Inc.

Representing the Medical Device Manufacturers Association (MDMA):

Mr. Timothy Krauskopf
Thermo Electron Corporation

Mr. David M. Link
EXPERTech Associates

Marcia Yaross Ph.D.
Allergan

Least Burdensome Proposal

I. Introduction

Section 205 of the Food and Drug Administration Modernization Act of 1997 included the concept of "least burdensome" to ensure that FDA consider the "least burdensome" valid scientific evidence "necessary" to demonstrate a reasonable assurance of device effectiveness or substantial equivalence to predicate devices with differing technological characteristics. The least burdensome concept does not reduce the scientific standard for effectiveness; this concept is intended to carry through Congress' longstanding purpose included in the "Medical Device Amendments of 1976" to avoid over-regulation of devices.

In examining the concept of least burdensome, the Least Burdensome Industry Task Force recognizes that good science requires judgment be exercised by both sponsors and FDA during the development process. This judgment is influenced by the scientific training, experience, and level of knowledge of the people involved. Interactive communication is often required for full comprehension of the issues to arrive at the most appropriate questions and the methodology with which to answer them. The Task Force believes that the most appropriate least burdensome approach, in its most basic form, is predicated on two principles:

Are the correct questions being asked?

What is the most appropriate and reasonable way to answer these questions?

A fundamental concept underlying least burdensome is that substantial equivalence or effectiveness must be demonstrated by appropriate and valid scientific information, evidence, or data and that no compromise can be made on this issue. Least burdensome is not a way for either the FDA or Industry to "cut corners" regarding the generation of data to support a product application. The ideas we present here are concepts the Task Force believes can be used as a guide by industry and FDA reviewers and managers to judge if the correct questions are being asked and if the ways chosen to answer them are indeed least burdensome.

II. Hierarchy of Increasing “Burdensomeness” to Establish Effectiveness

The following presents increasing levels of burden that should be considered in determination of the “least burdensome” appropriate means of establishing substantial equivalence or effectiveness. Before proceeding to each higher level of burden, FDA staff should identify the specific scientific question that must be resolved to establish substantial equivalence (Class I or Class II devices) or effectiveness (Class III) that cannot be answered at a lower level of burden. Also, as 510(k)s are inherently less burdensome to FDA and industry than PMAs, the same principle should be applied during “de novo classification” to ensure that the PMA route is not mandated unnecessarily.

For product modifications, it is assumed that the current 510(k) or (draft) PMA modifications guidance document will be consulted first to determine if prior review by FDA is required. When prior review *is* required, postmarket surveillance studies should be considered, whenever possible, as a potential tool to reduce the premarket level of burden by one or more levels.

Level of Burden	Comments
Document to file - no FDA prior review required.	Sponsor to maintain evidence of effectiveness in design history file (for Class I, II devices) or submit in annual report to PMA (Class III devices).
Laboratory bench testing; animal studies	Submit verification and/or simulated use-validation in 510(k) or PMA/PMA supplement when statutory threshold for submission is reached (e.g., new indication for use).
Retrospective clinical data, published literature, well-documented case histories and other reports of significant human experience per 21 CFR 860.7(c)(2)	Submit in 510(k), PMA supplement or original PMA, as appropriate, when non-clinical data cannot address relevant questions.
Partially controlled studies, historically controlled studies, and objective trials without matched controls per 21 CFR 860.7(c)(2)	Submit in 510(k), PMA supplement or original PMA, as appropriate, when available, less-formal clinical results cannot address relevant questions.
Well-controlled, prospective clinical trials	Submit in 510(k), PMA supplement or original PMA, as appropriate, when no less burdensome form of study design can address relevant questions.

III. Least Burdensome General Principles

The following lists represent general concepts that should be applied when implementing a least burdensome approach as well as concepts associated with higher levels of burden deemed unwarranted by industry. Following the list of general principles is a list of real-life examples including both industry experience and specific guidance documents that illustrate both situations where an overly burdensome approach was applied and cases where a least burdensome approach was followed.

A. Concepts that promote a least burdensome approach

1. Appropriate application of risk vs. benefit in determining approval criteria.
2. Acceptance of historical data, when data specificity is adequate, for established therapies in lieu of well-controlled prospective clinical studies
3. Application of a premarket/postmarket balance for data requirements particularly when considering long term information requirements
4. Acceptance of state of the art principles in test methods, verification and validation methods, and clinical study design.
5. Consistent acceptance of guidance documents and standards
6. Consistent requirements for a manual method vs. automated method
7. Application of a hierarchical approach to least burdensome beginning with the lowest level of burden.
8. Consideration of "accepted medical practice" in approval decisions
9. Good communication across FDA of least burdensome approaches to submissions.

B. Concepts that may result in unwarranted burden

1. Necessity of a submission unclear
2. Ineffective use of early collaboration meetings or other meetings leads to prolonged decisions on approval criteria and delays in product approval.
3. FDA requirements exceeding those in guidance documents or recognized standards
4. FDA should not require clinical data in 510(k)s when substantial equivalence to predicate has been shown with other types of testing

5. FDA's justification for moving a product from a 510(k) submission to a PMA is sometimes unclear. Clearer justifications on FDA's part would allow sponsors to better address FDA's concerns.

6. As technology rapidly advances, burdensome questions/requirements are often imposed on sponsors as a result of FDA's lack of familiarity with a particular technology.

7. FDA's justification for its approach when denying sponsor's approach is often not clear or detailed enough making it difficult for a sponsor to understand FDA's concerns.

IV. Least Burdensome Examples

Favorable Approaches to Least Burdensome

Example 1

When the sponsor proposed new uses within an approved general indication for an electrosurgical device, the agency allowed a least burdensome approach. Rather than having the sponsor conduct clinical trials, the agency cleared the new indications based on available clinical data and data from animal models. However, it remains questionable if an application for uses clearly within the general indication should be required at all.

Illustrated principles:

- Appropriate application of risk vs. benefit in determining approval criteria
- Acceptance of historical data, when data specificity is adequate, for established therapies in lieu of well-controlled prospective clinical studies
- Application of a hierarchical approach to least burdensome beginning with the lowest level of burden.

Illustrated principle for unfavorable approach

- Necessity of a submission unclear

Example 2

When the sponsor made substantial changes to the design--including hardware, software, and operation system changes--of its thermal ablation device, the agency approved the PMA supplement based upon laboratory data and engineering design analysis.

Illustrated principles:

- Appropriate application of risk vs. benefit in determining approval criteria
- Application of a hierarchical approach to least burdensome beginning with the lowest level of burden.

Example 3

The agency has adopted a “least burdensome” approach to the approval of alternate sewing ring configurations for heart valve sewing cuffs. In this case, DCRND worked with the Office of Science and Technology to review the requirements for heart valve cuff changes. Collectively, they determined that “clinical data would not be necessary to validate changes in diameter of the sewing ring diameter of less than 15%, as long as the overall diameter of the orifice has not been changed (e.g., if the additional material is being added to the sewing ring, the additional material should not interfere with the flow).” This policy was clearly stated policy on pages 46 and 47 of version 4.1, 10/14/94, of the Draft Replacement Heart Valve Guidance.

Illustrated principles:

- Acceptance of state of the art principles in test methods, verification and validation methods, and clinical study design.
- Application of a hierarchical approach to least burdensome beginning with the lowest level of burden.

Example 4

The FDA Cardiovascular Devices Advisory Panel recommended the approval of two trans-myocardial revascularization (TMR) devices recognizing that longer term safety data needed to be collected. In order to gain the data necessary to support safety, a post-market trial was required. This allowed patients to have access to this promising new technology and the FDA to gain additional patient data

Illustrated principles:

- Appropriate application of risk vs. benefit in determining approval criteria
- Application of a premarket/postmarket balance for data requirements particularly when considering long term information requirements

Example 5

Initial PMA approvals for implantable cardioverter defibrillators (pre-Temple report) were based on clinical studies using the historical survival of sudden death survivors without ICDs as the control. Approval required a minimum of 100 devices followed for one year. Had randomized studies using standard drug therapy been required, clinical studies would have been much larger and longer duration. For example, nearly 10 years later, the NIH funded AVID study proved the superiority of ICDs over drug therapy. This study was conducted with third generation devices which were significantly improved over first generation devices and involved nearly 1000 devices. The results of the initial PMA approval studies using clinical controls are consistent with the AVID results. Had randomized studies been required, the approval and acceptance of ICD therapy would have been delayed for several years.

Illustrated principles:

- Appropriate application of risk vs. benefit in determining approval criteria
- Acceptance of historical data, when data specificity is adequate, for established therapies in lieu of well-controlled prospective clinical studies

Unfavorable Approaches to Least Burdensome

Example 6

The OB/GYN Division is requiring a multi-center study with a control group of electrosurgery to support a PMA for endometrial ablation. Literature is available regarding the outcomes and risks associated with electrosurgical endometrial ablation. Patients have refused to participate in the study knowing that they could be randomized to the electrosurgery control group.

Illustrated principles:

- Appropriate application of risk vs. benefit in determining approval criteria
- Acceptance of historical data, when data specificity is adequate, for established therapies in lieu of well-controlled prospective clinical studies
- FDA's justification for moving a product from a 510(k) submission to a PMA is sometimes unclear. Clearer justifications on FDA's part would allow sponsors to better address FDA's concerns.

Example 7

The FDA required invasive, interstitial temperature measurements in a large patient population when every medical advisor and clinician presented their professional opinion that the increased risk to the patients and liability to the physician was not worth the risk and that the safety data could be obtained through other means. This was despite submission of data correlating mathematical computer modeling, muscle equivalent phantom measurements, *in vivo* animal models, and a number of human interstitial mappings. Although hundreds of data points could be obtained in a few patients to accomplish the goal of reconstructing a three-dimensional heating pattern, the FDA guideline specified an exact, unreasonably larger, number of patients assuming that only one or two measurements could be obtained from each patient. There was no third party arbitration that the sponsor felt it could go to contest requirements like this.

Illustrated principle:

- FDA's justification for its approach when denying the sponsor's approach is often not clear or detailed enough, making it difficult for a sponsor to understand FDA's concerns.

Example 8

The application of antimicrobial agents to implantable cardiovascular devices provides an opportunity for the agency to balance the risk of a modified device that has an established clinical history with the potential benefit to the patient when establishing the requirements for approval.

Many cardiovascular surgeons are concerned about infection in their patients. The practice of "pre-dipping" implantable cardiovascular devices in antibiotics is currently widespread. The surgical community is requesting that manufacturers provide devices that are treated with antimicrobial agents. The risks associated with the application of a small quantity of a known antimicrobial agent to an approved device are quite low. The risks are dependent upon the antimicrobial agent employed. For instance, antibiotics would include the associated risk of antibiotic resistance. That risk, however, could be minimized by the selection of an agent that is not considered a first line antibiotic in the physicians' armamentarium. Safety and effectiveness data for the appropriate antimicrobial agents are well defined through *in vitro* and animal data and by existing data from systemic use or use with other devices. The risk associated with the use of an approved device would be low, and further, would be well characterized by the existing safety and effectiveness data for the device.

The benefit to the patient, however, could be great. While the frequency of infection following cardiovascular surgery is low, the mortality and morbidity associated with infection is high.

These cardiovascular devices that have an established clinical history and are treated with antimicrobial agents, then, offer an ideal opportunity for the agency and the manufacturers to accept a low risk in providing the devices to the surgical community. These devices also have the potential for high benefit to the patient if infection of the device can be prevented. Requirements for approval of these devices should, therefore, be less burdensome because of the favorable ratio of risk vs. benefit.

Illustrated principles:

- Appropriate application of risk vs. benefit in determining approval criteria
- Consideration of “accepted medical practice” in approval decisions

Example 9

A company developing a bipolar device for electrosurgical endometrial ablation was required by the OB/GYN Division to submit a side by side tissue destruction comparison with a monopolar device in human extirpated uteri despite the fact that testing in turkey breasts had been the standard for such performance testing. This resulted in the company spending significantly more money and effort to provide the data in extirpated uteri. Interestingly enough, the data the sponsor collected in turkey breast was identical to the data seen in extirpated uteri, confirming the historical use of testing in turkey breasts.

Illustrated principles:

- FDA requirements exceeding those in guidance documents or recognized standards
- Acceptance of state of the art principles in test methods, verification and validation methods, and clinical study design.
- FDA’s justification for its approach when denying the sponsor’s approach is often not clear or detailed enough making it difficult for a sponsor to understand FDA’s concerns.

Example 10

Different divisions within ODE require significant differences in data needed for 510(k) submissions. This difference is illustrated by different data requirements for a Diagnostic ultrasound 510(k) reviewed by DRAERD and a patient monitoring 510(k) reviewed by DCRND. Although both devices are Class II, DCRND required far more data. This situation has not improved since FDAMA--DCRND still appears to require more data for submissions of Class II devices than DRAERD. In a FY1998 experience, a 510(k) for a diagnostic ultrasound catheter that was subject to joint review by DCRND and DRAERD resulted in DCRND requesting data that DRAERD had expressly stated would not be needed according to the device-specific guidance document for diagnostic ultrasound. DCRND did not appear to be familiar with nor inclined to consider the applicable device-specific guidance as part of the review process. The discrepancy was elevated to the Branch Chief level and resolved favorably, however at a considerable time/effort drain for the company involved.

Illustrated principle:

- Consistent acceptance of guidance documents and standards

Example 11

Software development using graphical programming has historically been impossible because the FDA seems to cling to the need to have line by line source code. Text based programming (C-code) is burdensome and takes 3 to 4 times as long to program costing money, time, and is much more difficult to debug. Graphical based programming has all the components that the FDA desires for development, yet to our knowledge, to date everyone has done their development work in graphical based software and then been forced to rewrite it all in C-code to get FDA approval.

Illustrated principle:

- As technology rapidly advances, burdensome questions/requirements are often imposed on sponsors as a result of FDA's lack of familiarity with a particular technology.

Example 12

In addition to requirements for maximum coefficients of variation for cholesterol testing, FDA has required acceptance criteria for maximum "% misclassifications," the percentage of test results that err from the "true value" from one side to the other of a "cutpoint" between ranges of values, i.e., causing shifts among classifications of under 200, 200 - 239, or 240 or over mg/dl. This requirement is unnecessary and duplicative of the basic requirements for accuracy and precision. Further, as this % misclassifications is potentially biased by the distribution of cholesterol values in the subject population, it places an undue burden on sponsors to obtain a "typical" distribution of test values.

Illustrated principle:

- FDA's justification for its approach when denying the sponsor's approach is often not clear or detailed enough, making it difficult for a sponsor to understand FDA's concerns.

Example 13

Automated blood culture systems are class I devices on the reserve list. The systems consist of an instrument and reagent; a patient sample is inoculated into the reagent, which will support the growth of any bacteria in the sample and the instrument detects growth if it occurs. The device does not identify the organism. Manual blood culture reagents are class I exempt.

FDA draft guidance currently requires the applicant to perform analytical studies that consist of inoculating very small quantities of each of several dozen bacterial strains into the growth medium (reagent) and showing that they grow and growth is detected by the instrument. The guidance then requires the applicant to conduct clinical studies at multiple sites, involving two thousand or more patient samples, in order to demonstrate that bacteria, when found in the sample, will grow and the instrument will detect growth. Because the analytical studies alone are so comprehensive and the test is qualitative only, the clinical studies add no new information about the ability of the instrument and the reagent to show and detect growth.

Illustrated principles:

- FDA should not require clinical data in 510(k)s when substantial equivalence to predicate has been shown with other types of testing
- Consistent requirements for a manual method vs. automated method
- Application of a hierarchical approach to least burdensome beginning with the lowest level of burden.

Example 14

Immediately after the Temple report, FDA rejected the use of the PMA clinical data base from first generation implantable cardioverter defibrillator (ICDs) as controls for studies in support of PMA approval for second generation devices. The historical study had been completed only months before and the study size (more than 1000 patients) provided greater statistical power than a concurrent control yet the historical control was rejected based on the “fear” of bias. Currently, previous PMA clinical studies are generally accepted as historical controls for the approval of next generation devices.

Illustrated principle:

- Acceptance of historical data, when data specificity is adequate, for established therapies in lieu of well-controlled prospective clinical studies

Example 15

For PMA approval of cardiomyoplasty devices, FDA required a randomized study using current drug therapy as the control. Cardiomyoplasty devices were designed to treat patients with advance heart failure where standard drug therapy can at best offer only temporary relief. The study was ultimately abandoned despite encouraging early results because of difficulties recruiting patients. After four years only 103 of a required 400 patients had been enrolled. One of the major problems was the loss of patients when randomized into the control arm. FDA needs to take a less burdensome approach for breakthrough devices designed to treat life-threatening diseases where existing therapies are not effective. For such devices, the potential for benefit justifies the less burdensome approach.

Illustrated Principles:

- Appropriate application of risk vs. benefit in determining approval criteria
- Acceptance of historical data, when data specificity is adequate, for established therapies in lieu of well-controlled prospective clinical studies

Example 16

A company spoke with FDA a few months ago to discuss Clinical trials for 2 Hepatitis A assays (anti-HAV total and anti-HAV IgM). They noted that the interference tests for these assays included spiking samples of serum and plasma with known concentrations of lipid, hemoglobin and bilirubin, and then testing the "doctored" samples to see if these substances interfered with our assay results (by paired testing of spiked and "natural" samples). A FDA reviewer insisted that spiked samples were unacceptable to FDA and that they should use natural samples containing elevated levels of those substances for conducting our interference assessment.

FDA suggested that the sponsor have volunteers eat a couple of hot dogs and then draw blood samples on them. The company argued the scientific merit of this suggestion, but to no avail. NCCLS EP7-P does not discount either approach.

Illustrated principles:

- Consistent acceptance of guidance documents and standards
- Application of a hierarchical approach to least burdensome beginning with the lowest level of burden.

Example 17

While more of a general matter, FDA has moved away from true substantial equivalence for 510(k)'s when forcing companies to use FDA's preferred "gold standard." FDA's paradigm for 510(k) clinical studies for IVDs gets more and more complex, to the point that they may as well be mini-PMAs. This includes comparison to multiple predicate devices and to presence/absence of disease. The legal standard of demonstrating equivalence to a legally marketed predicate is clearly not being followed.

Illustrated principle:

- Self-explanatory

Example 18

FDA is now requiring a Class III 510(k) device approved for delivery of “ionic solutions” to go through the NDA process for individual drugs. The drug has been used in clinical practice with this device for many years as a 510(k) approved product with a good safety profile and documented results noted in the scientific literature. The drug has been commercially available for over 40 years and has a well-established safety and efficacy profile. Through the NDA process the sponsor is being required to re-prove the efficacy and safety of this well-established drug (in-vitro testing, animal studies, pK studies, phase II & III clinical studies, etc), when the sponsor should just be evaluating the effectiveness of the delivery mechanism (device) in a clinical trial(s). The drug and device will not be packaged together and it seems that the lead agency should be CDRH rather than CDER since it is really about proving the effectiveness of the delivery mechanism that a PMA could appropriately address.

Illustrated principle:

- Appropriate application of risk vs. benefit in determining approval criteria

Example 19

FDA would not allow the sponsor to use the special 510(k) for a software upgrade. The rationale for the decision is that FDA wanted to upgrade its database of 510(k) information. The sponsor had to submit the change via a traditional 510(k) with all the data supporting the change.

Illustrated principle:

- Consistent acceptance of guidance documents and standards

V. Guidance Documents Examples

Favorable Approach to Least Burdensome

Example A

The draft document entitled "Intraocular Lens (IOL) Guidance Document" dated April 13, 1998, identifies those data required to establish safety and efficacy of a wide variety of potential device modifications. Based on the potential impact of a given modification, the modification may be classified as:

- No prior approval required (update in annual report to PMA)
- Non-clinical studies only required
- Limited, confirmatory clinical study required
- Full study adequate for new device required

Illustrated Principles:

- Appropriate application of risk vs. benefit in determining approval criteria
- Application of a hierarchical approach to least burdensome beginning with the lowest level of burden.

Unfavorable Approaches to Least Burdensome

Example B

Title: Diagnostic Ultrasound Guidance Document

The guidance document requires submission of acoustic output data rather than a certification that testing has been completed; data would be subject to inspection under the Design Control portion of a quality system inspection. Therefore, it should not be required in the submission. Also, the guidance requires submission of Doppler sensitivity data which FDA has stated will not be used as part of the SE decision. If the data is not needed for an SE decision, it is difficult to understand the need for the data. Therefore, the requirement for the Doppler sensitivity data should be deleted from the document.

Illustrated principle:

- Self-explanatory

Example C

Title: Guidance on Premarket Notification for Washers and Washer Disinfectors Intended to Process Reusable Medical Devices

Title: Guidance on the Content and Format of Premarket Notification Submissions for Liquid Chemical Sterilants and High Level Disinfectants

Companies have submitted extensive comments on these documents noting the concerns regarding application of least burdensome principles.

Example D

Title: Concerns for Mycobacterial susceptibility testing when there are established interpretive criteria (NCCLS) for both the drug and the organism

This draft guidance represents FDA's current thinking on submissions for antimicrobial susceptibility testing (AST) for first line drugs used in the treatment of tuberculosis. This guidance requires analytical testing for a variety of drug resistant strains of *M. tuberculosis* and clinical testing involving several thousand patients. It also requires the applicant to include test results for a CDC panel of rarely isolated organisms ("one of a kind bugs"), in internal studies and at external sites. It also requires samples from all discrepant results and resistant results to be sent to two FDA selected third party arbiters for "definitive" resolution, in addition to any mechanism the protocol includes for resolution of discrepant (e.g. testing at a clinical site other than the one that produced the original result.) FDA also has suggested, but has not required, that treatment outcome information from the patients tested would be most appropriate. That, however, addresses not only the appropriateness of the diagnosis, but also the effectiveness of the antibiotic treatment. If clinical testing is needed at all, let the sites do the reconciliation of discrepant by sending the resistant and discrepant, blind coded, to a site other than the one that identified them.

Illustrated principles:

- FDA should not require clinical data in 510(k)s when substantial equivalence to predicate has been shown with other types of testing

ATTACHMENT III



**Food and Drug Administration
Modernization Act of 1997**

FDAMA

**FDA PLAN
FOR
STATUTORY
COMPLIANCE**

November 1998

Time Frame	Relevant Statute	Percentage of First Actions Within Time Frame		Overdue*
		FY 1999 Performance Plan Goal	FY 1997 Baseline (Estimate)	
PDUFA:				
Review Priority NDAs within 6 months (CDER) (PDUFA II commitment letter)	Section 101(4) of FDAMA. FD&C Act Sec. 505 (b)	90 percent	100 percent	0
Review Standard NDAs within 12 months (CDER) (PDUFA II commitment letter)	Section 101(4) of FDAMA. FD&C Act Sec. 505 (b)	90 percent	99 percent	0
Review Priority NDAs/PLAs/BLAs within 6 months (CBER) (PDUFA II commitment letter)	Section 101(4) of FDAMA. FD&C Act Sec. 505 (b) for NDAs. None for PLAs/BLAs.	90 percent	100 percent	0
Review Standard NDAs/PLAs/BLAs within 12 months (CBER) (PDUFA II commitment letter)	Section 101(4) of FDAMA. FD&C Act Sec. 505(b) for NDAs. None for PLAs/BLAs.	90 percent	100 percent	0
Review priority efficacy supplements within 6 months (CDER & CBER) (PDUFA II commitment letter)	Section 101(4) of FDAMA. FD&C Act Sec. 505 for NDAs. None for PLAs/BLAs.	90 percent	100 percent	0
NON-PDUFA:				
Review ANDAs within 180 days (CDER)	FD&C Act Sec. 505(j)	60 percent	54 percent	142
Review and act on Blood and source plasma PLAs/BLAs within 12 months (Internal time frame) (CBER)	No statutory requirement.	70 percent	83 percent	4
Review PMAs within 180 days (CDRH)	FD&C Act Sec. 515(d)(1)(A)	50 percent	65 percent	0
Review 510(k)s within 90 days of receipt	FD&C Act Sec. 510(k) and (n)	90 percent	98 percent	0
Review food and color additive petitions within 360 days. (CFSAN) Goals are based on 360 days. FY 1997 baseline based on 180 days (statutory requirement).**	FD&C Act Sec. 409 and Sec. 721	30 percent	24 percent (within 180 days)**	52
Review NADAs and ANADAs within 180 days (CVM)	FD&C Act Sec. 512(c)(1)	None	75 percent	6

* The number of applications overdue at the end of FY 1998.

** For petitions received in FY 1996, using the previous petition review procedure, 24 percent of petitions received "first action" within 180 days. CFSAN re-engineered the petition review process in FY 1998 and redefined "first action." FY 1997 figures and FY 1999 are not directly comparable.

FY 2000 Performance Goals are not identified in this Plan. Specification of these goals is dependent upon final determination of the President's FY 2000 Budget submission to Congress.

**DEPARTMENT
of HEALTH
and HUMAN
SERVICES**

**Fiscal Year
2000**

Food and Drug Administration

*FY 2000 Performance Plan
and Revised Final FY 1999
Performance Plan*

MEDICAL DEVICES AND RADIOLOGICAL HEALTH

Program Strategic Goals

Strategic Goal 1:

Ensure that medical devices intended for human use are safe, effective and properly labeled by assuring that premarket submissions are properly processed within the specified time frames as directed by law.

Resources: \$70,325,000 639 FTEs

Performance Goals:

- Increase the on-time percentage of Premarket Approval Application (PMA) first actions (within 180 days) and Humanitarian Device Exemption (HDE) first actions (within 75 days) completed from 67 percent in FY 1998 to 85 percent in FY 2000 and 95 percent by FY 2002.⁷
This goal supports the accomplishment of the NPR High Impact Agency goal, Faster Access to Important New Medical Devices
- Review and complete 85 percent of Premarket Approval Application (PMA) supplements for new indications within 180 days in FY 2000 and 95 percent by FY 2002.⁷
- Review and complete 85 percent of complex 510(k) (Premarket Notification) final actions within 90 days in FY 2000 and 95 percent by FY 2002.⁷
- Review and complete 95 percent of 510(k) (Premarket Notification) first actions within 90 days.⁷
- Complete 95 percent of Investigational Device Exemptions (IDE) "Agreement" meetings and Premarket Approval Application (PMA) "Determination" meetings within 30 days.⁷
This goal supports the accomplishment of the NPR High Impact Agency goal, Faster Access to Important New Medical Devices

Rationale:

Medical devices intended for marketing in the United States are subject to rigorous premarket review by the FDA. Prior to marketing a device, manufacturers must seek FDA safety and effectiveness approval of their products. FDA is responsible for assigning marketed medical devices to a regulatory category (Class I—General Controls; Class II—Special Controls; Class III—Premarket Approval). FDA reviews: 1) Premarket

⁷ Achievement of this performance goal target level is dependent upon passage of User Fee legislation and establishment of management systems to implement user fees by the beginning of FY 2000.

MEDICAL DEVICES AND RADIOLOGICAL HEALTH

Baseline Data:	<u>PMA's Only</u>	<u>PMA's & HDEs</u>
	FY 1996: 51%	Not applicable
	FY 1997: 79%	Not applicable
	FY 1998: 83% (estimate)	67% (estimate)
	FY 1999: 70% (target)	65% (target)

Goal Statement: Review and complete 85 percent of Premarket Approval Application (PMA) supplements for new indications within 180 days in FY 2000 and 95 percent by FY 2002.

Data Sources: CDRH Premarket Tracking System and Receipt Cohorts

Baseline Data:	FY 1997: 65%
	FY 1998: 86% (estimate)
	FY 1999: 70% (target)

Goal Statement: Review and complete 85 percent of complex 510(k) (Premarket Notification) final actions within 90 days in FY 2000 and 95 percent by FY 2002.

Data Sources: CDRH Premarket Tracking System and Receipt Cohorts

Baseline Data:	FY 1996: 65%
	FY 1997: 70%
	FY 1998: 72% (estimate)
	FY 1999: 65% (target)

Goal Statement: Review and complete 95 percent of 510(k) (Premarket Notification) first actions within 90 days.

Data Sources: CDRH Premarket Tracking System and Receipt Cohorts

Baseline Data:	FY 1996: 94%
	FY 1997: 98%
	FY 1998: 99.5%
	FY 1999: 90% (target)

Goal Statement: Complete 95 percent of Investigational Device Exemption (IDE) "Agreement" meetings and Premarket Approval Application (PMA) "Determination" meetings within 30 days.

****This goal supports the accomplishment of the NPR High Impact Agency goal, Faster Access to Important New Medical Devices****

Data Sources: CDRH Premarket Tracking System and Receipt Cohorts

ATTACHMENT IV

“TALKING WITH STAKEHOLDERS ABOUT FDA MODERNIZATION”

Presentation in Connection with April 28, 1999, FDA Stakeholders Meeting in Atlanta, Georgia

Nancy Singer
Special Counsel
Health Industry Manufacturers Association

Docket No. 99N-0386

Good afternoon. My name is Nancy Singer and I am special counsel for the Health Industry Manufacturers Association. The Health Industry Manufacturers Association (HIMA) is a Washington, D.C.-based trade association and the largest medical technology association in the world. HIMA represents more than 800 manufacturers of medical devices, diagnostic products, and medical information systems. HIMA's members manufacture nearly 90 percent of the \$62 billion of health care technology products purchased annually in the United States, and more than 50 percent of the \$147 billion purchased annually around the world.

I appreciate the opportunity to be here. Since this is the Office of Regulatory Affairs site, my remarks today will focus on the question, “What action do you propose to enable FDA’s Office of Regulatory Affairs to focus resources on areas of greatest risk to the public health?”

It is HIMA’s belief that FDA, working with device manufacturers, has implemented many changes that have focused the agency’s resources, improved the efficiency of FDA inspections, and made the enforcement process more equitable. These activities have a direct bearing on the public health. Cooperative efforts toward efficiency and fairness need to continue so that industry can work with FDA to enable patients to have timely access to safe and effective medical devices.

Medical device companies see themselves as innovators in the diagnosis, cure, or treatment of disease or injury. Their success depends on allowing patients early access to their technically advanced, safe, and effective devices. FDA officials see themselves as the guardians of the public health. Their mandate is to foster the introduction of new technology and to ensure that the devices designed to diagnose, cure, or treat disease or injuries do not inadvertently cause harm. One of the ways FDA accomplishes its mandate is through the inspection of device manufacturers. During the past few years, many officials in the Office of Regulatory Affairs (ORA) and the Center for Devices and Radiological Health (CDRH) have begun to view industry as a partner rather than an adversary.

FDA Enforcement in the Early 1990s

In November 1990, David Kessler became the Commissioner of Food and Drugs. In speeches, he repeatedly stated that FDA enforcement “needed to be taken up a notch.” One of his initiatives was to decentralize the power for enforcement actions and delegate authority to officials in FDA district offices to send warning letters. The district officials were instructed not to be predictable in their enforcement actions. They were to go into a firm, spot regulatory violations, and then go on to find different regulatory violations in other companies. These initiatives caused companies to be suspicious of FDA because they were fearful of unpredictable and inconsistent regulatory actions.

Stimuli to Change

In 1994, HIMA polled the industry regarding its concerns about FDA enforcement policies and developed recommendations to improve the inspection process. In meetings with officials from FDA’s Office of Regulatory Affairs and CDRH, HIMA suggested items such as:

- Conducting preannounced inspections.
- Annotating the FDA 483 with completed or promised corrective actions
- Requiring that annotations be put in context (e.g., the investigator examined 50 complaints and found that 3 had not been reported as MDRs).
- Issuing close out letters after inspections.

A group of FDA officials received similar input from the Medical Device Industry Initiatives Grassroots Task Force, an industry group consisting of representatives of national and regional medical device associations.

Cognizant of its diminishing budgetary resources and of the reasonableness of the suggestions presented, FDA, in 1996, implemented a pilot program that included the items noted above. The agency subsequently surveyed the investigators and the companies being inspected, and found that the respondents in both groups believed that the pilot program improved the efficiency of inspections and the quality of communication between the investigator and the company. The program was so successful that, in March 1997, the features of the program became part of FDA’s standard operating procedures for conducting medical device inspections. The program is currently being piloted in other centers.

To solicit additional ideas on how to further improve the inspection process, from 1996–1997, FDA met with industry officials from medical device companies in various cities,

including Atlanta, Dallas, Nashville, Boston, Charlotte, and Orlando. Some of the suggestions coming out of these meetings included:

- Conducting joint training for industry and FDA investigators on the new requirements.
- Providing the establishment inspection reports (EIRs) automatically to companies after they have been inspected.
- Excluding from warning letters items that have been corrected or for which corrections have been promised.
- Increasing the time for companies to respond to FDA 483 observations, and acknowledging their response in the warning letter.

FDA Response to Industry Suggestions

Joint Training. In response to the industry suggestion on joint training, FDA's Southwest Region conducted joint training for FDA and industry personnel on how to comply with the MDR requirements. FDA also worked with the Food and Drug Law Institute and with national and regional device associations to present periodic teleconferences on FDA requirements for members of the industry and FDA officials. Additionally, the agency conducted joint training on how to comply with the design control portion of the new quality system regulation.

Establishment Inspection Reports. FDA has instituted a program under which it automatically provides EIRs to companies after their FDA inspections. This program has proven to be very successful, with companies better able to understand FDA's conclusions about their firm's state of compliance.

Warning Letter Pilot. Prompted by one of the industry's pressing concerns about the impact that warning letters had on their corporate image and stock price, a committee of the Medical Device Industry Initiatives Grassroots Task Force working with FDA officials designed an 18-month pilot program intended to preclude FDA from sending warning letters to companies who had corrected or were in the process of correcting deficiencies. The way the program works is as follows. Beginning March 29, 1999, after a domestic device investigation, a company with a good compliance record with FDA requirements will be given 15 working days to respond to deficiencies that would have previously triggered a warning letter. If the response is deemed to be satisfactory, then a warning letter will not be issued. Instead, FDA will issue a postinspectional notification letter. The letter will state that while the inspection found quality system deficiencies which, if not corrected, would warrant a warning letter, the company's written response has satisfied FDA that the company has taken or will take appropriate corrective actions. If, at a later time, FDA observes that the deviations from the quality system regulation

have not been remedied, the agency may take regulatory action (seizure, injunction, and civil penalties) without notice.

The program also addresses situations that would have warranted a warning letter for failure to submit a 510(k) application or for labeling violations. Under this program, companies, in most instances, will receive an untitled letter within 30 working days of the FDA inspection. Companies will have 15 days to respond to FDA. CDRH will then have 30 days to consider the firm's response. If the firm's response is satisfactory, FDA will send a postinspectional letter similar to the one discussed above. HIMA applauds the agency for this initiative as it provides the device industry with the opportunity to make corrections and forego the receipt of a warning letter without diminishing the agency's authority.

Inspection Evaluation Survey. For years, industry has made various allegations about the lack of uniformity in FDA inspections. In an attempt to get accurate data, a committee of the Medical Device Industry Initiatives Grassroots Task Force, in cooperation with University of California Irvine's Center for Statistical Consulting (UCI), designed a medical device inspection evaluation survey to provide a mechanism by which industry can provide anonymous feedback to ORA and members of the public regarding the FDA inspection process. The survey, which began on March 1, 1999, will be piloted for one year.

Upon completion of an FDA inspection, the investigator will fill out the top portion of the survey that contains background information about the company and the devices it manufactures, the name of the investigator, the FDA district, whether or not a 483 was issued, and the reason for the inspection. After completing the form, the investigator will give it to an official at the firm that is being inspected, ask him or her to complete it, and return it in the stamped envelope to UCI.

Data will be entered and analyzed at UCI, with specifics about companies and investigators kept confidential. UCI will analyze the data at the end of six months and at the end of one year. To show trends in satisfaction and perceived problems, a comparison of the responses both nationally and by individual districts will be made. HIMA believes that the evaluation will provide concrete data about what is going on during the FDA inspection process and where and how the process can be improved.

Quality System Inspection Technique (QSIT)

For years, members of the industry complained that FDA investigators inspecting their companies focused on individual deviations from the good manufacturing practice regulations rather than on whether their company had a quality system in place that was designed to

manufacture safe and effective products. In 1998, an ad hoc group of FDA and industry officials developed recommendations to address these concerns.

Based on the group's recommendations, a CDRH team led by Tim Wells developed a new systems approach for FDA inspections, which they called the Quality System Inspection Technique (QSIT). QSIT is based on the premise that the quality system regulation has seven major subsystems whose requirements intersect. The subsystems are

Management controls.

Design controls.

Corrective and preventive actions.

Production and process controls.

Record/document/change controls.

Material controls.

Facility controls.

During an initial inspection, an FDA investigator will examine whether the company has the first four subsystems in place, and whether it is manufacturing products under the procedures required by those subsystems. If a company has an inspection following which no official action is indicated, subsequent inspections will be more limited. HIMA supports this program and predicts that it will result in focused and efficient inspections.

Conclusion

FDA officials working with industry have made tremendous progress in allowing FDA to focus its resources to improve the manner of conducting inspections and making the procedure for initiating regulatory action more equitable. This interactive exchange needs not only to continue, but also should be used as a model for how FDA can protect the public health by working with industry to improve all aspects of the regulatory process.