Science at Work in CDRH:

A Report on the Role of Science in the Regulatory Process

Final Report

Submitted by the
External Review Subcommittee
Center for Devices and Radiological Health

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I. Introduction

The mission of the Center for Devices and Radiological Health (CDRH) is to promote and protect the health of the public by ensuring safe and effective medical devices and safe radiological products. The Center's public health mission requires working with a broad spectrum of stakeholders, ranging from consumers to medical professionals to the regulated industry. All of these expect CDRH to manage risks presented by advancing technology and changing use patterns and to do so with effective use of organizational resources.

The Center programs have been shaped with stakeholder input. Center management is well underway in implementing the FDA Modernization Act (FDAMA), and it appears to have managed available resources responsibly. Although five years ago the Center had an unacceptable backlog in medical device applications, through programmatic reengineering and increases in productivity the backlog has been eliminated.

Yet rapid changes in culture and technology threaten to overwhelm the Center's limited resources. Medical technology is changing rapidly, information systems are evolving so fast that e-mails have transformed traditional communication, scientific disciplines are merging, and the business of health care (as well as the manufacturing of medical products) is becoming global.

External pressures are compounding the problem. As Congress and the Administration balance the budget by shrinking government, CDRH must justify resource needs. At the same time, internal shifts have compromised the Center's science base, and its infrastructure is eroding in areas such as information systems, laboratory equipment, and training. Personnel issues are also affecting the Center's ability to do its job with at least a third of the Center's staff being eligible for retirement. Before institutional knowledge is lost, it is vital to share and capture this expertise.

In the midst of this change, CDRH must ask itself how it can continue being an effective agent of consumer protection and health promotion and how it can mold itself into the medical device and radiological health agency of the future - one that embodies predictability, timeliness, flexibility, transparency, interactiveness and effectiveness. To accomplish this, CDRH has developed a strategic plan and is beginning the implementation phase. The Center expects to update CDRH's mission, assess its current situation, envision the future and identify strategic issues, set goals and strategies, obtain feedback and support from staff and stakeholders, guide implementation and institutionalize a scientific approach to carrying out its mission.

The assumptions that underlie the plan are that the Center views science as the fuel for the regulatory engine. The plan aims to assure that CDRH will consider products from concept to obsolescence, i.e. the total product life cycle (TPLC), will meet all statutory responsibilities, meet its own quality standards, consider stakeholders as partners, and will follow an approach that is least burdensome while maintaining regulatory effectiveness and integrity. The Subcommittee endorses these assumptions and aims, but in addition adds the importance of limiting the influence of non-scientific factors.

The CDRH document on Goals and Strategies includes four areas: the total product life cycle (TPLC); magnet for excellence; meaningful metrics; and knowledge management. Intrinsic to these four areas is the fact that CDRH is a science-based organization with unique scientific expertise. Its regulatory decisions, from approving and clearing new products to the surveillance of existing ones, depend on asking and answering the right scientific questions in a predictable, transparent, and timely manner. In making these decisions, CDRH must identify relevant scientific issues, develop and collect evidence to address the issues, and then assess and judge the evidence. If CDRH is to do this, it must maintain its scientific expertise and be poised to adapt to new scientific and technical challenges for the future.

To help assure the quality and relevance of the Agency's regulatory decisions, the FDA Commissioner has directed CDRH and the other FDA Centers to examine how science is used in their respective organizations. This includes an assessment of whether the needed scientific expertise is available currently, whether it is effectively used, and a determination of the scientific expertise needed for the future. This has led to the external science review presented in this report. The Subcommittee appointed to conduct this review, and which has authored this report, only hopes that its findings and recommendations will provide CDRH with the help it is seeking.

II. Science Review Background, Subcommittee Charge, and Objectives

The review of the individual FDA Centers by Subcommittees of the FDA Science Board began three years ago with the Center for Biologics Evaluation and Research (CBER) and more recently included the Center for Food Safety and Nutrition (CFSAN). The summaries of these reviews were presented publicly at the Science Board with recommendations to the Commissioner of the FDA. These initial science reviews examined only the peer review process and the research programs of CBER and CFSAN. Their emphasis was primarily on laboratory research, although epidemiological and statistical research programs were also reviewed.

CDRH could have structured its external review in a similar manner; however, it chose to broaden its review. Reasoning that science is the fundamental building block of almost all of the organization's activities, the Center director decided to look at the role science plays throughout CDRH, and in their regulatory decisions. With the theme, "Science at work", the purpose of the review was to assess the quality of science across the organization and its relevance to the organization's regulatory mission.

The CDRH External Science Review Subcommittee charge originated from FDA's Science Board. The charter provides for the assembly of a committee with at least 2 members from the FDA's Science Board. CDRH assembled this committee with 13 members (see Attachment 1) from academia, industry, and government agencies. The Subcommittee was diverse, not only with respect to the source of the members, but also from their areas of expertise and experience, as indicated by the following: two cardiologists, one neurosurgeon, three biomedical engineering faculty, one statistician, two medical device company representatives, one software expert from NASA, one

human factors expert, and one non-US government (Canada) regulatory agency representative.

The Subcommittee's objectives were to make observations, conclusions, and recommendations regarding CDRH's use of science and scientific expertise, its overall structure, and its readiness for the future. Furthermore, The timing of this science review is fortunate, in that it comes during the formative stage of the Center's strategic plan and at a time where over the next five years there will be a significant number of retirements. This provides CDRH with a unique opportunity, and it is hoped that the recommendations of the Review Subcommittee will help the Center better utilize its scientific resources, both internal and external.

Following an Internal Review that is described in the next section, the external process started with the convening of the CDRH External Science Review Subcommittee on June 19 for an orientation session. This meeting was hosted by the Petit Institute for Bioengineering and Bioscience on the campus of the Georgia Institute of Technology in Atlanta, Georgia. This was followed by a three-day meeting held on July 24-26, at multiple CDRH buildings located in Rockville, Maryland. The Subcommittee agenda included the review of case studies, role-playing in focus sessions, and interviews with foreign government, industry, and CDRH staff. The Subcommittee made observations, drew conclusions, and developed recommendations. Finally on August 8, 2001, a subgroup drafted the Subcommittee's report and this was finalized through a series of electronic exchanges. On November 16, 2001 the Subcommittee's final report with their findings and recommendations will be presented to FDA's Science Board, the Commissioner of the FDA, and to the CDRH leadership.

III. Process of Science Review

The approach taken was simply to review "science at work" within CDRH. To this end, the Subcommittee considered both an overview of the Center's purpose, structure, and function, as well as an in-depth review focused on a specific device type, i.e., electrical stimulation devices. This allowed the Subcommittee to view the science-based regulatory decision-making process in action along the total product life cycle, from concept to obsolescence. Even though much of the focus of this science review was on electrical stimulation devices, the Subcommittee believes that its findings and recommendations have a more general application to the enhancement of science in CDRH's regulatory decision making.

A. Internal Review

An important part of the total science review process and an important input to this Subcommittee was the internal review conducted by CDRH. When in July 1999, CDRH Senior Management decided to conduct a science review, it was agreed that the focus of the review should be on a single cross cutting technological area in order to perform a detailed assessment that was sufficiently detailed but also manageable. The field of electrical stimulation devices was chosen because it was felt that these products would

effectively illustrate the depth and breadth of science in the Center, how and when scientific expertise is brought to bear on regulatory decision-making, and why science is essential to protecting public health.

Twelve internal experts in the electrical stimulation field, chosen to represent all of the Offices of the Center (predominately composed of non-managerial staff) were appointed to this Science Review Team and this internal group was officially charged with developing a protocol for the Center's Science Review. The objective for this review was to investigate whether CDRH is a science-based organization, has taken a broad view of science in the Center, and has taken the necessary steps to develop and enhance the required science base. During the course of the development of the Science Review, the establishment of a long-range strategic management plan for the Center was initiated. Concepts from the Science Review Team helped to shape and provide the underpinnings of the Center's Total Product Life Cycle paradigm. This Team also proposed to Senior Management that the science review look at case studies involving as many regulatory activities across the life cycle as possible.

The specific product areas chosen for the case studies were cardiac pacemakers, cochlear implants, deep brain stimulators and external defibrillators. These four were chosen because they illustrated different scientific issues at different points in the product life cycle, recurrent scientific issues at different points in the product life cycle, diverse scientific issues within a single phase of the total product life cycle, and the challenges in identifying and bringing all appropriate internal science-related resources to bear on a specific issue in a timely manner.

Once the framework for the science review was established, this proposal was discussed with FDA Senior Management and the independent FDA Science Board. It was agreed that a report resulting from an internal evaluation would provide an external committee with the prerequisite information to conduct its review. CDRH Senior Management nominated Branch Chiefs and Division Directors from all of the Center's Offices to conduct the internal evaluation. This Internal Subcommittee of ten and the Science Review Team together finalized the protocol.

The ground rules for the internal review included:

- the review not be a retrospective evaluation of individual decisions, or their correctness, rather an instrument to evaluate the overall role of science in the Center's decision-making;

- the review not focus primarily on "process," i.e., on the methods employed to do the job, but have process enter the assessment only to the extent that it might help identify the activities performed and shed light on CDRH's use of science in decision-making**;** and

- the review be reflective of the Center's current practice, with a 5-year historical boundary being imposed (while some areas covered during the review, such as the developmental history of cochlear implants, required looking into earlier time

periods, the standard practice was to consider procedures/decisions made during the past 5 years).

In February 2001, the internal science review was initiated. The Internal Review Committee began by conducting in-depth interviews of CDRH staff that worked on the four case studies, as well as interviews with their supervisors. The Internal Review Committee members doing the interviews did not participate directly with the case studies being evaluated. They identified the case study issues for this evaluation.

In addition to these interviews, the Internal Review Committee asked each Office Director to document: a series of issues ranging from an assessment of Scientific decision making in the Office, including how information comes in, how issues are identified, and how science is used in those programs/functions, to an identification of the core competencies that lead to good science and how CDRH can provide for this. Based on the findings from the case study interviews and the responses from the Office Directors, the Internal Review Committee drafted an internal review report. This report was provided to the External Review Subcommittee at the June 19, 2001 Orientation meeting in Atlanta, Georgia.

Subsequent to this orientation and prior to the on-site CDRH review, the following information was provided to the Review Subcommittee:

- CDRH Current Situation Analysis;
- Recommendations and Observations From the CDRH Science Review Team and Internal Review Committee;
- Top Ten List of Greatest Challenges & Problems for Science-Based Regulation at CDRH; and
- Top Ten List of CDRH Recommendations to Itself for Science-Based Regulation.

This Subcommittee commends CDRH for the substantive nature of this internal review and the spirit in which it was conducted. Not only did it provide a meaningful self-assessment by CDRH, but together with the additional information provided, the Subcommittee received a foundation of knowledge from which it could launch its own review.

B. External Review

For the external part of this review, the Subcommittee's agenda included reviewing CDRH's overall structure, seeing science in use by reviewing multiple cases studies on electrical stimulation devices, conducting in-depth interviews with CDRH staff on these cases, challenging their actions and decisions, interviewing European and Canadian government officials regarding their respective regulatory processes, and role-playing using historical data in focused sessions with CDRH staff. The Subcommittee was given a wealth of information. This was provided in many different ways and ranged from reviewing documents to interviewing staff, industry, and foreign government regulatory officials.

As noted previously, the Subcommittee's objectives were to make observations, conclusions, and recommendations regarding CDRH's use of science and its readiness for

the future. Although in many ways this external review was both extensive and exhaustive, the Subcommittee did not have time to directly review the use of science in the Office of Compliance. Furthermore, the Subcommittee in no way believes that it has the knowledge to offer recommendations at a micro-management level. Rather, the Subcommittee has attempted to provide recommendations of a more overall nature, leaving it to CDRH and FDA to determine how changes that are needed should be implemented.

1. Documents Reviewed

At the orientation session held in Atlanta, the Subcommittee was provided with a variety of documents, proposed agenda items for the July 24-26 meeting, and other information. This included: panel questions, a broad overview of the Subcommittee task, Total Product Life Cycle (TPLC) and Science Based Regulation materials, in depth case studies, and a product listing for an on-the-spot review. The Subcommittee had the opportunity to review these with CDRH staff. At that point, the Subcommittee shaped the final agenda and panel questions and assigned review teams for the case studies.

During the July 24-26, 2001 panel meeting, the Subcommittee requested additional information regarding the budget and structure of the Center, as well as on specific 510(k) notifications and premarket approval applications. The Subcommittee reviewed this information and interviewed the staff accordingly.

2. Interviews

a) CDRH staff

Case Study Review Teams

The Subcommittee decided to assign two to three members to be responsible for reviewing in depth each of the four different case studies: Cardiac Pacemakers; Deep Brain Stimulators; Cochlear Implants; and Automatic External Defibrillators. These four Subcommittee review teams interviewed a variety of CDRH staff, ranging from front line reviewers to mid-level management. CDRH staff included anywhere from seven to 15 people at any given time with, for example, some of the following expertise represented: clinicians, engineers, statisticians, audiologists, physical therapists, nurses and other scientists. A wide spectrum of expertise was involved in these interactive dialogue sessions. In each of these interviews, a portion of the time mid-level management was excused from the session to provide an environment in which staff could be totally open and honest. As stated earlier, these case studies were selected because, in combination, they covered the major aspects of the Total Product Life Cycle model. Although the focus was on electrical stimulation devices, it was felt that the issues identified were generic and, hence, conclusions drawn from the review of these case studies would be generally applicable to other device areas.

On-the-spot Reviews

The Subcommittee tested the quality of the scientific reviews by requesting to see documents about the decisions that CDRH made in the last 5 years on electrical stimulation devices. Through this process, the Subcommittee was given free access to any information individual members deemed of interest. CDRH staff provided all requested information and coordinated interviews with respective reviewers regarding their decisions. Several front line reviewers were interviewed regarding their decisions and asked to summarize the issues relating to the submissions and overall review.

Role Playing

In order to give the Subcommittee a better idea of the difficulties CDRH staff faced in making science-based regulatory decisions, the Subcommittee had the opportunity to role-play as CDRH staffers during the meeting, using two actual scenarios—one a pre-IDE situation and the other involving a postmarketing problem. In the pre-IDE session, the Subcommittee had to deal with a new device to manage cardiac arrhythmias. Fundamental questions were raised, including what expertise in software was needed, what data were necessary to support the intended use of the device, and how the review could be completed in a timely manner.

In the postmarket session, the Subcommittee was placed in the position of dealing with a safety issue regarding anti-theft devices interfering with pacemakers and implanted cardiac defibrillators. This focus session involved working with adverse event reports and collaboration with another federal agency.

Union and Senior Management

The Subcommittee interviewed the union (NTEU) and Center senior management regarding issues and challenges that CDRH will face in the future. The union management included the NTEU FDA Chapter President and two CDRH union stewards. CDRH senior management interviews included several of the office directors (OST, OSB, ODE) and division directors (OSB and ODE).

b) Industry Interviews

CDRH arranged interviews with individuals from four companies (Dr. Eric Fain, St. Jude Medical; Paul Citron, Medtronic; Peter Jacobson, ELA Medical; Dr. Steven Staller, Cochlear Corp) in the industries that the case studies involved. The Subcommittee was allowed to talk candidly with the industry representatives regarding their perspective on CDRH science and expertise, and the Center's overall readiness for the future. These four industry representative provided small versus large and US based versus non-US based perspectives, in addition to a broader device industry perspective on the FDA use of science.

c) International Interviews

To bring a global perspective into the picture, the Subcommittee interviewed two foreign government officials, one from the United Kingdom and one from Canada, regarding

their regulatory processes. From these two interviews, the Subcommittee was able to compare the U.S. with both Canada and Europe.

Dr. David Jefferies, Director of the Medical Device Agency (MDA) in the United Kingdom, explained regulatory classification and the role of notified bodies in approving medical devices in Europe. He noted the small size of the U.K. regulatory staff compared with that of CDRH, and the use of outside experts and committees. For analysis of new medical devices, the EU relies on independent commercial entities, designated notified bodies. Notified bodies assess conformance to the essential requirements as specified in the Medical Devices Directive, Active Implantable Medical Devices Directive, or *In-Vitro* Diagnostics Directive (i.e., the European equivalents to the U.S. *Code of Federal Regulations* applicable to medical devices and *in- vitro* diagnostic products). The notified bodies are supported by fees collected from manufacturers for premarket reviews and quality system audits, with the integrity of the process based on a combination of government oversight by a Competent Authority in the country the notified body is registered and the manufacturer's legal responsibility to comply with national medical device laws (i.e., the transposition of the EU directives into national law).

The notified bodies place their major emphasis on confirming that devices meet technical specifications and comply with appropriate international or European standards, with lesser emphasis placed on clinical trials or performance (either pre-market or post-market). Dr. Jeffries stated, however, that Europe needs more clinical investigations before marketing medical products, and explained the drawbacks inherent in relying solely on notified bodies in approving new medical products.

Although notified bodies have the responsibility for premarket evaluation and approval, which allows for CE marking of medical devices, the MDA has the authority to take appropriate regulatory action on marketed devices in the U.K. Postmarket events that result in product failure or patient injury, for example, are reported to the Competent Authority in the country in which the event occurs. In the U.K. such reports are submitted to MDA. Dr. Jeffries noted the small size of the U.K. regulatory staff compared with that of CDRH, and the need for greater reliance on use of outside experts and committees.

Ms. Beth Pieterson, a member of this Subcommittee and the Director of Medical Devices Bureau Health Canada provided her perspective on Canada's regulatory structure and processes. The information she provided suggested that Canada was a hybrid of the European and American systems.

IV. Findings

The Subcommittee made its evaluation of CDRH science-based decision-making and future preparedness with an emphasis on: 1) focus of the scientific questions, 2) scientific breadth and depth (content), 3) communication and integration of science, and 4) timeliness of decision-making. The Subcommittee viewed science in the *broad sense*,

incorporating scientific, engineering, medical, physiological, and procedural approaches and findings. In this section its findings are presented, and in this the Subcommittee has grouped these observations and findings into three areas: scientific expertise, human resource issues, and organizational and process issues.

A. Scientific Expertise

To provide a basis for making judgments about the scientific expertise of the Center for Devices and Radiological Health (CDRH), the Subcommittee reviewed the organization of CDRH as related to scientific personnel, heard presentations of four case studies and asked numerous questions about them, conducted interviews of four industry representatives about the quality of scientific judgments as related to applications submitted by their companies, talked to personnel from the Office of Science and Technology and from the Office of Device Evaluation, and conducted "on-the-spot" reviews of a number of past decisions. From these multiple different perspectives of the Center, the Subcommittee came away convinced of the commitment of the Center and its personnel to the public welfare.

The Subcommittee was further convinced of the willingness of the staff to work hard, often on tasks unlikely to be recognized, and to struggle with and resolve conflicting goals of timelines versus complete scientific knowledge. The Subcommittee thought that the staff made and continues to make decisions that are, on the whole, balanced and well-founded in terms of their underlying science. The fundamental challenge to the Center is to make decisions quickly and at the same time on a sound scientific basis, so that beneficial technology can be available and harmful technology can be removed from public use without delay.

The External Review Subcommittee found this Center to be an agency staffed by excellent people who are doing a good job in dealing with their assigned tasks. At the same time, the Subcommittee's judgment, consistent with that of the Center's staff, was that there is stress in the system and room for improvement, especially as one looks out toward future years. This is elaborated in the findings in the following paragraphs.

1. Science and the Regulatory Decision-making Process

The Subcommittee strongly reaffirms the fundamental principle that good science is critical to good decision-making within the CDRH. Scientific and engineering expertise is a core component of the decisions on the substance of the questions that come before the Center, and well founded decisions require substantial scientific judgments. In the case studies presented to the Subcommittee and in other studies selected for on-the-spot examination by the Subcommittee, the vital issues always involved the science, engineering, and related physiological and medical issues underlying the question at hand. The need for sound science is broadly understood in reaching good decisions on complex new initiatives.

The presence of strong scientific knowledge allowed rapid approvals to be issued, notwithstanding paperwork or procedural problems, and also allowed serious potential

problems in devices already in use to be detected before many people were affected by them. A consistent finding in the interviews with industry representatives was that they were frustrated by delays that they saw as being merely procedural or bureaucratic but were supportive of, and in some instances welcomed, those conversations with the Center revolving around substantial, relevant scientific, engineering, or medical issues.

2. The Present Level of Scientific Expertise in the CDRH

The overall high quality of CDRH reviewers, medical officers, scientists and engineers was evident throughout the presentations. Some staff members are recognized authorities in their fields through publications and standards bodies. The range of expertise across diverse topics --- atrial pacing, bones density, and batteries, as examples --- was impressive. In-depth expertise exists on several topics studied in the labs of the Office of Science and Technology and expertise in some sections of the Office of Device Evaluation is considerable.

Nonetheless, it also was evident to the CDRH staff and to the Subcommittee that expertise across fields is uneven. For example, there are no medical officers who are neurologists or psychiatrists and there appeared to be no behavioral or cognitive scientists. Although the Subcommittee review was limited to electrical stimulation devices, it would not be surprising if there were gaps in knowledge in other scientific areas important to CDRH. In other fields central to some review judgments, such as human factors, or computer science (especially software reliability), expertise is limited to a few people who are spread across too many tasks. Further, use of outside experts is limited by organizational barriers, budgets, and time constraints, by concerns about confidentiality and conflicts, and by legal requirements for action within restricted time windows. It should be noted that these factors could adversely affect a scientific approach. Even when the CDRH has expertise within the organization as a whole, the responsible individuals within the Office of Device Evaluation are not necessarily aware that such expertise is present, because they have no detailed database (electronic or otherwise) as a catalog. Finally, the level of expertise among the staff about the clinical environment in some cases is limited, so decisions may be sometimes rendered that are problematic when applied to clinical trial designs. One example raised by a Subcommittee member appeared to have been a clinical trial design that was scientifically valid, but may not have had sufficient ethical review from a clinical perspective.

3. The Increasing Complexity of Applications

The Subcommittee reviewed data on the numbers of applications submitted each year over the last decade and discussed with the staff the complexity of these applications. Over time, for a given kind of device, its technology, device maturity, and the associated clinical uses of devices move from investigational levels into widespread use. The CDRH has done a good job of reclassifying devices into categories requiring less review or no review when that is justified by increased knowledge and experience. Thus**,** even as the use of medical devices has increased substantially over the past decade, the number of applications requiring review has remained approximately constant.

The complexity of the applications requiring review has increased, however, even as the total numbers remained constant. Increased complexity has occurred because the devices are intended to address more complex medical issues (e.g., atrial versus ventricular stimulation), because the intended patient population changes (e.g., use in children), because issues arise involving uncertain medical or physiological events (e.g., those in the brain), and because of unanticipated interactions of medical and non-medical devices (e.g., electronic anti-theft systems in stores with implanted stimulators**)**. Issues arise about human factors of the users (do children report failures in the same way?), about proper statistical design, and about highly specialized topics (different lithium battery technologies).

The increased complexity and limited internal resources sometimes puts the responsible reviewer in a difficult position to make judgments in fields where the evaluator's experience or knowledge is lacking, or, recognizing the limited knowledge, to cause delays in decisions by asking for information that is irrelevant or would not be needed by a more expert evaluator. Increased complexity also means that more staff time is required to prepare for meetings with industry representatives, and more time is required of individual staff members to respond to a single application. Increasing complexity also places great demands on the staff for up to date scientific knowledge of a changing field, with a corresponding need to give continuing education to the staff a high priority (see Staff section of Findings).

4. Science and the Long-Term Regulatory Role

The Subcommittee was concerned about the balance between various CDRH commitments, how these relate to the Total Product Life Cycle paradigm, and, more broadly, how these relate to the overall CDRH mission. On the whole, CDRH processes are driven by the timelines of required actions, ones that constitute a major part of each day's workload and that involve deadlines placed on the Center for action within a certain number of days. Since decisions can be controversial and subject to criticism, there is substantial pressure to focus on each one immediately rather than to include consideration of longer-term goals. Thus, it is unsurprising that timeliness has become the basis for evaluation of individuals and organizational components, to the detriment of scientific and other benchmarks.

It may be that at present too much emphasis has come to be placed on the timeline aspect of the Center's charge. Staff time spent on development of guidelines (guidance documents), standards, and peer-reviewed papers should be encouraged through the use of metrics that recognize such activity. Such activities and documents often will have a greater beneficial effect, per unit of staff time expended, than does an individual review, even though the benefit is not as easily documented and occurs some months or years later. The Subcommittee believes that working on long-term activities is desirable. Unsolved was how to do it more than at present, when time is at a premium and guidance documents are 10 years old and far out of date. Necessary mechanisms are currently lacking for a systematic process that leads to periodic review and updating of guidance documents.

Correspondingly, it was evident that the Total Product Life Cycle paradigm (TPLC), where each phase of the review is used to improve the next, was a good basis for the Center. Within a TPLC framework, the segment of the cycle receiving the least emphasis was the feedback loop from post-market review of one device to pre-market design of its successor. This segment of the cycle is most heavily dependent on recording present experience and passing that on to the next generation of designers (and reviewers/evaluators). In this regard, it was noted by staff that there is no general catalogue or electronic database of decisions reached, or the basis for them, so that undue weight is placed on individual people *remembering* what happened in some earlier, related situation.

While the benefits of retaining experienced people are always large, it is not a good practice to rely on that as extensively as is done now. Further, because of pressures on staff time and limited recognition for extra effort, only a small portion of accumulated staff knowledge makes its way into standards. Even with the unique perspective of the CDRH staff, it may not be possible to recognize all of the failure modes in recently designed systems.

5. The Leveraging of External and Internal Expertise for ODE

The Office of Device Evaluation (ODE) is the largest Office within the CDRH, comprising about 40% of the total number of CDRH employees. ODE is required to conduct reviews within strict time limits and within prescribed bounds of legal authority. It is the initiator of and has administrative control over most CDRH device reviews.

It seemed to the Subcommittee that there was a strong tendency for the Office of Device Evaluation to operate primarily “in-house", in fact if not by plan. This practice may derive from its relative administrative simplicity or from the time pressures of day-to-day work. Also, according to ODE staff, access to external expertise is too complex to be suitable for dealing with most situations, for outside experts are not readily available within the time and legal restrictions present. Access to such expertise must be facilitated and encouraged in all areas, e.g., biomedical engineering, behavioral science, statistics, medical, and ethical. Outside sources include both individuals and organizational resources within entities such as the AMA, American College of Cardiology (ACC), North American Society of Pacing and Electrophysiology (NASPE), Blue Cross/Blue Shield, and others.

The Subcommittee was interested in learning about the use of third parties, e.g. the notified bodies in Europe, registrars for quality system audits in Canada, and third party reviews to a limited extent by the FDA. The Subcommittee recommends that CDRH examine the feasibility of increasing the use of third parties in the United States as a mechanism to direct available CDRH resources to critical science issues and to those activities that can only be done within CDRH.

6. Metrics for Quantity, Timeliness, and the Quality of Decision Making

Most CDRH decisions involve science at some level. The level ranges from simple and "apparent to a scientifically schooled reviewer" (e.g. a judgment that some paperwork involves no substantial scientific issue) to the highly advanced (as when reviewing a new kind of medical device based on newly understood physiology interacting with a new technology). The Review Subcommittee came away convinced that at each level CDRH staff work conscientiously to try to apply science, broadly understood, in an appropriate way. This has the nominal but too often abstract support of management. The careful application of good science routinely appears to be done without support of, and perhaps sometimes *in spite* of regular operating procedures, which track the number and timeliness of applications processed. Reviewer evaluations tend to be based on volume metrics rather than the quality of scientific analyses.

Subcommittee members were surprised to find that there is no ongoing, systematic retrospective review within CDRH of some fraction of decisions, either as a measure of quality control or as a metric of individual and collective staff performance. Such evaluations are routine in industry or academic centers and can be accomplished by internal staff or sometimes by outside review. There is no doubt as to the capability of CDRH to review the Center's performance. In meetings with the Subcommittee, CDRH's professional expertise and its ability to identify strong and weak points was evident when discussing Center performance. What is missing is an overall administrative plan for such scheduled systematic reviews to occur and a plan for use of any metrics that might result.

There is a need for metrics to assess quality and complexity as well as just timeliness. A possible classification metric system that FDA might consider is based on decisions similar to the ACC/AHA Guidelines for implantation of pacemakers and antiarrhythmia devices (J Am Coll Card 1998;31:1175-1209 (A-B-C on p.1177). A decision based on this would be more transparent and informative than currently possible. This is because it institutionalizes the reality of non-scientific influences in the decision making process. This type of metric addresses the influences related to safety and effectiveness, such as the status of the clinical trial, the complexity of technological issues, regulatory and legislative issues (Congressional inquiries), and public concerns.

7. Scientific Expertise for the Newer, Breakthrough Technologies, including Combination Products

Even as it recognizes the good job done by CDRH staff on most tasks and in most decisions taken now, the Review Subcommittee has a great concern about whether CDRH will have the right expertise in future years. The concern comes because of the changing nature of devices to incorporate cellular or tissue-engineering components, because of the highly differentiated organizational structure of the present CDRH (which tends to replace departing staff with persons holding the same expertise), because scheduling and evaluation rewards short-term goals, and because there is little internally-generated review of quality of work.

CDRH's limited funding presents a two-fold concern. First, in comparison with most new medical, scientific, or engineering facilities created with expenditures of hundreds of thousands of dollars and comparable operating budgets, CDRH funding level is inadequate to maintain the broad number of programs needed. Second, CDRH seems to be poorly organized to take advantage of outside resources that have the needed funding.

B. Human Resource Issues

During the three-day session, the Subcommittee had discussions with many CDRH staff. The Subcommittee was impressed with the quality, professionalism and dedication of the staff. It was evident that staff have the scientific expertise related to their positions, and that they strive to use their expertise to impact the safety and effectiveness of medical devices used in the United States. At the same time, staff brought to the attention of the Subcommittee areas of weakness involved in human resource management in the Center. These include: recruitment and retention, gaps in scientific expertise, staff training and development, workload issues, promotion opportunities for scientists, reward and recognition.

1. Recruitment and Retention

The Subcommittee was presented with data showing that within the next several years, a significant percentage (30%) of the scientific staff will be eligible for retirement. However, there is apparently no recruitment strategy or succession planning in place to plan for the future. When asked, reviewers appeared unaware of how, or if, management plans for anticipated future staffing needs.

Additionally, the existing expertise will not be the same expertise that is needed for new technologies. In the discussion with industry representatives, a common theme was that the breadth of existing scientific experience is not sufficient for the future.

Several staff stated that dealing with the workload fully occupied them and that there is a lack of resources and time to plan ahead. There was also concern expressed regarding immediate loss of institutional memory due to the anticipated retirement of a significant number of staff and lack of electronic cataloguing.

Recruitment and retention of young scientists, engineers, and medical officers is, and will continue to be, a challenge. This concern was expressed repeatedly by the staff and by representatives of industry, and it also was recognized by the Subcommittee. The Subcommittee was told that young scientists frequently join CDRH and then leave for other opportunities within five years. Compensation packages, the work environment, and career opportunities at CDRH must be able to compete with those available in academia and industry.

CDRH must invest more and earlier in its technical staff to prepare for the assessment of rapidly evolving new technologies incorporated into medical devices and the growing number of combination products (i.e. biologic- or drug-device combinations). Without such investments, CDRH will likely lose critical technical expertise through increased turnover. An overall strategic staffing plan was not found to be a part of Center's

strategic plan. Furthermore, there appears to be no evaluation of what technical positions are needed to support the Center's objectives. The Subcommittee did not find critical success factors beyond essential job requirements nor did it find that incumbents were sufficiently evaluated.

2. Gaps in Existing Scientific Expertise

There does not appear to be an exact correlation between the scientific need to perform the work effectively and the current staff competencies. Both staff and the Subcommittee identified several areas where there is limited expertise to deal with current scientific issues. For example, there are gaps in neurology, behavioral sciences, and information technology. Lack of human factors expertise and software specialists was also noted. Considering the wide variety of expertise required by CDRH to carry out its mission, it is unrealistic for all of this expertise to be in-house. Some types of expertise may be needed for only a finite (rather than career) timeframe. This underscores the need to reach outside in order to bring specialized expertise to bear.

3. Staff Training and Development

The budget allocation for staff training and development is *woefully inadequate*. Each scientific non-laboratory position is allocated $1500 per year. This funding envelope includes all day-to-day expenses, such as pens and paper, as well as training and development and conference attendance. This level of support does not provide scientific staff with sufficient opportunity to remain current within their area of expertise, or prepare for the future scientific challenges that the Center faces. Funding for continuing education and development within scientific disciplines is inadequate and often competes with base salaries and research program funding. For example, entry-level junior scientists in OST, even those with Ph.D.s, are seldom given development opportunities during their first five years of tenure. Even among the most senior scientific staff, development opportunities are few. This calls into question the adequacy of some scientific reviews by scientists hired decades ago with little opportunity for continued training in their scientific discipline.

The Subcommittee believes that CDRH scientists may become regulators without sufficient scientific training and development. In ODE, branch and division management are given budgetary discretion for staff development. Typically, only one professional meeting per reviewer per year is funded, and these funds may be used instead to fund an academic course depending on the seniority of the staffer. In addition to the lack of available funding, lack of time for training and develop was identified. The workload clearly does not permit sufficient time for scientific staff to remain current.

4. Workload Issues

As stated in previous sections, with the emphasis on meeting submission review timelines, there appears to be too few staff to carry out the necessary activities as CDRH now functions. Bringing good science to bear takes time. It was also noted that lack of

time can prevent adequate quality assurance for the various CDRH activities. The review times and volume throughput have become the primary focus for the scientific evaluator.

Due to the workload that staff face, there is insufficient time to think ahead and plan for the future. For many special assignments, staff are asked to "volunteer" without any reduction in their other work. Staff are faced with competing priorities, such as completing application reviews on target and completing or updating guidances. Although the workload is a challenge within the organization, there do not appear to be any innovative approaches in taking advantage of external expertise to assist in the process. Several Subcommittee members commented that the scientific staff were overburdened with administrative tasks (e.g., paperwork) that prevent them from being completely focused on their science-related responsibilities and professional development.

The Subcommittee met briefly with union representatives. The union works with management on "quality-of-life" aspects. It appears that CDRH does not have any major management-union issues. The topics brought to the attention of the Subcommittee included promotion opportunities, work assignments and development opportunities in the Center. There was emphasis on assuring that every employee be treated with dignity and respect.

5. Promotion Opportunities

CDRH scientists expressed concern about their lack of promotion opportunities. The Subcommittee was told that managers can be promoted almost instantly, and that the process is also timely for staff who wish to switch to management. However, for those desiring to advance on a technical path, the promotion process is rigid, lengthy and cumbersome. The process inhibits the retention of good scientists. Promotion for scientists is linked, in part, to the number of presentations they make at meetings and conferences; however, the resources may not be available to attend such meetings.

6. Reward and Recognition

If scientists felt that they had adequate opportunities for advancement and were given adequate resources, both time and money, for training and development, it is possible that there would not be frustrations with the existing reward and recognition scheme. For example, entry-level junior scientists in OST, even those with Ph.Ds, are seldom given development opportunities during the first five years of employment. However, frustrations were expressed about current rewards and recognition approaches. For example, there is no reward for doing quality work, only for meeting deadlines. Or, the only reward for good work is more work.

There seem to be rewards and recognition of the quality of work, but no consistent standards to define high quality work other than timeliness. This encouragement occurs at the individual and work group level, but not necessarily at the branch, division, or office levels.

C. Organizational and Process Issues

Over the past several years CDRH has made science-based regulatory decision-making a top priority. In addition the Center has embraced the Total Product Life-Cycle concept and has begun developing a strategic plan that marries science-based decision-making with TPLC. If CDRH is to meet the stated objectives of the strategic plan, the Subcommittee has determined that more of the Center's budget should be allocated to science-based programs and technical staff development.

Without exception the reviewers and scientists interviewed demonstrated earnest commitment to their work. They take seriously the mission of CDRH to protect the American public by ensuring the safety and effectiveness of medical devices. They are dedicated to completing their assignments well and on time. However, they are often frustrated in their work by lack of resources, lack of clear direction from management (particularly when interoffice collaboration is required), lack of communication tools, and lack of development and promotional opportunities.

Although the overall number of premarket applications submitted for review is not changing appreciably, the complexity is increasing. The review staff is therefore continuously challenged with meeting statutory timelines for completion of reviews without sacrificing their quality. To further compound their efforts, budgetary limits within the Agency have hampered the Center's ability to replace staff lost to attrition. This results in excessive workloads for some and leaves gaps in scientific expertise necessary to perform comprehensive science-based reviews today as well as to prepare staff for the assessment of the emerging technologies of tomorrow. In addition, CDRH reviewers would prefer to rely less upon data from industry and more upon data generated independently within the Center, or by external contractors. Yet research programs are few, underfunded, and perhaps, not focused on the most current research needs.

A system of retrospective measurement and analysis of specific CDRH decisions and their quality is lacking. There does not seem to be a systematic attempt to assess the appropriateness of past decisions to learn from mistakes (either individual, group, or institutional), i.e., were decisions correct, consistent, and done with minimal resources as well as being timely. From a higher organizational focus, there is no periodic comparison of CDRH's mission with what CDRH is doing to fulfill that mission. Is it doing what is needed to evolve CDRH's professional expertise so as to be able to review new kinds of devices in a knowledgeable way? Do research projects achieve relevant goals and are those goals still relevant? There appears to be no quality metrics about CDRH as an organization.

1. Structure of CDRH

CDRH is made up of some 7 offices, 27 divisions, 85 branches, and employs 1,000 people. Approximately 65% of the staff members hold science-related positions. The volume of work performed within the Center is high, and includes premarket product reviews, postmarket surveillance and compliance activities, development of regulatory

guidance for the medical device industry, Center-directed research, and administrative tasks.

CDRH appears to be organized in what one Subcommittee member calls “semi-porous silos." The Center appears to be highly segmented and layered which makes communication and collaboration among the various offices, divisions and branches difficult and cumbersome. The lack of an appropriate electronic database has been noted previously. In addition, the existing structure requires a large management staff to oversee small groups of staff and can lead to unintended bureaucratic barriers to communication across the center and prevents clear leadership, ownership and accountability for decision-making. Theoretically the reviewer in charge of a submission or project can enlist help from other staff within the Center; but such “grass roots” efforts can be sluggish due to imposition on the already full workload of colleagues. These issues were illustrated in comments made by individual reviewers interviewed as well as in "Lessons Learned" in each of the four case studies reviewed by the Subcommittee: *communication and interoffice coordination can be achieved, but it is greatly facilitated when top management (i.e. office director or above) direct the process*, and in some instances, direct involvement of top management is necessary.

2. Office of Device Evaluation

Branches within the divisions of Office of Device Evaluation (ODE) do assign team leaders to manage application review projects. The team leader is responsible for ensuring the right people with the right technical and scientific expertise are brought together during the review period to provide input on the regulatory decision to be made. The team leader’s recommendations are reviewed by the Branch Chief and possibly by the Division Director. In most cases, this system works well. Most reviews are completed on time, and no major backlogs exist today compared to the significant backlogs that existed in the early 1990’s.

But at least in one case study (deep brain stimulation device), the team leader requested a specific scientific review of EMI compatibility to her management, but this request was denied. In this case the right scientific expertise was available within the Office of Science and Technology (OST), but not utilized due to a management decision that overrode the team leader’s request. This underscores the grass roots versus management interest/direction issue addressed in the previous section. The EMI question arose again late in the review process, and the request was then granted. As a result the OST reviewer cited various deficiencies in the sponsor’s data, requested additional information, which has further delayed the completion of the review. In this case more open communication across the offices early in the review process may have lead to an earlier resolution on the need for EMI review by bringing in the input from the OST EMC expert.

When there is a lack of sufficient internal scientific expertise needed to make regulatory decisions, one option is to contract that expertise externally. However, it appears that external experts are seldom used by the Center beyond those who sit on existing FDA Advisory Panels. Staffers interviewed cited conflicts of interest issues, lack of resources,

and a slow cumbersome process as reasons why external consultants are not used more frequently by CDRH. Although advisory panel members may be available quickly and at a reasonable cost, they often have conflicts of interest themselves that prevent them from taking a more active role in the review of submissions. The Center is then limited in its ability to bring the right expertise to bear in those instances where internal expertise is not available. A more liberal Agency or Center policy with respect to contracting external experts on an as-needed basis would help CDRH meet its science-based decision-making objectives without increasing headcount or overhead.

3. Office of Science and Technology

The Office of Science and Technology (OST) represents a major resource for CDRH. The organizational structure was established in the mid-1980s based on relevant technologies of that time: this past history has led to the current structure of four technical divisions, three of which are oriented towards engineering science and technology and one towards the life sciences.

While OST has been and continues to provide scientific support for scientific reviews when asked, and while OST staff have participated in many CDRH decisions, there was clearly a communications gap between ODE and OST. In part this gap reflects the limited knowledge within the ODE of the people in OST (since they work at a different site) and limited knowledge of the expertise held by OST staff. There are few support resources available to ODE personnel to catalog the expertise within OST (the database/catalogue issue again). Further, even when the research projects undertaken by the OST were judged quite pertinent to the CDRH mission, it was unclear whether or not these were the best set of projects to be done "in-house."

It should be noted that in some instances there are scientific programs ongoing within OST which were initiated more than 20 years ago. In any assessment of OST's scientific programs, there will need to be a prioritization, and in some cases, some programs may need to be abandoned and their resources redeployed. A concern is that the $4600 allotted per laboratory scientist for research support is insufficient and too small to undertake meaningful projects in many of the emerging scientific fields. A critical issue thus is the focusing of resources and programs so that OST can continue to be a resource and a leader within CDRH in emerging areas of science and technology.

Although the Subcommittee did not have the charge nor the time to carefully examine OST, it believes that now is the time to assess through an independent review how OST can prepare itself for the science and technology of this 21st century. OST needs to lead CDRH into these new areas, and the review recommended by this Subcommittee should focus on organizational, management, and programmatic issues.

4. Combination Products

Products combining devices, pharmaceuticals, and/or biologics have been made possible by technologic advance. Such products are likely to increase in importance and numbers in the next few years, and they represent an example of the complexity in products which CDRH and FDA as a whole will need to face. Whether these are regulated as devices or

other has depended on the primary intended use of the product; however, *a clear pathway for such products and guidelines for related regulations are needed.* This includes the degree of input from each regulatory Center, balancing safety and effectiveness with the desire for timely decisions. This may require creating a totally new structure within FDA. Whatever the case these combination products need to be regulated with an approach that embodies the philosophy of CDRH, one that is least burdensome, predictable, timely, flexible, transparent, interactive, and effective.

5. Communication Within and with Outside Organizations

As mentioned above the hierarchical structure of CDRH may inhibit good communication among the various offices. Although the office directors meet regularly to keep the communication channels open, there was some evidence among the reviewing and scientific staff of "competition" and perhaps perception of status differences among the offices, which may also limit communication and collaboration. The importance of interoffice communication and collaboration to the full implementation of a TPLC program within CDRH cannot be over emphasized.

To break down some of these communication barriers, an effective database and catalogue system based on information technology solutions must be employed. Several staffers expressed the need for quicker and more effective information sharing across the Center. Rapid access to regulatory decisions made and lessons learned, and internal/external resources prevent duplicative (and perhaps conflicting) decisions in the review of similar products or issues. Even though access to precedent decisions lead to efficient, complete, and consistent outcomes and the Center archives thousands of documents annually, it appears that data retrieval and access is unable to meet reviewers' needs. IT tools must be implemented to provide more efficient utilization of information among the staff.

As illustrated in the pacemaker interference case study, interagency communication and collaboration can be extremely beneficial to the solution of real-world problems not identified during the premarket review. However, there is no clear process or mandate for FDA collaboration across government agencies, such as with FTC, FCC, CDC, etc.

6. Regulatory Review Process

The review time statistics of CDRH are quite impressive. Premarket applications are generally reviewed within statutory timelines. Based on the case histories presented, the Center further appears to respond quickly and effectively to urgent issues as they arise. Balancing the need for sufficient scientific information with significance of the risk of the problem can be challenging, however, as evidenced in the automatic external defibrillator case study. In this case the two tools used by the Center team of experts and reviewers (i.e. Health Risk Analysis and Health Hazard Evaluation) seemed less than objective and lead to somewhat different risk assessments, which were then used to make the regulatory decision. The Center must also deal with a variety of non-science based influences. These range from public or industry-originated "scares" about certain products to Congressional or Administration policy directives.

Upon receipt, premarket applications are triaged by the branch chief within the appropriate reviewing division within ODE. The branch chief then assigns the review of the application to a lead reviewer. Although the assignment is intended to be based on the specific scientific expertise needed, or to the reviewer with the most experience with the particular type of medical device under review, assignments are more often based on distribution of workload. This system can result in an inefficient and potentially lower quality review and should be reconsidered.

The lead reviewer acts as a team leader, identifying and bringing together the right scientific personnel to conduct the review. However, one staffer stated that OST and other non-ODE resources are needed early in the review process, but timeclock pressures often preclude their use. This failure to use available OST resources may reflect either priority or process issues associated with interoffice collaboration. This again touches on the issue of process via grass roots versus management interest/direction, as addressed in a previous section.

There was concern expressed by some staffers that the scientific reviewers may be overburdened by excessive paperwork that could be done at a more administrative or managerial level. Movement of paperwork to administrative staff would free up valuable time of the scientific staff that could be better applied to more science-related activities.

Given fixed budgetary constraints, some variation on the notified body concept may be a relevant approach to addressing regulatory needs while allowing FDA to focus its limited funding on in-house tasks that cannot be done by external groups. Although a third-party review program has been implemented as provided for in FDAMA of 1997, it could be expanded to include a wider range of products (e.g., PMA supplements or those that require clinical data for premarket clearance), thus freeing up reviewing resources with the Center.

In each of the case studies presented, lessons learned were well articulated and fairly balanced. Upon questioning various reviewers involved in the individual cases, however, it appears that routine postmortem analyses do not occur, nor is information learned shared widely across the Center.

Taking all the above discussion on the CDRH Regulatory Review process in total, the Subcommittee concludes that CDRH does not have a comprehensive Quality System in place to support the execution of the FDA mission. Quality Systems, implemented in concert with international standards, e.g. the International Standards Organization (ISO) 9000 family, are common place in industry and have become a prerequisite for doing business. Academia and other government organizations have adopted similar quality systems. If CDRH were to be viewed as a business enterprise, its products would be: decisions on product approval submissions, guidance documents, comments and endorsement positions on standards, and actions on product problems encountered in use in the field. The Subcommittee saw no comprehensive process, as would be found in a typical Quality System, that addresses the quality of CDRH products.

V. Recommendations

Based on the observations and findings presented in the preceding section, the following recommendations are offered.

1. CDRH needs to communicate, both internally and externally, a clear vision of the fundamental role of science in the regulatory process. This vision should define the role of science in developing relevant guidance documents and in developing, modifying, and approving appropriate standards. The vision should delineate the role of science in determining how effectively CDRH responds to new technologies and facilitates the introduction of those technologies to users in a safe and effective manner. Development of a system for summarizing the scientific and other factors leading to guidances or approvals (or rejections) would be useful both for FDA, as it reviews its decisions, and for the public.

2. So that science can play this fundamental role, CDRH needs to rethink how it carries out its mission, prioritizes its activities, outsourcing those functions it can while still maintaining oversight, and reallocating its resources so as to expand its investment in science, in all Offices. As part of this rethinking, CDRH should examine its existing organizational structure as well as other regulatory models, with consideration for change to implement and support the TPLC concept. Given fixed budgetary constraints, one model would be for FDA to focus its in-house expertise on selected tasks, and delegate others to official notified bodies or similar entities that derive funding from non-governmental sources.

3. As part of its restructuring of activities to enhance the fundamental role of science, CDRH should assess and reconsider the structure of OST to focus on emerging science and technology; this assessment likely will require a separate review of OST.

4. CDRH should develop a plan for enhancing cross-office and inter-agency (e.g., FTC, FCC) communication and collaboration.

5. CDRH should establish an electronic database for liaison functions and internal and external expertise inventory.

6. CDRH should develop and implement a formal process for capturing institutional knowledge through more time spent on guidance documents, standards, other written publications, and archiving and retrieval systems, with written precedent files so that when a decision is reached it does not only remain in the "mind" of the reviewer. Professional credit should be given to the contributors, and the contributors should be rewarded.

7. In recognition of the large staff turnover anticipated in the next 5 years and in order to fill gaps in scientific expertise, CDRH should expeditiously perform an assessment of the current level and breadth of expertise and use this to develop a long-term strategic staffing and recruitment plan. Major gaps in expertise should be identified and filled during recruiting for staff replacements due to attrition and turnover. For each

position, the options of full-time, part-time, or contract (external) personnel should be considered.

8. CDRH needs to develop procedures and implement staff development/training opportunities to ensure that reviewer mandates for such issues as sample size or randomized trials are shaped by realistic clinical perspectives and relevant ethical considerations.

9. In recognition of its staff being its greatest resource, CDRH needs to streamline processes that encourage scientific growth within the staff and the maintenance of scientific expertise; these processes need to provide for a more inviting career path and a reward structure for scientific personnel, and will require a reallocation of budget resources so that stated goals of staff growth can occur.

10. CDRH should encourage and facilitate the use of internal but non-ODE expertise and also external expertise, including the development of operational and budget policies that promote a more liberal use of external experts.

11. CDRH should expand its outreach to and scientific interactions with industry and universities through visitor programs and the creation of appropriate forums for professional development and for information exchange between FDA staff, industry, and academia with particular emphasis on new scientific fields that may result in new medical devices within the next 5 years.

12. CDRH should develop a plan in collaboration with other Centers for the evaluation of combination products; this plan may require changes in organizational structure and operational procedures. Whether it is a new structure or some amalgamation of existing structure, the regulation of these products requires an approach that is least burdensome and embodies the philosophy of CDRH.

13. CDRH should develop and implement a quality evaluation and improvement program, and as part of this, the evaluation system should develop metrics for the assessment of quality as well as the timeliness of results. The focus of these activities should be to achieve high quality product reviews in a timely manner. Management should implement a system for recognizing, rewarding, and encouraging high quality product reviews and investigations.

14. CDRH should implement a quality system with both continuous evaluation and improvement programs in accordance with ISO 9000 or other relevant standards. The focus should be on CDRH as an organization with a specific mission and on the development of activities that contribute to high quality decisions making the most productive use of resources and with a high degree of consistency.

VI. Conclusions

In summary, this external review team believes that CDRH is doing an excellent job in carrying out its mission. Even so, with new products arising out of the biological

revolution and with breakthrough technologies which will be increasingly complex, CDRH will be significantly challenged.

This review thus was conducted in the spirit of assisting CDRH as it faces up to these challenges. The review consisted of a self-study carried out by an internal CDRH team followed by a three-day extensive (and exhaustive) assessment by an external review team. This external team found the internal self-study to be an important learning experience in its own right for CDRH and commends CDRH for the dedication, integrity, and commitment to excellence exhibited by this effort.

The external assessment, as represented by this report, provides an additional perspective. CDRH must institute major changes. The needed changes are reflected in the specific recommendations presented in the previous section. These changes are necessary if CDRH is to significantly increase the role of science in regulatory decision making. They include possible changes in structure and a rethinking of how the business of CDRH is to be conducted, a reinventing of the CDRH staff through strategic recruitment, the continuous professional growth of existing staff, and policies that reward staff for the quality of their scientific expertise. CDRH must reach out to external resources, including not only universities but also industry, to create partnerships that will accelerate making new technologies available that are both safe and effective so as to enhance patient benefit in America.

Finally, the Subcommittee appreciates the fact that these recommendations, if accepted, cannot be put into place overnight. The Subcommittee suggests that these recommendations be incorporated as explicit components of the CDRH strategic plan. Annual objectives derived from the recommendations should be established, communicated to the organization, and included in individual performance plans. Progress against meeting objectives should be monitored and appropriate actions taken if objectives are not met.

Attachment 1: CDRH External Science Review Subcommittee

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