

**AdvaMed's Written Testimony on
The Critical Path White Paper
at
Science Board
to the
Food and Drug Administration**

by

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AdvaMed appreciates the opportunity to comment on “Innovation, Stagnation: Challenge and Opportunity on the Critical Path to New Medical Products,” and applauds FDA’s focus on identifying opportunities and means to move important medical products from research to bedside. AdvaMed is the world’s largest association representing manufacturers of medical devices, diagnostic products, and medical information systems. AdvaMed’s more than 1,100 members and subsidiaries manufacture nearly 90 percent of the \$75 billion of health care technology products purchased annually in the United States, and more than 50 percent of the \$175 billion purchased annually around the world.

AdvaMed members range from the largest to the smallest medical technology innovators and companies. Nearly 70 percent of our members have fewer than \$30 million in sales annually.

The FDA paper’s underlying assumptions about device innovation are not supported by the publicly available data on device submissions

Because the paper makes it clear that its findings apply to drugs, biological products, and medical devices, we believe it is critical to identify key differences between the pharmaceutical and biologics industry and the medical device industry. The paper’s assumption that there is stagnation in the industry is based on metrics for drugs and biological products for the past ten years (see, e.g., the paper’s Figure 2, illustrating the decline in drug and biological product submissions and Figure 3, illustrating the escalation in investment for new drugs). FDA’s own Annual Report numbers demonstrate, however, that there has been *no* similar decline in the number of medical device submissions over the same time period. Indeed, there has been a statistically significant *increase* in both PMA and IDE submissions over the past ten years (see attachments). This is a critically important distinction between the pharmaceutical and device industries, and one that should be kept in mind while working to identify new methods for improving the speed to market for new medical products. Moreover, some medical device regulatory approaches may prove useful in addressing concerns about stagnation in the development process for drugs and biologics. Both the Agency and the pharmaceutical industry may wish to examine this. Most importantly to the medical device industry, there are areas where improvement could further facilitate the movement of innovative medical devices to the patient’s bedside. AdvaMed is very interested in these areas of potential improvement, of course, and we are looking forward to the discussion this afternoon to hear more about FDA’s proposed Critical Path Opportunities List.

Unique characteristics of device innovation are key

Medical device development has been characterized as a continuous, iterative process. This iterative and ongoing development process, characterized by constant product changes made in response to user needs and preferences, distinguishes medical technology innovation from pharmaceuticals development.¹ There is also a “learning curve” associated with practitioner use of medical technologies that may be longer than with drugs.² Further, the iterative improvements that mark medical technology innovation tend to parallel an increase in the skill level of practitioners, so that outcomes are dependent on both product performance and practitioner expertise.³

Innovations in medical technologies are not restricted to the premarket phase of their development. Instead, actual use of devices by practitioners in the clinical setting typically spurs additional refinements and improvements. Clinical adoption serves as the beginning of an iterative process of: feedback from medical practitioners, device redesign, use, and more feedback. Further, in addition to technological refinements, medical practitioners may use medical devices beyond their original intended uses and seek applications in other medical specialties.⁴

In addition, medical device refinements often result from advances in other industries—in materials science, bioengineering, molecular biology, and information systems, for example.⁵ The Lewin Group noted that many technologies are adaptations from other fields (e.g., lasers, ultrasound, magnetic resonance spectroscopy, and computing), and that many were developed through the interdisciplinary work of clinicians, physicists, engineers, and other scientists (e.g., medical lasers, cardiac pacemakers and defibrillators, cochlear implants, endoscopes, catheters, and cardiac imaging systems).⁶ This interdisciplinary character contributes to the evolutionary nature of medical technology development, and it lends a degree of unpredictability to the process. The benefits and effectiveness of a particular device technology may change as it evolves, and

¹ See Scott D. Ramsey, Bryan R. Luce, Richard Deyo, and Gary Franklin, “The Limited State of Technology Assessment for Medical Devices: Facing the Issues,” *The American Journal of Managed Care* (September 25, 1998), p. SP 191. See also Annetine Gelijns and Nathan Rosenberg, “The Dynamics of Technological Change in Medicine,” *Health Affairs* (Summer, 1994).

² Gelijns, “Comparing the Development of Drugs, Devices, and Clinical Procedures,” p. 166.

³ See C.R. Ramsay, A.M. Grant, S.A. Wallace, P.H. Garthwaite, A.F. Monk, and I.T. Russell, “Statistical Assessment of the Learning Curves of Health Technologies,” in *Health Technology Assessment* (2001), Vol. 5, No. 12. The authors note (on page 59) that both individual operators and institutions learn through experience. These “learning curves” complicate the evaluation of medical technology, and they are an impediment to rigorous assessment.

⁴ The Lewin Group, *Outlook for Medical Technology Innovation*, Report 1, *The State of the Industry*, p. 19.

⁵ The Wilkerson Group found that: “Virtually all device developments have adopted technology developed by other industries, rather than conducting basic component research. Contributions have been made by the defense, computer, telecommunications, aerospace, chemical, materials, and medical research industries.” The Wilkerson Group, p. 16.

⁶ The Lewin Group, *Outlook for Medical Technology Innovation*, Report 1, *The State of the Industry*, p. 19.

important refinements in medical technology may result from innovations in distant fields and industries that cannot be foreseen.

The Health Care Technology Institute provides a useful summary of the medical technology innovation process:

At its core, device innovation is a dynamic, complex, and incremental process. It is marked by uncertainties and unexpected twists, and it rarely moves in a linear, predictable pattern. It spans many different stages and activities—from development of a new idea, to diffusion of a new device, to refinement of an existing product. Among the host of factors influencing device innovation are market forces; federal policies, such as product liability, patents, and funding of research; and patient needs and demands. But perhaps most significantly, device innovation is a process that is rooted in the active day-to-day interchange between device users and device manufacturing companies. The relationship that often develops among these parties during the early stages of device innovation can be viewed as the beginning of a long-running dialogue.⁷

The principles of device regulation recognize the unique characteristics of device innovation

A review of the legislative history underlying the enactment of the Medical Device Amendments of 1976 shows that Congress designed medical device legislation with the broad diversity of devices in mind, and the realization that the one-size fits-all approach of drug regulation would not work for devices. Accordingly, Congress based the regulatory scheme on degree of risk, with the lowest risk devices subject to only basic requirements and the highest risk devices subject to more extensive premarket review by FDA. More recently, the Food and Drug Modernization Act (1997) codified certain medical device policies that enabled more streamlined review of devices, including exemption of many low risk devices from premarket review, early collaboration meetings, collaborative review process for premarket approval applications, and other similar provisions. Most importantly, it contained a “Least Burdensome” provision that required the FDA to identify and utilize the most expedient means to market for novel technologies that would assure device safety and effectiveness. FDA has found numerous opportunities to apply Least Burdensome methods to medical device review including the use of Bayesian statistics to reduce the number of subjects required in a clinical study, reliance on valid non-US data in lieu of clinical data from US populations, use of previously submitted information and data from published literature for approval of PMA supplements, and the use of objective performance criteria.

⁷ Health Care Technology Institute, “The Dialogue of Device Innovation,” p. iii.

Among the reasons for this Congressional focus on risk-based regulation was recognition that the medical device industry differs in significant ways from the pharmaceutical and biological products industries. First, the vast majority of medical device companies are small companies, with annual sales of less than 30 million. Second, the life cycle of the average medical device is about 18 months, after which the device is replaced by newer technology. Third, medical devices do not typically benefit from extended patent protection. Fourth, medical devices encompass a large range of products, from bandages and wheelchairs to in vitro diagnostic products to implantable cardioverter/defibrillators. For these reasons, there was a need for a regulatory system that would be flexible and efficient, and, since 1976, FDA has looked for ways to improve its pre- and post-market handling of medical devices. Most recently, it converted its GMP regulation to a Quality System approach closely harmonized to the internationally accepted ISO quality systems standard and required the industry to apply risk management principles to medical device design.

Issues remain to be addressed in the regulation of devices

FDA's White Paper offers an opportunity to address a number of problems associated with bringing innovative / breakthrough medical devices to market, and in fact, proposes the development of a Critical Path Opportunities List. AdvaMed certainly supports efforts to ensure that the regulatory pathways for approving the products of new technologies can keep pace with biomedical research.

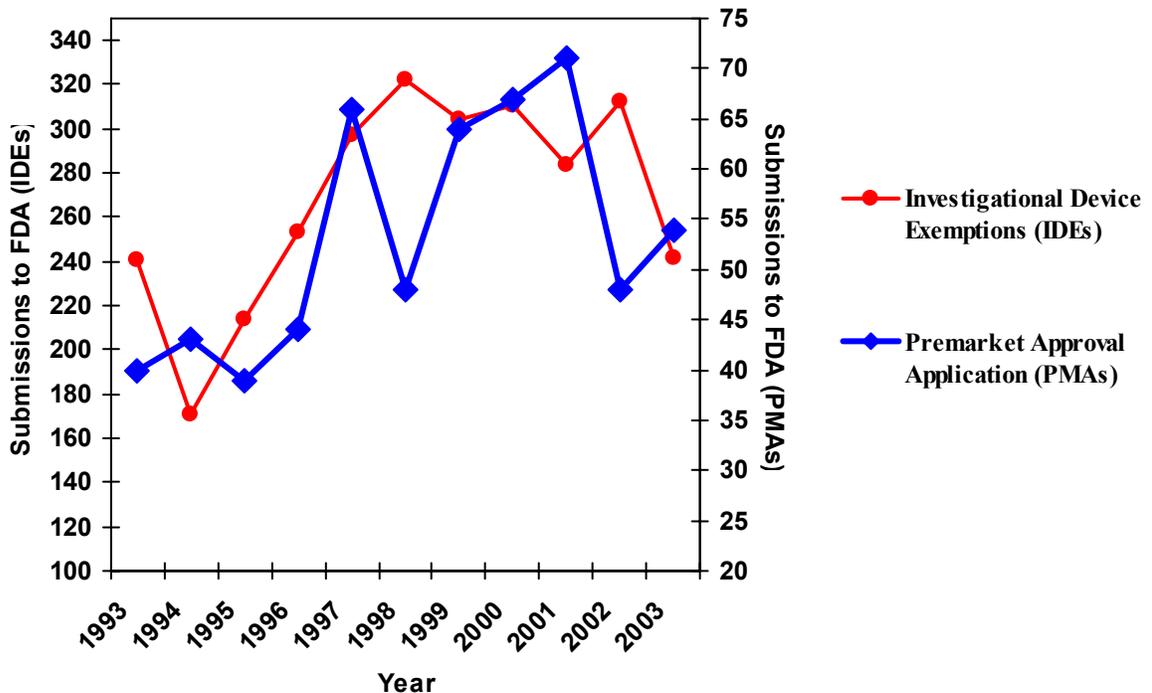
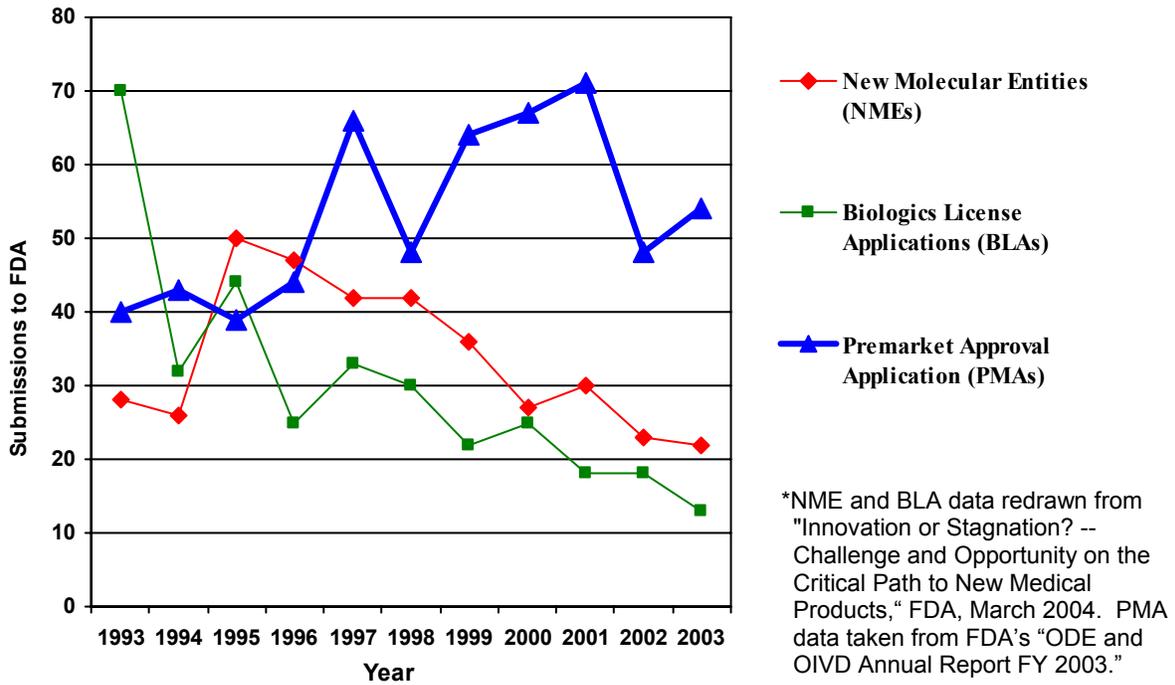
AdvaMed believes that review process issues, such as early communications, are an important part of improving the critical path. We also believe that the science used in device review could benefit from a critical look at the scientific expectations for new and novel technologies and whether those expectations are a roadblock to the advancement of patient care. Some of our initial candidates for the medical device Critical Path Opportunities List, then, include early communications, the expedited review process, clinical trial design issues for breakthrough products, the use of post-market mechanisms, and new approaches to in vitro diagnostic test development. We look forward to further refining this list as the process of working with the agency unfolds.

AdvaMed is pleased to work with FDA to enhance the movement of innovative products to the patients who need them

Given the number and the variety of medical devices, effective regulation is no easy task. The key challenge facing FDA as it regulates medical devices in the 21st Century is the same one that confronted FDA in 1976, when the agency was charged by Congress to regulate these products—balancing FDA's dual mission

of protecting and promoting the public health. AdvaMed is pleased to work with the Agency as it tackles this issue agency-wide for all medical products.

Attachments



* PMA and IDE data taken from FDA's "ODE and OIVD Annual Report FY 2003."