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AdvaMed
Advanced Medical Technology Association

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

Re: Docket No. FDA-2009-N-0247, Comments on Transparency Report

To Whom It May Concern:

The Advanced Medical Technology Association ("AdvaMed") is pleased to submit the following comments on the FDA's Transparency Task Force's May 19, 2010, report "FDA Transparency Initiative: Draft Proposals For Public Comment Regarding Disclosure Policies Of The U.S. Food And Drug Administration" ("Task Force Draft Proposals").

AdvaMed member companies produce the medical devices, diagnostic products and health information systems that are transforming health care through earlier disease detection, less invasive procedures and more effective treatments. AdvaMed members range from the largest to the smallest medical technology innovators and companies.

AdvaMed believes that greater transparency in FDA operations is a desirable goal. We support a number of the draft proposals and include in these comments some recommendations for areas not addressed by FDA. At the same time, however, transparency must be balanced against other objectives, and AdvaMed believes that many of the draft proposals would have a negative impact on the public health, innovation, American competitiveness, and legitimate business interests without corresponding benefits. Furthermore, new regulation to promote transparency to the public can be resource intensive and create additional workload for the Agency. These resource implications should be seriously considered, particularly in cases where the information FDA is proposing to disclose is already in the public domain by other mechanisms. If the Task Force determines that there is public health value in disclosing additional information about FDA's core program activities, it would be counterproductive to weaken those very same core programs by diverting FDA resources to the disclosure process.

Our comments are divided into three sections:

- Premarket information (proposals relating to the release of information on products that have not received clearance or approval and are unavailable to patients outside an investigational context).
- Postmarket information;
- Other proposals (Docket Management).

I. PREMARKET INFORMATION

The Task Force Draft Proposals include a number of recommendations that would result in the release of important and sensitive commercial proprietary information and/or trade secrets prior to approval or clearance and marketing of a device or diagnostic. This information is exempt from disclosure under the Freedom of Information Act as trade secret or confidential information.

These draft proposals, while well-intentioned, would have a number of negative effects. They would undermine intellectual property rights. They would create competitive harm, disadvantaging originator companies, especially small companies, relative to competitors. They would benefit foreign competitors, providing them with heretofore unavailable intellectual property and commercially sensitive information. Most important, they would reduce the attractiveness of financially risky investments in novel, breakthrough products; ultimately harming the public health by limiting the development of new treatments and diagnostics.

By contrast, the public health benefits alleged from release of this information—primarily information on products that cannot legally be sold to patients—are minimal or nonexistent because patients have no access to these products outside of a highly controlled investigational context. Within the investigational context, an elaborate set of rules exists for ensuring investigators are fully informed about investigational devices, protecting patients, and informing them of the location of investigational sites and opportunities.

To appreciate the concerns about disclosure of premarket information that is protected from disclosure under the law as confidential or trade secrets, it is important to understand the market dynamics underlying device and diagnostic innovation. Patents provide less protection for devices and diagnostics than they do for drugs or biologics. This is because competitors can often "engineer around" patents once they understand the basic principles of the device. Accordingly, the opportunity for return on investment in device and diagnostic development is highly dependent on the period of market exclusivity that is gained by being the first to market with a new product. The more quickly competitors can market a competing product, the lower the return to the innovator.

The result is that any information potential competitors can gain about a device during the development stage can significantly reduce the value of the innovation. Information need not be elaborate technical specifications. Anything that helps identify the product an innovator company is developing can start another company down the same development path and reduce the value of the innovation. Congress recently reemphasized the importance of confidentiality in all premarket stages of device development. In the Food and Drug Administration Amendments Act of 2007 (FDAAA) Congress provided an exception for public disclosure of clinical trial information on "Clinicaltrials.gov" until after, and if, the device or diagnostic is cleared or approved for marketing.

Just this year, the Patient Protection and Affordable Care Act included provisions designed to bring transparency to the financial relationships between device makers and physicians. Congress specifically delayed from public disclosure payments to physicians related to device development. Public disclosure of these payments is required four years after the payments occur or after the product is approved or cleared for marketing, whichever comes first. This protection was provided even though the only information that would be revealed would be the name of the physician, the amount of the payment and the general purpose of the payment, *e.g.*, consulting. Even that information was understood to give potential competitors clues to product development that could undermine the product's ultimate value.

The disclosures included in the draft proposals include information from the earliest to the latest stages of product development with information provided ranging from the relatively general to the very specific. AdvaMed's comments on the specific proposals are discussed below.

8. FDA should disclose the existence and, when asked, confirm the existence or non-existence of investigational applications. For investigational applications, the disclosure should include the name of the application sponsor, the date the application was received, the proposed indication(s) or intended use(s) of the product, and the proposed proper and/or trade name of the product, if available.

Disclosure of an investigational application would be very damaging to companies, and to small innovative companies in particular, because it would alert potential competitors to key information about the device—its intended use and the indications for use. A competitor company, including foreign companies, could very well use this information to consider starting development of a product of its own or seek other sources of information about the device that would help give it a jump start on designing a competing product using the same basic idea.

Not only would disclosure of this information hurt companies from a competitive perspective, but it also makes device companies less attractive to venture capital firms, which generally will not invest in firms that have lost any competitive advantage. Today with the economy still suffering, losing any head start advantage will threaten investments in small device companies.

While the potential short-term damage to the interest of individual innovator companies and the long-term damage to the value of investment in developing new treatments and cures are clear, the public health benefits posited as a reason to initiate this draft proposal are weak. The FDA suggests that:

- The draft proposal would encourage patient enrollment in clinical trials that are underway or likely to be started, particularly those trials that may not be posted in ClinicalTrials.gov.

- Public availability of this information may reduce the potential for public confusion about the development of a particular product.

- Disclosing the fact that FDA has received an investigational application will not allow a competitor to copy the formulation of a product or reverse engineer the device.

We strongly disagree with these contentions. The disclosure will not result in the benefits FDA describes, and FDA fails to recognize or even acknowledge the fundamental need for protection of confidential information. The only clinical trials that are not currently posted in ClinicalTrials.gov are trials for devices and diagnostics, with delayed posting as provided in the law as described above. This delay not only largely coincided with FDA's regulations, but acknowledged the public health benefit of maintaining the confidentiality of device development and innovation. Moreover, abrogating this important protection would likely add little or no patient benefit, because patient enrollment in clinical trials is the responsibility of the innovator company, not the FDA, and if public availability of data on the trials is necessary to encourage enrollment, the innovator company can choose to make the data available on "Clinicaltrials.gov" or it can increase advertising outreach for subjects.

It seems likely that posting of minimal data on the existence of an IDE is more likely to increase rather than reduce public confusion about development and availability of a particular product, because in the absence of a public posting, the public is unlikely even to be aware that the product is under development. Moreover, the posting of this limited information would likely result in public inquiries requesting additional information, which FDA, by law, cannot provide, increasing rather than reducing public confusion. In any event, it is unclear how "reducing the potential for public confusion about the development of a particular product" would advance the public health.

Finally, while it is true that the proposed disclosure would not, by itself, allow a competitor to copy the design of a product or reverse engineer the device, this does not mean that the information would have no value to a competitor. As noted above, the proposed disclosure could start a competitor down the same development path earlier than would otherwise be the case and also might encourage the competitor to seek other information that would provide more details on the product under development. Indeed, FDA's current regulations provide that if the existence of an IDE has been publicly disclosed or acknowledged by the company,

the agency has discretion to "disclose a summary of selected portions of the safety and effectiveness data, that is, clinical, animal, or laboratory studies and tests of the device, for public consideration of a specific pending issue." 21 CFR § 812.38(b)(2). However, for companies that have not publicly disclosed or acknowledged their IDEs, these innovative companies would be competitively disadvantaged, punished for their efforts as first to file an investigational application and could lose their investment funding.

9. FDA should disclose: (1) whether an investigational new drug application (IND) has been placed on hold, terminated, or withdrawn, whether an investigational device exemption (IDE) has been terminated or withdrawn, or whether an investigational exemption for a new animal drug has been terminated and (2) if an IND has previously been placed on hold, whether and when the hold is lifted. A statement should be included that such actions may be taken for various reasons, only some of which relate to safety or effectiveness.

With respect to an IDE, the problem with disclosure of information on whether an IDE has been terminated or withdrawn or whether an existing hold has been lifted raises the same issues as disclosing the existence of an IDE. In many cases, the withdrawal or termination of an IDE does not signify that the company has ceased development work on the product; it may only indicate the need to do further development of a device, or a decision to examine device-related data or information before continuing a study, or an economic decision by the IDE sponsor.

FDA offers the following rationale for disclosure of the information:

- It is important to inform the public when a clinical hold has been imposed or when FDA has decided to terminate an exemption. That way, individuals that are interested in enrolling in the clinical trial or are already enrolled can take steps to limit exposure to unnecessary risks.

- Providing the status of clinical trials does not disclose information that could be used by competitors to 'free-ride' off the sponsor's innovative effort. In some cases, the existence of clinical trials is already public.

It is clear that participants in a trial have an interest in knowing that the trial has been stopped or terminated, especially if the termination is due to a safety issue. Persons not enrolled in the trial have no such interest because they have no access to the treatment in question and thus have no need to take steps to limit their exposure to any risks associated with the treatment.

Patients already enrolled in a clinical trial, however, are already protected through FDA's existing regulations. Specifically, under the IDE regulations, a sponsor must ensure "that any reviewing IRB and FDA are promptly informed of significant new information about an investigation." 21 CFR § 812.40. Indeed, a "sponsor who determines that an unanticipated

adverse device effect presents an unreasonable risk to subjects shall terminate all investigations or part of investigations presenting that risk as soon as possible." 21 CFR § 812.46(b)(2) (requiring termination within "5 working days after the sponsor makes this determination and not later than 15 working days after the sponsor first received notice of the effect"). Moreover, for significant risk devices, if the sponsor wishes to resume a terminated investigation, the sponsor must obtain IRB and FDA approval. 21 CFR § 812.46(c). For non-significant risk devices, the sponsor may not resume a terminated investigation without IRB approval, and if the investigation was terminated under (b)(2) because of an unreasonable risk to subjects, then the sponsor also must obtain FDA approval in addition to IRB approval. 21 CFR § 812.46(c).

If these regulations are insufficient to assure that trial participants are promptly notified of any safety risks to which they may have been exposed as a result of participating in the trial, further requirements for disclosure of information to trial participants should be considered, but there is no public health interest advanced by informing the public at large.

As discussed above, the Task Force's statement that disclosing clinical trial status could not "be used by competitors to 'free-ride' off of the sponsor's innovative effort" is not correct. Competitors clearly want to know as much information as possible about a competitive product's development so that they can use that information in their own product development efforts and decision-making. The draft proposal's handing over of such information, in fact, does give competitors a "free-ride" and will surely stifle innovation.

10. FDA should disclose the fact that an NDA, NADA, ANDA, ANADA, BLA, PMA, or 510(k) application or supplement was submitted (or resubmitted) to the agency at the time the application is received by FDA. The disclosure should include the name of the application sponsor, the date the application was received, the proposed indications or intended use of the product, and the proposed proper and/or trade name of the product, if available.

As in the case of the previous draft proposals, disclosure of this information gives potential competitors substantial information that may spur development of a competing product much sooner than would otherwise be the case.

FDA states two rationales for the proposal:

- Will provide helpful information to a patient "eagerly awaiting a treatment for a particular disease and [who] wants to know when that treatment may be available. Disclosing whether, and when, a marketing application has been submitted for a specific use will provide helpful information to these individuals, and ease some of the current frustration that stems from the FDA's restrictions on providing this type of information."

- The information may increase agency accountability, presumably by allowing patients to raise questions about agency failure to make a timely decision on a product.

The first rationale is flawed, because it provides patients with unhelpful information. The knowledge that a PMA or 510(k) application has been filed does not provide access to treatment or actionable information as to when treatment may be available. To the extent patients actually make decisions based on this information, it is likely to be counterproductive. Patients hoping for the approval of a new treatment may fail to take advantage of existing treatments in the hope that something better will soon be available. Given the uncertainties of the timing of FDA approval of any given product and the fact that the product may, in fact, not be approved at all, encouraging patients to delay treatment in hope of a new cure may be harmful to patients. Moreover, the information proposed to be provided is so limited that it would be difficult for an individual patient to have any real idea of the utility of the treatment for his or her individual case, even if the device were ultimately to be approved. Thus, knowing that an application is filed with the agency creates a speculative and abstract possibility of treatment and diagnoses with no tangible benefit to the public.

The rationale that disclosing this information may increase agency accountability by pressuring the agency to make timely decisions is not supported by current experience.[1] Moreover, the agency has decried recent situations in which it claims that decision-making on a particular product was driven by public pressure, not science. Information is already publicly available on overall agency performance. For example, as part of the negotiations for device user fees, FDA established performance goals for the agency to meet that relate to review times. *See, e.g.*, MDUFA 2007 Commitment letter, http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/UCM109102.pdf. Moreover, in the device context, the Office of Device Evaluation (ODE) already publishes FDA review times for marketing applications in its annual reports, which are accessible to the public. *See, e.g.*, ODE, Annual Performance Report Fiscal Year 2008 at 5 and 8 (showing average total FDA review days from filing to approval for all original and panel track PMAs, and average FDA time from receipt to final decision for 510(k)s). While the timeliness and comprehensiveness of data on FDA performance can and should be improved, it is highly unlikely, and data do not support, that this proposal will not achieve that objective.

11. FDA should disclose that an unapproved NDA, ANDA, NADA, ANADA, BLA, or PMA, or uncleared 510(k) has been withdrawn or, if FDA determines that the application was abandoned by the sponsor. If the drug, biological product, or device is associated with a significant safety concern, FDA should provide a brief description of

[1] Some companies choose to make this type of information publicly available. There is no evidence that this speeds FDA consideration of the products in question.

the product, the use for which approval was sought or obtained, and the identified safety concern.

FDA's draft proposal has two components:

- Disclosure that a product application has been withdrawn or abandoned by a sponsor;

- A more detailed description of the product and of the safety concerns associated with it, if the application was withdrawn or abandoned because of a safety concern.

It is important to understand that the fact that a sponsor has withdrawn or abandoned a product application does not mean the product has no value or that withdrawal is the end of the line for product development. The sponsor may decide that the FDA is unlikely to approve the product based on the evidence submitted and may wish to submit a new application after developing more data, or the sponsor may believe that the underlying product still has merit but needs more development work before FDA can approve it. As in the case of the FDA's draft proposals discussed above, knowledge of the withdrawal could assist competitors, especially if the more detailed information associated with a product withdrawn for safety concerns is provided.

The counterbalancing public health benefits cited in support of the draft proposal, by contrast, are not significant enough to justify the policy. The FDA rationale cited is:

- The European Medicines Agency discloses this information.

- The fact of withdrawal allows interested individuals and the investor community to provide funding or seek other opportunities for the product.

- If the public knows the request for approval or clearance has been submitted, disclosure that it has been withdrawn could be important to patients who may be awaiting new treatments for their disease.

- FDA makes available a detailed summary of safety and effectiveness information about a product that is the subject of a PMA withdrawn by the FDA. But if a sponsor withdraws or abandons the device for safety and effectiveness reasons, that information is not made public. Disclosure would allow researchers studying the device or a closely-related device to use that information to protect patients from identified and potential risks.

- If information concerns an off-label use of a marketed product, health care professionals and patients would have access to information that could influence decisions about whether to use the product for that off-label use.

With regard to the first justification, the European Medicines Agency (EMA) discloses when a marketing authorization application has been withdrawn and information about the EMA's evaluation of the product. However, the EMA only reviews drugs for human and veterinary use, *see* Regulation (EC) No 726/2004, and therefore EMA policy is inapplicable to the device industry. As noted above, early knowledge about products under development has substantially negative implications for the device industry.
With regard to the agency's second justification, the Task Force states that disclosure of this information would provide opportunities for investors to provide additional development funding or to pursue development of the product through an alternate route. Because the originator company has an interest in securing additional funding and retains intellectual property rights to the product in the event that someone else might try to pursue it, the originator company has ample motivation to make the data public if either of these options is more appealing than continuing development work with its own funds.

As discussed in our comments on draft proposal #10, it is not helpful to patients and may even be counterproductive to provide information on products that have not been approved.

The last two FDA justifications relate to providing more detailed information about a withdrawn or abandoned product when the product is withdrawn for safety or effectiveness reasons. The Task Force maintains that disclosing when and why an application is withdrawn or abandoned for a significant safety reason "should allow researchers studying the same molecule or device, or a closely related molecule or device, to use that information to protect patients from the identified and potential risks." Public disclosure, however, is unnecessary to achieve this objective. Device sponsors are required promptly to inform any reviewing IRB and FDA of significant new information about an investigation, and to provide investigators "with the information they need to conduct the investigation properly." 21 CFR § 812.40; *see also* 21 CFR § 812.150(b)(1) (Sponsors also are required to report to FDA, all reviewing IRBs, and all participating investigators the results of the sponsor's evaluation of an unanticipated adverse device effect within 10 working days of the sponsor first receiving notice of the effect). Thus, the agency will be aware of significant new information and can act accordingly, especially in regard to investigations of closely related devices. Therefore, under the current regulatory framework, researchers will be informed if there is an issue either with the same device or a closely related device being studied.

No investigation of an unapproved device involving significant risks to human subjects may be conducted without FDA approval. FDA takes account of any risks that may be relevant to a new product that have appeared in approved or withdrawn applications in determining whether or not to grant an IDE or what conditions to place on the IDE.

The Task Force's reference to FDA's safety and effectiveness summary for a withdrawn PMA is technically correct but not terribly relevant. Although FDA has authority under 21

U.S.C. § 360j(h)(1)(A) to issue a safety and effectiveness summary where the agency has withdrawn its PMA approval, the agency has rarely, if ever, used this authority.[2]

Finally, the draft proposal attempts to justify the release of information about a withdrawn submission for a new indication for a marketed device on the grounds that if the information concerns an off-label use, "health care professionals and patients would have access to information that could influence decisions about whether to use the products for that off-label use, if such use is not otherwise prohibited." Of course, this situation applies only to a likely insignificant subset of applications, and the FDA has other and more effective ways of addressing this situation than posting a notice of a voluntary withdrawal.

If a sponsor withdrew or abandoned a marketing application for a new use because of a safety concern regarding that use, the FDA could take several actions. For example, the FDA could issue a safety alert, public health notification, or "Dear Doctor" letter warning the public or health care providers about an off-label use, or require a labeling change warning of the hazards of such use. Additionally, FDA could discuss with the manufacturer the need for a field correction, which could take the form of revised labeling with strengthened contraindications, warnings, or precautions. Thus, the agency has ample resources at its disposal to ensure that any knowledge related to an off-label use is appropriately disseminated to physicians and patients.

13. FDA should disclose the fact that the Agency has issued a refuse-to-file or complete response letter in response to an original NDA, BLA, or an efficacy supplement for an NDA or BLA at the time the refuse-to-file or complete response letter is issued, and should, at the same time, disclose the refuse-to-file or complete response letter, which contains the reasons for issuing the letter.

As with Draft Proposal #15, which is discussed in more detail below, we believe that disclosing the existence of a refuse-to-file or complete response letter and the letter itself could cause significant competitive harm [3] Neither a refuse-to-file letter nor a complete response letter indicates the end of the product review, and a company still has a very strong interest in keeping its product development efforts confidential. Additional work will continue on a product in these circumstances, while competitors will have advance notice of areas to address or avoid, placing the initial submitter at a significant competitive disadvantage.

Indeed, FDA itself recognizes that, for example, when CBER issues a complete response letter after reviewing the file, it is because questions remain or additional data are needed prior to approval. The letters request additional information needed to complete the review of the BLA. Similarly, the agency's Web site explains that with respect to refuse-to-file

[2] A search of publicly available records fails to reveal a single summary of safety and effectiveness of a withdrawn PMA.

[3] The rationales for Draft Proposals #13, 14, and 15 are all the same, and we have the same objections for this Draft Proposal as are stated in our response to Draft Proposal #15.

(RTF) letters, "CBER's initial decision on whether or not to file a BLA or supplement will be based upon a threshold determination as to whether the information submitted to support licensure is sufficiently complete to permit a substantive and meaningful review" and "an RTF is not a final determination concerning potential approvability; it can be an early opportunity for the applicant to develop a complete application, but will delay, at least for a time, a full review of the application." Thus, clearly FDA itself expects that in both situations a company will do more work. Indeed, our comments in response to Draft Proposal #15 pertaining to AI letters and "not approvable" letters apply equally to refuse-to-file letters and complete response letters.

In sum, FDA's rationale for this disclosure is not supported by the facts, and disclosing this information would be detrimental to the public health. Release of important commercial information prior to approval would have a number of negative effects while the alleged public health benefits are minimal or nonexistent. While this specific proposal is not directly device related, as we discussed in response to item 15 below, the policy behind it is incorrect and will not advantage patients, physicians, or companies that develop treatments and diagnostics for patients.

15. FDA should disclose the fact that the agency has issued a "not approvable" letter in response to a PMA for a medical device and the fact that FDA has issued an "additional information (AI)" letter in response to a 510(k) submission, and should, at the same time, disclose the "not approvable" letter or "additional information (AI)" letter, which contains the reasons for issuing the letter.

It is important to keep in mind that neither a "not approvable" letter nor an AI letter is the end of the line for the product. In both cases, FDA is indicating deficiencies in the application that the sponsor may try to remedy by providing the requested data or information. In fact, as many as half of all 510(k)s receive an AI letter at some point before they are cleared. Alternatively, the sponsor may take the same basic product idea, modify the design, or conduct additional studies to address deficiencies revealed in the letter, and start a new application. The letters not only disclose the fact that the sponsor has been developing the product in question but also often include fairly detailed information on product specifications, trial design, and other information that could be of immense value to a competitor to further its own device at the expense of the initial submitter, thereby creating competitive harm to the initial submitter. The chilling effect on innovation and investment in breakthrough products that would result far outweighs the speculative gains associated with making such information public.

The public health arguments for the policy are articulated by FDA as follows:

- The information may be valuable to patients and health care providers who want to know whether, and when, a new treatment will become available.

- If approval is for an off-label use, it could affect the decision to use the product off-label.

- Investors may be provided with information that may allow for the most efficient use of limited research dollars.

- Disclosure of the letter enhances the credibility of the FDA's decisions by revealing the basis for the decision.

In fact, publication of a "not approvable" or AI letter provides no information about the likely availability of a device or the timing of its availability and any speculative information such letter does provide has little public health value. The argument seems to imply that patients are foregoing alternative treatments while waiting for approval of a new treatment, and availability of the "not approvable" or AI letter would help them decide whether to continue to wait. Since neither the "not approvable" letter nor the AI letter provides a clear indication on the ultimate likelihood of the product being approved or disapproved or the timing of approval or disapproval, it would be highly speculative for a patient or provider to base treatment decisions on such letters.

Supplemental applications to put a new use for a previously approved product on-label apply to a limited subset of applications. To the extent that a failed attempt to get a currently off-label indication on-label reveals significant problems of safety or efficacy with the off-label use, the proper choice for the FDA is to inform the public and medical profession immediately using the authorities discussed in our comments on Draft Proposal # 11—not to ask practitioners and patients to wade through a "not approvable" or AI letter that may or may not clearly identify the issue nor represent the FDA's final decision on the issue. As noted earlier, FDA can issue a safety alert, public health notification, or "Dear Doctor" letter warning the public or health care providers about an off-label use, or require a labeling change warning of the hazards of such use. Additionally, FDA could discuss with the manufacturer the need for a field correction, which could take the form of revised labeling with strengthened contraindications, warnings, or precautions. Thus, the agency has ample resources at its disposal to ensure that any knowledge related to an off-label use is appropriately disseminated to physicians and patients.

The argument about investors being able to use limited research dollars more efficiently is unconvincing. Manufacturers who provide most of the research investment oppose the draft proposal because it is likely to result in less innovation, therefore, it is hard to see on what basis FDA would make an alternative judgment. Investors who fund companies must conduct due diligence on these companies, including reviewing the regulatory files that would contain correspondence between the companies and the agency. Thus, for all intents and purposes, this information is already available to investors who commit to keep the information confidential, and not made public to the potential detriment of the persons seeking funding.

Finally, the draft proposal is justified by the argument that disclosing a "not approvable" letter or AI letter "enhances the credibility of FDA's decisions by revealing the basis for the agency's decisions not to permit the marketing of a product and furthers the goal of more transparent and open government called for by the Administration." The credibility of the agency rests on its track record for approving safe and effective products, not on revealing the basis of its decision not to approve the marketing of a particular product and certainly not on its release of an AI letter which is simply one step in the process of final decision-making. While transparency in government operations is desirable as a matter of general principle, it does not mean it is desirable in every circumstance. In this case, it would appear to serve no useful public purpose while creating a significant negative impact on a key public health goal, namely, the creation of safe and effective treatments and cures.

16. FDA should disclose relevant summary safety and effectiveness information from an investigational application, or from a pending marketing application, if the agency concludes that disclosure is in the interest of the public health, which includes when FDA believes it is necessary to correct misleading information about the product that is the subject of the application.

The problems with disclosure of the premarket information—particularly of the relatively detailed type of information described here—have already been extensively discussed. The benefits the Task Force suggests are:

- The advancement of science;
- Protection of patients who may use products;
- Efficient use of limited resources available for research; and
- Selective publication of clinical trial results which has, in the past created a misleading impression of the safety and effectiveness of the product with negative implications for public health. This is particularly pronounced when the product is used off-label.

The Task Force does not elaborate how disclosure of this information would advance science. As discussed extensively above, the chilling effect on innovation and investment in breakthrough products that would result far outweighs the speculative gains associated with making information that will become public when the product is approved available prematurely.

Except in the case of approved products for which a new, currently off-label use is being sought, this information has no value for protection of patients who may use the product, because the product is not available to patients outside the investigational context.

The argument about efficient use of resources available for research has been discussed extensively above. Potential investors already have ample information available, and speeding research on competing products creates a competitive harm to the originator company and is not a legitimate policy objective.

The last issue, that selective publication of clinical trial results has created a misleading impression of the safety and effectiveness of a product, is only relevant in the context of a current or potential off-label use—not for a product only available within an investigational context. As noted previously, FDA has ample authorities available to deal with this potential problem.

Currently, FDA cannot even disclose the existence of an IDE unless its existence has previously been publicly disclosed or acknowledged by the device sponsor. 21 CFR § 812.38(a). Where its existence has been publicly disclosed or acknowledged, "FDA may, in its discretion, disclose a summary of selected portions of the safety and effectiveness data, that is, clinical, animal, or laboratory studies and tests of the device, for public consideration of a specific pending issue." 21 CFR § 812.38(b)(2). Importantly, this summary "may not contain trade secret of confidential commercial information, including confidential safety and effectiveness data." 45 Fed. Reg. 3732, 3746 cmt. 90 (Jan. 18, 1980). But where the IDE has not been publicly disclosed or acknowledged, "no data or information in the file are available for public disclosure." 21 CFR § 812.38(b)(3) (noting exceptions for banned devices and a report of an adverse effect to the study subject who experienced such effect).

For a pending marketing application, again it is the agency's role to determine the safety and effectiveness of a product. If at the end of the review, FDA determines a device submission does not meet its regulatory burden, then the agency can issue a Not Substantially Equivalent order or not approve a PMA. Importantly, FDA's regulations specifically state that, "If the existence of a PMA file has not been publicly disclosed or acknowledged, data or information in the PMA file are not available for public disclosure." 21 CFR § 814.9(c); *see also* 51 Fed. Reg. 26342, 26345 cmt. 13 (noting disclosure of the existence of a PMA that had not been publicly disclosed or acknowledged "would have limited benefit to the general public at such time and could adversely affect the commercial interests of the applicant.")

17. FDA should convene a group of internal and external stakeholders to discuss the possible uses of non-summary safety and effectiveness data from product applications, the circumstances under which it would be appropriate for sponsors to disclose non-summary safety and effectiveness data from applications submitted to FDA, and if appropriate, the format and the method by which disclosure should occur.

AdvaMed strongly disagrees that any proposal to disclose non-summary safety and effectiveness data from product applications should be subject to further discussion. The Task Force has not identified a problem that should be addressed, and for FDA to disclose this information without authorization from the sponsor would reverse long-standing policies to prevent competitive harm that have withstood the test of time.

Indeed, this information is routinely found to be confidential commercial information, which is barred from disclosure under 5 U.S.C. § 552(b)(4). *See, e.g.*, The Department of Justice Guide to the Freedom of Information Act (2009 Edition) at 324-326 (explaining "Numerous types of competitive injury have been identified by the courts as properly cognizable under the competitive harm prong, including the harms generally caused by disclosure of:...(8) raw research data used to support a pharmaceutical drug's safety and effectiveness...").

The Task Force has provided neither an evidentiary nor a logical basis to justify discussions of considering this change in policy and this proposal does not warrant implementation, particularly given all the other more pressing demands on the agency's resources.

II. POSTMARKET INFORMATION

To the extent the draft proposals seek to strengthen compliance with the FD&C Act, we fully support them. For example, if FDA posts the summary of the most common inspection observations, its current Agency Workplans, and recently filed court cases, we believe this information will educate individuals and firms and enhance compliance with the law. In contrast, some of the draft proposals may cause confusion and mislead the public as well as foreign regulators; it is critical that FDA fully assess and avoid any unintended consequences of disclosure. For example, any publication of the termination of recalls must be timely. Additionally, summarizing adverse event information without providing the proper context for those adverse events may very well lead patients and health care professionals to reach incorrect conclusions resulting in negative, and not positive, public health outcomes. We caution FDA to be cognizant of these outcomes as the agency evaluates these draft proposals.

1. FDA should expand the areas in which it provides the public with online access to public information from adverse event reports about FDA-regulated products submitted to FDA, in a format that is searchable and allows users to generate summary reports of this information, including, if known and as applicable, the trade name and/or established name of the product, dosage, route of administration, description of the adverse event, and the health outcome. Adverse event report information should continue to be disclosed with a clear disclaimer about the limits of the information.

Medical Device Report (MDR) information, by its nature, is anecdotal with inherent limitations. Indeed, the Task Force has acknowledged these limitations: (1)"there is no certainty that the reported event was actually caused by the product;" (2) "reports do not always contain enough detail to fully evaluate an event;" (3) "there is no way of knowing the actual number of adverse events that may be associated with a product because of under-reporting;" and (4) "FDA also does not know the actual number of people or animals that have been exposed to a product because sales data and other available proprietary product distribution information, the best estimates available to FDA, do not necessarily equate to product use."

Despite these limitations, FDA currently posts MDR information on its web site. The information is searchable and useful, allowing users to search by problem, device class, brand name, manufacturer, event type, 510(k) or PMA number, and event date range. Because of the inherent limitations with MDR information, FDA posts a disclaimer on the MAUDE search page: "MAUDE data is not intended to be used either to evaluate rates of adverse events or to compare adverse event occurrence rates across devices." Therefore, we do not believe it is necessary to expand this area for public access.

Furthermore, FDA has recently added the Total Product Life Cycle (TPLC) report to its web site which generates a comprehensive summary report for each device product code. The TPLC report displays for a chosen product code all premarket reviews listed by manufacturer and decision; device problems; and recalls listed by class, year, and manufacturer. Through a link away from the TPLC web site, FDA warns users that: "Adverse events from the MAUDE database cannot be used to determine the *rate* of adverse events for a particular product or to compare adverse event rates between products. Manufacturers submit reports according to their regulatory requirements. Submission of the report does not mean the device caused the adverse event. In most cases, further investigation is necessary to understand the cause of the adverse event."

AdvaMed does not object to improving the accessibility to existing public information and summary reports on adverse events. It is important, however that FDA improve disclaimer information and accessibility to these disclaimers. Improved disclaimer information will reduce the probability of consumers and health care professionals reaching inaccurate conclusions regarding medical device performance. Disclaimer information should be prominently displayed on each search and summary page, i.e., the user should not have to actively select a separate screen to view disclaimer information.

The current FDA disclaimers for the MAUDE database and the TPLC summary report are not adequate to inform the public that summary data may be misleading. The disclaimer should disclose that MAUDE and TPLC information is inadequate to enable and support a conclusion regarding safety or effectiveness of a device. Most importantly, the disclaimer should warn consumers not make health care decisions on initiating or discontinuing the use of medical devices based on adverse event reports without consultation with their health care provider.

3. In the weekly FDA publication, FDA Enforcement Report, FDA should disclose when the U.S. Department of Justice files a case seeking enforcement action on FDA's behalf in a court of law and the final determination of that case, if known.

AdvaMed supports the disclosure of this information in the FDA Enforcement Report with the caveat that this should not be posted until the person or company that is the subject of the enforcement action receives notice of the action.

4. FDA should post on its Web site all Agency Workplans (i.e., the annual Office of Regulatory Affairs Annual Field Workplan) that are older than five years, starting with the FY 2001 Workplan.

AdvaMed agrees that Agency Workplans should be posted on FDA's Web site, but disagrees that only Workplans older than five years should be posted. Workplans older than five years may reflect the policies of prior administrations and be so outdated that they offer limited to no value. Instead, current Workplans and those for the prior two fiscal years would demonstrate to the public the agency's approach to protecting the safety of FDA-regulated products.

The agency concern that posting more contemporaneous information will allow persons to predict agency enforcement priorities and thereby circumvent the law is highly speculative and ignores the deterrent effect that disclosure of this information will likely have. In contrast, only disclosing past information, under this thinking, would disclose information that is near useless because it would have no current applicability. Importantly, FDA has the authority to inspect any facility where FDA-regulated products are processed and the disclosure of its Workplans in no way limits this authority or its ability to enforce the law. Moreover, the Task Force recognizes that agency priorities and plans may shift in response to public health concerns, and thus what is outlined in the Workplans may be revised and parties cannot assume that the Workplans are cast in stone. The agency often inspects facilities based on adverse event reports, recalls, or competitors' complaints and one can never predict when one of these events will occur and trigger agency interest. Thus, regulated industry has no guarantee, nor should it have, that FDA will or will not conduct an inspection at any given time, and the disclosure of Agency Workplans will in no way change this circumstance. In other words, providing current information that may increase compliance should not be undermined by a concern that has no effect on FDA's day to day inspection and enforcement capabilities.

Finally, to a certain extent FDA already discloses its enforcement priorities through the publication of Warning Letters, letters generated to industry as a whole, public remarks by FDA officials, and court filings (see Draft Proposal #3). For example, in a 2009 public presentation, the Director of FDA's Office of Regional Operations described how FDA was increasing its overseas inspections of facilities regulated by the agency for fiscal year 2010. *See* The Pink Sheet, "FDA Ratchets Up Overseas Inspections For FY 2010 – 924 for Drug Activities" (Nov. 2, 2009). Thus to assert that disclosing Workplans may allow parties to circumvent the law fails to consider the many ways in which FDA already identifies its enforcement priorities, the purpose of which is deterrence. Disclosing recent Workplans is positive, because it provides a comprehensive statement of important compliance areas for industry focus.

5. FDA should disclose the outcome of the filer evaluation for importers or third parties working on behalf of importers.

The Task Force's rationale for this draft proposal is:

- To provide filers an incentive to provide accurate information about imported products.

- To arm importers with information that will allow them to select filers that have a track record of providing accurate information

AdvaMed has no objection to the proposal as stated, however we look forward to further detail as to the implementation of this proposal.

6. FDA should disclose the name and address of the entity inspected, the date(s) of inspection, type(s) of FDA-regulated product involved, and the final inspectional classification—Official Action Indicated (OAI), Voluntary Action Indicated (VAI), or No Action Indicated (NAI)—for inspections conducted of clinical trial investigators, Institutional Review Boards (IRB), and facilities that manufacture, process, pack, or hold an FDA-regulated product that is currently marketed. The disclosure of this information should be timed so as not to interfere with planned enforcement actions.

There may be some circumstances where disclosure of the address of a facility and the type of FDA-regulated product at that facility could raise national security issues. For example, if a facility played a significant role in the blood supply or offered a product that is used by soldiers at war, disclosing the address and type of FDA-regulated product could compromise national security. Therefore, AdvaMed urges FDA to work with the United States Department of Homeland Security to identify locations of potentially sensitive use products and to take security issues into consideration in disclosing any information.

We oppose making this inspectional information publicly available because foreign regulators could misinterpret the information. For example, a foreign regulator could inappropriately exclude products manufactured at those facilities from the market or could take targeted actions against the company based on the inspectional information.

Additionally, the disclosure of this information is more relevant to persons or firms that have received Warning Letters. Where inspections result in no objectionable conditions or any objectionable conditions found do not meet the threshold of regulatory significance, there is little value in disclosing the proposed information. Thus, this draft proposal should be limited to Warning Letter recipients only.

7. FDA should generate, and share with the public, information about the most common inspectional observations of objectionable conditions or practices that are made during inspections of FDA-regulated establishments and post that information online on a regular basis.

Posting summary information about the most common inspectional observations based on Quality System Regulation (QSR) categories is beneficial, as long as company names and

addresses are not used. Importantly, the information must be in summary form and in a useful format to assess the strengths and weaknesses of industry's overall Good Manufacturing Practices (GMP) performance. Also, FDA should identify the number of inspections by jurisdiction, *e.g.*, device, drug, etc.

18. When a system is set up that provides FDA with authority to require companies to submit certain information to the Agency when they initiate an action to recover or correct a product that is in the chain of distribution, FDA should disclose this information as soon as practicable after receiving this information from the firm.

The Task Force states that its draft proposal depends upon receiving authority to require firms conducting voluntary recalls to provide FDA with information about the identity of the product, the estimated number of products subject to recovery or correction, the reason for the action to recover or correct the product, and the geographic distribution of the product. However, 21 CFR Part 806, Reports of Corrections and Removals, already requires device manufacturers to report this information to FDA when a correction or removal is initiated to (1) reduce a risk to health posed by the device; or (2) to remedy a violation of the FD&C Act caused by the device which may present a risk to health. 21 CFR § 806.10(a). Such reports must be submitted within 10 working days of initiating such correction or removal. Thus, any action related to devices with an impact on the public health is already required to be reported to FDA.

FDA stated the following rationales favoring disclosure of this information:

- Disclosure will "ensure that useful, actionable information is provided to the public about a problem with an FDA-regulated product so that consumers can make informed decisions in response to a recall announcement."
- "With ready access to key information about a recalled product, health care providers can better evaluate a patient's condition and provide appropriate care."

Currently, all recalls are identified in FDA's weekly published Enforcement Report. Regarding additional disclosure to the public, we recommend press releases, but only for Class 1 recalls that involve situations where "there is a reasonable probability that the use of, or exposure to, a violative product will cause serious adverse health consequences or death." 21 CFR 7.3(m)(1).[4]

To post additional information–especially for Class 2 and 3 recalls that are numerous and where the possibility of harm is remote–would be more likely to saturate the public and make

[4] In contrast, a class 2 recall is defined as a situation "in which use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote." Class 3 recalls are defined as "a situation in which use of, or exposure to, a violative product is not likely to cause adverse health consequences." 21 CFR 7.3(m).

the public less responsive to recalls, in particular those that present potential serious health harms, *i.e.*, those in Class 1. In sum, we believe the best public health strategy is to use extra disclosure methods for those recalls that merit that treatment, *i.e.*, Class 1 or § 518(e) mandatory recalls.

20. If FDA determines that a recall is terminated, that information should be disclosed to the public. A recall is considered terminated when FDA determines that all reasonable efforts have been made to remove or correct the product in accordance with the recall strategy and when it is reasonable to assume that the recalled product has been recovered, corrected, reconditioned, or destroyed.

If a termination notice to a company is timely, AdvaMed supports publicly disclosing recall terminations. However, if the recall is completed and any potential danger abated, a delayed notice of termination could do more harm than good. A late notice of termination benefits no one. It lengthens the time a company appears to be subject to a recall, and could confuse users about the status of their devices. If the termination notice issues within a reasonable time (e.g. 60 days) from when the recalling company has notified FDA that the recall is completed, and includes the date that the company completed the recall, we would endorse issuance of such public notices.

21. FDA should post untitled letters on the FDA Web site, and, if requested by the recipient of the letter, the response to the untitled letter, as appropriate.

AdvaMed opposes this Draft Proposal. Untitled letters are particularly useful in situations where a company's practices and conduct are not clearly illegal, *e.g.*, where the line between what is acceptable and what is violative is unclear, such as is often the case with advertising claims. In addition, as the Task Force acknowledges in its Draft Proposal, "not all of the information provided in untitled letters reflects problems with FDA-regulated products that may pose a direct risk to the public health."

The FDA stated rationales for posting untitled letters are that:

- Information in untitled letters reflects problematic practices and potential public health risk associated with products.
- The public has an interest in learning about firms and individuals that violate the FD&C Act because that information may inform decisions about whether, or from whom, to purchase a product.
- Similarly situated companies may use the information to determine what activities and practices FDA finds violative and modify their own behavior.

The first and third goals could be satisfied without causing harm to companies by deleting all company identifying information from the posted letter. However, the second goal causes us to recommend against publishing such letters.

Untitled letters have been used successfully for years to obtain voluntary action from industry when it is unclear that a practice is violative or presents a health concern. Publication under these circumstances would appear to be punitive. Currently, the difference between FDA disclosing a Warning Letter and not disclosing an untitled letter is intentional and should not be removed. Indeed, disclosing untitled letters would effectively elevate them to the status of warning letters, impugn a company's products or practices where no violations or no public health issues may exist. Moreover, stating that publishing such letters to identify law violators is unreasonable. At most, the allegations in FDA letters are exactly that and no more. They are not judicial or administrative law determinations of violations following the exercise of due process. Untitled letters can be, and are, enormously useful and can avoid potential violative conduct and engender cooperation. We, therefore, strongly recommend against the publishing of such letters.

III DOCKET MANAGEMENT PROCESS

2. FDA should change its current practice so that comments submitted at www.regulations.gov from people self-identified as individual consumers are posted on that Web site in the same manner as other comments. In the Federal Register notice soliciting public comment, FDA should adequately inform commenters about the public disclosure of their comments on www.regulations.gov.

AdvaMed agrees with this proposal. Publication of consumer comments will allow the public to learn about the viewpoints of individual members of the public, not only trade associations or academic institutions, for example. With respect to posting comments online, comments from individual consumers should be treated in the same manner as comments submitted by others. FDA should adequately inform the public of the ways they can submit comments to the docket. The public should be adequately informed that comments submitted to www.regulations.gov are subject to disclosure online.

Sincerely,

Janet Trunzo
Executive Vice President
Technology and Regulatory Affairs