

July 18, 2011

Representative Henry A. Waxman  
Ranking Member, Committee on Energy and Commerce  
U.S. House of Representatives  
2322A Rayburn House Office Building  
Washington, DC 20515

Dear Mr. Waxman:

I write in reply to your request for comments on the report entitled "FDA Impact on U.S. Medical Technology Innovation: A Survey of Over 200 Medical Technology Companies" by Dr. Josh Makower, Dr. Aabed Meer, and Ms. Lyn Denend. I understand that you have asked several journal editors to review it as they might a submitted manuscript. The topic of medical device regulation by the FDA, including device approval and safety oversight, is of major importance because these products directly affect the health and quality of life of many patients in the United States. Accordingly, there is a need for rigorous research that provides good data to inform the issues of the timeliness and appropriateness of the FDA medical device approval process, and that provides reliable information to compare the efficiency, effectiveness, cost-benefit, and burden of the US and European processes for medical device approval and regulation.

The report by Makower et al is based on a survey of industry executives and was designed to collect information about how the US and European premarket regulatory processes for medical devices compare, about the cost and time involved to navigate the US premarket regulatory processes, and about aspects of the US premarket regulatory processes that are most challenging to innovators. Based on responses from 204 unique companies, the authors report that "survey respondents viewed current US regulatory processes for making products available to patients (the premarket process) as unpredictable and characterized by disruptions and delays" (on page 6 of their report); that the "FDA compared unfavorably to European regulatory authorities" (page 7) in terms of time from companies' first communication about a device to receiving approval to market the device (page 6), as well as in terms of predictability, reasonableness, transparency, and overall experience (page 7); and that the "suboptimal execution of FDA premarket regulatory processes has a significant, measureable cost to US patients in the form of a device lag" (page 7).

The report by Makower at al has several important limitations, including, but not limited to, a selected study population, a low survey participation rate, lack of verification of apparently subjective data, unclear data reporting, and issues surrounding interpretation of the findings for the US and European comparisons. These issues reduce and limit the validity of the reported findings.

First, it appears that those who responded to the survey were from a select group, selected based on invitations to participate limited to companies in the MDMA, NVCA, and medical technology state associations. The study does not provide sufficient information to judge whether this small sample is representative of US medical technology companies. In addition, the survey response rate is low, increasing the likelihood of selection bias, particularly if the invitation to participate indicated the reason for the survey; in that case, respondents may have been more likely to participate if they were dissatisfied or had negative experiences with the FDA process.

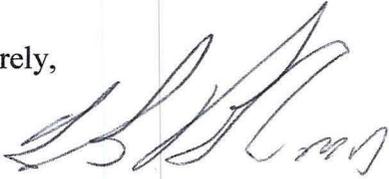
Second, the study report does not include the survey instrument or details about survey development and validation, so it is not possible to determine whether the questions were formed in a neutral way, or whether their wording or ordering may have created leading questions or a biased response. Based on the results, it appears the questions were designed to assess respondents' impressions, and opinions, and other subjective measures. There does not appear to have been any attempt to assess the accuracy of these subjective responses, for example, by requesting data through correspondence or internal documents, or by auditing a subset of companies and obtaining objective corroborating data.

In addition, it is unclear whether the responses were based on a respondent's overall opinion of the process at FDA or a company's single recent experience. It also appears that different participants received different surveys and that some companies provided more than one response to some items. However, the authors do not provide information about the number who did so, which questions these responses addressed, whether these multiple responses were aggregated with others, or whether there was clustering by company. Moreover, it is not clear whether all respondents had experience with both the US and European systems, or whether in some cases the comparisons were made between responses of subsets of individuals who did not respond to both sets of questions.

Third, there are several issues with interpretations related to the comparisons of the US and European regulatory processes. The authors interpret FDA approval time lines as being long, but without any background information or benchmark as to what constitutes appropriate time frames; the comparison with EU does not necessarily provide a benchmark of appropriateness, only of an alternate process. Throughout the report, the authors indicate that the delay in approval and availability of devices compared to the EU has resulted in worse care being available for US residents. However, the authors do not provide any evidence that this delay or lack of availability leads to adverse health outcomes. In addition, the authors do not provide data indicating that the EU system is comparable to the US system with the exception of the approval process/time frame. There may be other factors that mitigate the effects of a shorter time frame in the EU, and there may be other differences with respect to the regulatory system and environment between the US and EU that have not been assessed.

Even though the authors have acknowledged several of these important study limitations (page 19 of their report), such acknowledgement does not mitigate the threats to validity created by these methodological issues. Given the extent of these limitations, the inferences and conclusions that can be reliably drawn from this report are limited. When the findings of a statistical survey and report cannot be considered definitive, they may be viewed, at best, as hypothesis generating, perhaps leading to a more thorough exploration in more rigorously designed future studies.

Sincerely,

A handwritten signature in black ink, appearing to read 'H. Bauchner', written in a cursive style.

Howard Bauchner, MD  
Editor in Chief, *JAMA* and Scientific Publications