

February 24, 2010

Division of Dockets Management (HFA-305)
U.S. Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2009-N-0575

Dear Sir or Madam:

The Medical Device Manufacturers Association (“MDMA”) appreciates the opportunity to comment on the questions posed and issues raised in the Food and Drug Administration’s (“FDA’s”) public announcement of a February 9, 2010 meeting entitled *Incorporation of New Science Into Regulatory Decisionmaking Within the Center for Devices and Radiological Health*.¹ MDMA is a national organization representing hundreds of innovative, entrepreneurial medical technology companies. MDMA’s mission is to ensure that patients have access to the latest advancements in medical technology, most of which are developed by small, research-driven medical device companies. As such, MDMA supports FDA’s commitment to exploring meaningful, predictable and transparent means of incorporating new science into regulatory decision-making in a manner that fosters innovation, encourages advances in science and medicine, and focuses on the public health.

We appreciate FDA engaging in this ongoing dialogue regarding FDA’s regulation of medical devices. We are optimistic that, through these discussions with industry, including the small, entrepreneurial businesses which predominately characterize the medical device industry, a transparent, fully-defined pathway for utilizing new scientific information during FDA’s regulatory decision-making process can be articulated and achieved. We believe that this process can and should incorporate new scientific information without immobilizing Agency action or resulting in unwarranted or unnecessary reactions. The challenges imposed on industry by vacillating review goals and inconsistently applied standards stifle medical device innovation and are ultimately detrimental to the public health. Regulatory confusion or inconsistency results not only in unnecessarily delayed product approvals, but also in more expensive products for device manufacturers and ultimately for patients. Diminished patient access to safe and effective medical devices because of either delayed approval or prohibitive costs is contrary to FDA’s overriding purpose of protecting the public health.² In light of these concerns and as discussed in additional detail below, MDMA would encourage FDA to (i) define

¹ 74 Fed. Reg. 67237 (Dec. 18, 2009).

² See Hamburg, Margaret A. and Joshua M. Sharfstein, *The FDA as a Public Health Agency*, NEJM, Vol. 360:2493-2495 (June 11, 2009)(“What has remained constant is the agency’s ‘overriding purpose,’ in the words of the Supreme Court, of protecting the public health.” quoting *United States v. Bacto-Unidisk*, 394 U.S. 784 (1969)).

the parameters of relevant terms central to discussing these issues; (ii) articulate clear standards that FDA will employ for classifying the relevance or importance of new information or technologies; (iii) specify that FDA's evaluation and assessment of new information will be consistent with FDA's risk/benefit assessments; (iv) based on this risk/benefit assessment, FDA will specify what, if any, action (i.e., new standards for product approvals, withdrawal of product approvals, new clinical trial requirements) should result from the new information; and (vi) permit industry participation in the development and vetting of any resulting action.

I. Adapting to New Scientific Information

FDA should clearly define "New Scientific Information." MDMA agrees with FDA's stated goal of achieving a reasonably consistent, flexible process for responding to "changes in science." Moreover, MDMA appreciates that FDA's regulatory decision-making process must be able to adapt as science evolves and as new information emerges about the risks or benefits of particular medical devices. Indeed, MDMA fully supports FDA in its goal of utilizing clear and convincing information and reliable scientific data in its regulatory decision-making pathways consistent with FDA statutory and regulatory requirements. It is clear, however, given the case studies proposed for the Public Meeting's discussion and FDA's fluid use of the terms "new science" and "information" in the announcement of the Public Meeting, that, unless these terms are clearly defined as an initial matter, it is unlikely FDA will achieve the desired "predictable adaptability."

Specifically, in FDA's proffered Case Studies,³ FDA utilizes the following examples as new science: "a pattern of Medical Device Reports (MDRs) that have been submitted to CDRH calls into question the safety of the device when used in the long term for its cleared use,"⁴ "a compelling peer-reviewed publication reports that an attempt to replicate these clinical trial results was unsuccessful,"⁵ "CDRH learns from other compelling peer-reviewed studies in publication that the surrogate does not reliably track the expected clinical outcome."⁶ MDMA is not suggesting that, based upon the limited description of these scenarios, such information could not constitute new scientific information for the Agency's consideration. Instead, MDMA would encourage FDA to clearly articulate and define what it intends new scientific information to include and provide guidance on how it concluded that the information described in these hypothetical case studies constituted relevant new information for FDA regulatory review. We note, for example, that the FDA highlights the "peer-reviewed" nature of the report and in Case Study 2 the studies were "compelling and peer-reviewed." One option for describing "new scientific information" would be to hold potentially relevant information to the same standard of "valid scientific evidence" that FDA employs in the approval process. MDMA strongly encourages the Agency to provide a clear framework for evaluating and understanding "new scientific information."

³ Avl. At <http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm191579.htm#case>. (last visited 2/2/2010).

⁴ Case Study 1: Scenario A.

⁵ Case Study 1: Scenario B.

⁶ Case Study 2.

FDA’s review of and response to new scientific information should be consistent with its statutory and regulatory requirements. MDMA believes that FDA should clearly articulate its standard for evaluating new scientific information and, in particular, the factors that FDA intends to apply in determining whether or not the information triggers the need for additional agency action. In other words, what factors will the Agency consider in determining whether new scientific information is important? This standard should be consistent with FDA’s statutory and regulatory requirements, including the requirement that new scientific information should provide clear and convincing evidence that FDA action should be taken in light of FDA’s statutory obligation to conduct a risk/benefit assessment.⁷

For example, in Scenario A of Case Study 1, FDA posits a pattern of Medical Device Reports that call the safety of the hypothetical device into question. However, this statement is provided without a discussion as to how this new information affected FDA’s risk-benefit assessment of the device. MDMA believes this risk/benefit balancing is crucial in assessing whether the new information warrants any action. Although FDA’s background discussion seems to suggest that the Agency intends to evaluate new information in light of its traditional risk-benefit assessment (“new information gathered about the risk-benefit profile of a device on the market may justify requiring additional data on similar types of devices during premarket review, in order to provide sufficient confidence in the product’s safety and effectiveness”), FDA should confirm that all new information will be subject to this assessment and that the new information and its significance will consistently be assessed in light of the product’s risk-benefit profile.

Moreover, FDA currently has extensive authority to take necessary action to respond to new information which clearly establishes that the risk-benefit profile of a product is altered by clear and convincing new information. MDMA agrees that FDA should articulate a flexible and predictable system for assessing appropriate action, consistent with its authority, in light of clear and convincing new scientific information which affects the risk-benefit profile for a product. For example, this process should contemplate interaction with the manufacturers’ of all devices potentially affected by the new information. There are instances in which new information may garner the need for manufacturers to generate additional data to more fully understand the new information. Conversely, there are also instances in which manufacturers may already possess the additional data necessary to understand the new information or when the new information can be understood or clarified by contextual factors. It is therefore critical that FDA provide manufacturers with an opportunity to review and analyze the new information and provide available context or further clarifying data. FDA’s proposed process for evaluating and responding to new information should also recognize that some new information may be inconclusive or controversial. In such instances, FDA should utilize the appropriate Panel or Advisory Committee to obtain recommendations on how to respond to the new information, particularly if the matter involves a product or issue that the Panel has previously considered. MDMA recommends that FDA provide a clearly drafted framework for responding to new information, either through promulgated regulations or guidance documents, that results in a measured, reasonable response that (i) weighs the validity and credibility of the new information, (ii) provides an opportunity for meaningful discussion with the affected manufacturer (or

⁷ See, e.g., 21 U.S.C. § 360c(a)(2)(C) (FDA must “weigh[] any probable benefit to health from the use of the device against any probable risk of injury or illness from such use.”).

manufacturers) regarding FDA's assessment of the new information, (iii) utilizes FDA's Panels and Advisory Committees, as necessary and (iv) results in a written standard for addressing the new information that is clearly articulated to all potential manufacturers.

Indeed, in the event new information signals a significant risk to patients that outweighs any corresponding benefit, then FDA should coordinate with the device manufacturer(s) to timely notify appropriate audiences, including the public, of the new information and the corresponding risks. Absent clear evidence, however, the new information should be considered but should not necessarily be the basis for additional requirements, conditions, or restrictions on individual or whole classes of products, regardless of where the product is in FDA's regulatory pathway. FDA should not apply new standards to any products until it has scrutinized and analyzed the new information through its delineated process and determined that new standards or actions are required. Moreover, FDA should establish an effective date for the imposition of any new standards established as a result of new information and explicitly provide that the standards will not be retroactively applied in instances where the risk profiles of products already marketed are not significantly affected. Once the new standards are established, FDA should ensure that they are consistently applied to all affected devices.

FDA routinely makes decisions and assessments regarding a product relying on less than ideal information. FDA has the ability to monitor, through post-marketing requirements, the ongoing risk-benefit profile of a product. In instances in which new information clearly and convincingly negatively affects the risk-benefit profile of a product which is undergoing premarket review, FDA should, through a clearly defined process, ensure that the sponsor's data addresses the new risks. However, responding to the new information need not require expensive, lengthy or disproportionate randomized, blinded controlled clinical trials. Instead, FDA should establish, through its paradigm for incorporating new information into the review process, that bench testing, additional post-market requirements, or other less rigorous testing may suffice, and, where they do suffice, are preferred. MDMA strongly believes, however, that unless the new information clearly and convincingly demonstrates that currently approved medical devices are exposing patients to significant risk of harm that is disproportionate to its benefit profile, FDA product approval or clearance should not be impacted. Therefore, in Case Study 1, Scenario A, if FDA concludes that the new MDR pattern provides clear and convincing evidence that Device Y may have a different risk-benefit profile than its predicate device, FDA should establish through, well articulated procedures, how Device Y's sponsor should address this safety risk information in their data. Moreover, if FDA believes that the new evidence clearly and convincingly demonstrates that the predicate device about which the MDRs relate has a new risk-benefit profile which affects FDA's approval or clearance determination, FDA currently has the ability to take necessary action.

FDA should provide written guidance to affected medical device manufacturers regarding new standards resulting from new scientific information. As FDA acknowledges in its background discussion, "CDRH has sometimes incorporated new science into our regulatory decision-making on an ad hoc, non-transparent basis. Such an approach can result in inconsistent regulatory expectations and less predictable decision-making." In light of this recognition, FDA should identify and implement a process that (i) provides affected manufacturers and interested parties with early access to new information, (ii) encourages informal and formal dialogue between the Agency and the manufacturer regarding

the significance of the new information and its effect on the medical device's risk-benefit profile, and (iii) provides written guidance on the resulting requirements or modifications to the regulatory pathway for the device based upon the new information and the resulting interaction between the Agency and interested parties.

MDMA is highly sensitive to the importance of protecting confidential information in the context of product development, review and approval and recognizes that the Agency will need to address competing interests in connection with the disclosure of certain information to support the creation of new standards and the protection of confidential information. Nevertheless, MDMA urges the FDA to avoid creating a system which would impose new and changing obligations on sponsors or manufacturers in instances where they do not have sufficient access to the information giving rise to the new requirements.

II. Adapting to Novel Technologies or Novel Uses of Existing Technologies

FDA has historically recognized that it makes decisions and operates with less than ideal information.⁸ Indeed, the Federal Food, Drug and Cosmetic Act permits FDA to withdraw its approval or clearance when FDA determines that the medical device, among other things, no longer satisfies the standards for premarket approval.⁹ MDMA reiterates FDA's concern from the Background Discussion to the meeting notice that "creating too many regulatory requirements raises costs and prevents products from reaching consumers." Such an outcome is clearly contrary to protecting the public health. Consequently, FDA should rely heavily on its already extensive post-marketing regulatory authority to require post-approval studies to confirm its premarket risk-benefit analysis. It would be detrimental to innovation and product development to require clinical trials that are disproportionate to the potential market for the medical device. FDA should ensure that its premarket review is reasonable in light of the product at issue, and that, when data warrants additional oversight, FDA has the ability to require and monitor post-approval studies.

Further, we would strongly caution FDA to avoid establishing any review standards for novel technologies or novel uses which result in the Agency trending away from its statutory and regulatory standards of assessing products based upon whether there is reasonable assurance of the device's safety and effectiveness and instead adopting review thresholds which essentially result in FDA self-determining and only approving the "best" or newest technologies. It is not FDA's role to restrict public availability of products to just those deemed "safest" or "best," which in many instances could also result only in the most expensive products being available. Older technologies often cost less than "new and improved" technologies, and efforts to restrict the use of "older" devices which continue to be safe and effective for their intended uses, will likely result in additional (and unnecessary) costs to the health care system. Furthermore, new technologies are often not available in sufficient quantities to serve an entire market for a particular device type, and any effort by FDA to only permit the "best" or "safest" technologies through efforts to restrict access to older technologies could result in some patients

⁸ See Hamburg, Margaret A. and Joshua M. Sharfstein, *The FDA as a Public Health Agency*, NEJM, Vol. 360:2493-2495 (June 11, 2009).

⁹ 21 U.S.C. § 360e(e)(1).

having no access to medically necessary devices. Such an outcome would be detrimental to public health and unnecessarily limit patient access to safe and effective products.

III. Enhancing CDRH's Technical Competence and Analytical Capability

MDMA encourages the FDA to continue to take proactive steps to encourage CDRH staff to interact routinely and regularly with industry representatives. Furthermore, MDMA strongly believes that industry and FDA will both benefit from ensuring that all CDRH staff receives routine and regular training on FDA statutory and regulatory policies and procedures as well as FDA's guidance, policies and procedures. Our members have experienced numerous instances of inconsistent application of FDA's authority and responsibility by different members of CDRH staff. Indeed, in light of the recent efforts to increase CDRH staff, we would encourage the Agency to implement additional training for all staff on technical and regulatory issues and concerns.

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MDMA appreciates FDA's continuing attention to ensuring that the Agency develops a predictable and flexible process for responding to new scientific information. Specifically, MDMA encourages the Agency to continue to create transparency in its processes for evaluating and assessing new information and to work with industry to determine how new information affects individual product's risk-benefit profiles. It is essential that, in the absence of clear and convincing new safety information which creates unsustainable risks for a product, FDA not attempt to retroactively apply new standards to previously cleared or approved medical devices.

Thank you for the opportunity to provide our comments. If we can provide additional assistance as FDA evaluates and formalizes its predictably adaptive approach to incorporating new scientific information into its regulatory decision-making processes, please do not hesitate to contact the undersigned.

Respectfully Submitted



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