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Docket No. : FDA-2015-D-4803

Leslie Kux, Assistant Commissioner for Policy
Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

MITA Comments, Re: Public Notification of Emerging Postmarket Medical Device Signals ("Emerging Signals"): Draft Guidance for Industry and Food and Drug Administration Staff

Dear Ms. Kux:

As the premier trade association representing the manufacturers of medical imaging equipment and radiopharmaceuticals, the Medical Imaging & Technology Alliance (MITA) is responding to the public docket on the draft guidance on Public Notification of Emerging Postmarket Medical Device Signals ("Emerging Signals").

General Comments

MITA and its members believe that Public Notification of Emerging Signals draft guidance as written would have significant unintended and undesirable consequences for all stakeholders. MITA urges the Agency to consider withdrawing this draft guidance. If, however, the Agency decides to move forward with guidance, MITA maintains that this version raises several significant concerns that must be addressed before the guidance is finalized. Most importantly, we believe that the need for public notification of emerging signals needs to be carefully weighed against the potential for patient confusion, undue alarm of the public, and the impact of such notifications on manufacturers of medical devices. We also believe that the addition of clearer criteria one or more flow charts could be helpful in further understanding the process by which the Agency intends to determine whether the public notification of an emerging signal is needed. These concerns are detailed below.

Patient and Medical Community Confusion and Undue Alarm

While there are merits to FDA intent to promptly inform the public of higher risk and safety issues, doing so without sufficiently clear evidence of the risk or safety issue could potentially result in misleading information to the public. On lines 93-96 of the draft guidance, FDA states

"a communication regarding an emerging signal may lack certainty about the significance of the information, including whether it represents a new, potentially causal association, or a new aspect of a known association (e.g., increased rate or severity of event), between a medical device and one or more adverse events or outcomes." This lack of certainty and the inability to identify the significance of information shared through this mechanism will only contribute to confusion and may lead to misinformed treatment decisions. This may also create a heightened level of public concern that may be unwarranted and which could lead patient and clinicians to unnecessarily avoid or stop using the device in question. This could lead to reduction in the use of safe and effective medical devices and could have a negative impact on patient care, significant financial ramifications for manufacturers as well as negatively impact a manufacturer's reputation.

Furthermore, if the information is not fully validated and the Agency is not providing any recommendations, it is unclear what benefit patients and the medical community will receive from prematurely hearing of perceived signals.

Validation and Verification of Data

In the draft guidance, the Agency does not provide details on how information about emerging signals will be gathered. In fact, the draft guidance indicates that the FDA would make decisions based upon "all available information" but does not define or identify the sources of that information, the kind of information it deems informative or the analytical process by which a decision is made. The draft guidance does not outline how the FDA intends to filter the source of emerging signal information for false or exaggerated claims against companies or how such sources could be used for competitive motives.

On lines 130 and 195, the draft guidance suggests that the FDA will consider the reliability of the data underlying the emerging signal. The agency does not define what is considered "reliable data" or what criteria the Agency will use to ensure that the data is reliable. FDA must define reliable data and the criteria that the Agency will use to determine reliability of data. MITA believes that it is crucial for the FDA to consider the validity of the data being used and define minimum verification requirements before issuing public notification of an emerging signal. It is also important that the FDA process for reaching the conclusion that public notice of an emerging signal is necessary be transparent to affected manufacturers.

Finally, in Section III, the FDA lays out factors for evaluating and communicating about medical device emerging signals. However, many of these factors are poorly defined. For example, on lines 192-194, the Agency indicates that they will consider if "the information represents a new, potentially causal association, or a new aspect of a known association (e.g., **increased rate or severity of event or reduced benefit),** between a medical device and **one or more adverse events or clinical outcomes".** MITA strongly requests that the FDA provide additional information regarding how the Agency defines the "increased rate or severity" and whether one

adverse event is sufficient to spur an emerging signal notice as is inferred from the language quoted above.

Lack of Manufacturer Input

As mentioned earlier, MITA is concerned that the draft guidance does not outline how the manufacturer would be involved in coordinating any public safety effort with the Agency when there is reason to believe there is an emerging signal. MITA objects to the lack of manufacturer input included in the draft guidance. It is important that the Agency engage manufacturers while the available information is being reviewed to determine if public notification of an emerging signal is required. Such consultation would ensure that manufacturers are afforded due process as well as ensure that the Agency is, in fact, relying on all potential sources on information. In addition, the manufacturer is uniquely qualified to discuss with the FDA whether the data collected is sufficient to spur a public notification, what other data may be available and identify any actions that may be prudent to address the concerns.

Lack of complete timeframes

In lines 202-204, requirements are included for reassessment if the FDA does not issue an emerging signal and receives additional information. In these cases, the Agency is required to reassess the communication within 30 days. However, there is no timeframe to reassess an emerging signal if it has been issued and additional information is received that indicates that the signal poses no additional risk. Additionally, Section IV recommends that the Agency update the communications on the website at least twice per year. Twice per year does not seem to be sufficient when all other timeframes in the draft guidance are 30 days. MITA members are concerned about the lack of clear timeframes of how the Agency will communicate when additional information is available. MITA believes that it is important that the FDA provide timely information when an emerging signal is considered "cleared".

<u>Open Questions</u>

There are many open process related questions upon review of this guidance.

- The draft guidance does not seem to consider that there will be situations where public notification of an emerging signal is released and the emerging signal is later found to have no public health impact.
    - What happens if FDAs perceived signal cannot be confirmed or is false?
- What is expected of manufacturers whose products leads to or is a subject of an emerging signal notice?
    - How specifically will the FDA address such situations?
- There is no clear indication of how FDA would determine when an issue is considered an emerging signal or clear delineation of FDA's criteria for deciding to take action.
    - What would be the basis for the decision?
    - How will the FDA manage the communication?

    - Will the decisions be based on classes of devices? Types of devices? Or specific to a manufacturers product line?
- What recourse do the manufacturers have in such situations? In line 181-186, the FDA admits that the communication on emerging signals is not intended to infer causal relationships or recommendations to stop using the device.
    - How does the FDA intend to communicate these nuanced thoughts?
    - MITA recommends that the Agency add specific language to the template on Page 8 to address this issue.
- There are several systems in place which already address the postmarket and it is unclear what emerging signals will provide versus these current systems. What will emerging signals provide that FDA feels the current postmarket systems do not provide?

Line(s)	Text	Comments/Proposals
59-64	For the purposes of this guidance, an emerging signal is new information about a medical device used in clinical practice 1) that the Agency is monitoring or analyzing, 2) that has the potential to impact patient management decisions and/or alter the known benefit-risk profile of the device, 3) that has not yet been fully validated or confirmed, and 4) for which the Agency does not yet have specific recommendations.	This text is unclear and more information is needed specifically regarding the Agency's process for determining what is considered a signal, and more importantly why communicating this information prematurely (i.e. *that has not yet been fully validated or confirmed, and for which the Agency does not yet have specific recommendations*) is beneficial to the public.
98-105	Timely communication about emerging signals is intended to provide health care providers, patients, and consumers with access to the most current information concerning the potential benefits and risks of marketed medical devices so that they can make informed treatment choices based on all available information. Such communication may also reduce or limit the number of patients exposed to the potential risk while the issue is being further evaluated. In addition, communicating emerging signals may also promote enhanced vigilance on the part of clinicians, risk managers, patients and consumers, who may respond by increasing their reporting	Current regulations require manufacturers of medical devices to continually evaluate risks associated with their devices as they emerge through post-market monitoring activities and initiate corrective actions. These actions are communicated to healthcare providers and patients and in many cases the FDA. This information is also posted on the FDA website and is publically available. Inaccurate, or incomplete information from the FDA and a lack of clear guidance or recommendations on how to react to the information being shared, will cause confusion and may lead to misinformed treatment decisions.

	to FDA. This may in turn assist the Agency in further understanding the emerging signal.	
113-120	All medical devices have benefits and risks. Health care providers, patients, and consumers must weigh these benefits and risks when making health care decisions. FDA weighs probable benefit to health from the use of the device against any probable risk of injury or illness from such use in determining the safety and effectiveness of a device. However, not all information regarding benefits and risks for a given device may be fully known or characterized prior to the device reaching the market. New information about the safety and/or effectiveness of the device often becomes available once the device is more widely distributed and used under real-world conditions of actual clinical practice	Current regulations require manufacturers of medical devices to continually evaluate risks associated with their devices as they emerge through post-market monitoring activities and initiate corrective actions. These actions are communicated to healthcare providers and patients and in many cases the FDA. This information is also posted on the FDA website and is publically available.
134-137	Emerging signals may include, but are not limited to, a newly recognized type of adverse event associated with a medical device, an increase in the severity or frequency of reporting of a known event, new product-product interactions, device malfunctions or patient injuries potentially related to improper device use or design, or a reduction in benefit to the patient.	In regards to "a newly recognized type of adverse event," such information should already be communicated and available to the public via Maude Database, MDRs. Manufacturers are also required by regulation to initiate corrective actions to protect the public from reported adverse events and any new risks that are identified through post market surveillance. As stated above, MITA requests that FDA provide a further explanation of the term "newly recognized type of adverse event".
142-149	The gathering and interpretation of the additional data needed to fully characterize an emerging signal can be complex, and it may take weeks or months to conduct the analyses to understand the implications of the signal for device performance and for its clinical significance. In addition, in certain circumstances, the FDA may collaborate with other federal and state public health agencies, or elect	As stated in the guidance, interpretation of data and characterization of emerging signal can be complex. Therefore, industry urges the FDA to involve the manufacturer when it is determined that there is an emerging signal. This would prevent the need to prematurely communicate to the public, allow for a thorough analysis of the issue and identify corrective actions if necessary. Further, this will reduce the time and

	to seek recommendations from one of its Advisory Committees to assist in evaluating available information pertaining to a signal. These factors contribute to variability in the amount of time needed to sufficiently evaluate an emerging signal and to determine whether public communication of specific recommendations and/or regulatory action are warranted.	effort expended by the Agency.
155-156	Seriousness of the adverse event(s) (e.g., severity and reversibility) relative to the known benefits of the device;	As stated above, information regarding adverse events should already be communicated and available to the public via Maude Database, i.e. MDRs. Manufacturers are also required by regulation to initiate corrective actions to protect the public from reported adverse events and any new risks that are identified through post market surveillance. MITA requests that FDA provide a further explanation of the term "newly recognized type of adverse event".
166	Potential for preventing, identifying, monitoring or mitigating the risk	Industry urges the FDA to involve the manufacturer when it is determined that there is an emerging signal. This would prevent the need to prematurely communicate to the public, allow for a thorough analysis of the issue and identify corrective actions if necessary.
172	Accuracy and availability of information already in the public domain.	Accuracy of information is difficult to assess if not all necessary information is available. This is especially true as some information in the public domain does not include input from the manufacturer. Industry urges the FDA to involve the manufacturer when it is determined that there is an emerging signal. This would prevent the need to prematurely communicate to the public, allow for a thorough analysis of the issue and identify corrective actions if necessary.
181-186	The decision to provide public information about a medical device emerging signal is intended to give health care providers, patients and consumers access to *the most current information* about an emerging signal. It does not mean that FDA has	As stated above, inaccurate, or incomplete information from the FDA and a lack of clear guidance or recommendations on how to react to the information being shared, will cause confusion and this may lead to misinformed treatment decisions.

	concluded that there is a causal relationship between the medical device and the emerging signal. Nor does communicating about the emerging signal mean that FDA is advising health care providers, patients, or consumers to limit their use of the device.	It is also difficult to imagine that the information is "*the most current information"* if the information is incomplete and hasn't been properly analyzed.
195-197	2. the available information is reliable and supported by sufficient strength of evidence; and 3. the information could have important clinical implications for patient management decisions and/or could it significantly alter the known benefit-risk profile of the device.	Please consider that conflicts of interest might affect the information which is provided to FDA in regards to the benefit-risk profile of a beneficial device or a device based beneficial therapy/intervention (e.g. cost pressure of healthcare institutions and health insurance providers). The source of information which has been used as evidence should be made publicly available for each case to allow clarification if applicable.
199-200	FDA staff should conduct an initial assessment of the need to communicate about an emerging signal within 30 days of receiving the information.	Industry urges the FDA to involve the manufacturer when it is determined that there is an emerging signal. This would prevent the need to prematurely communicate to the public, allow for a thorough analysis of the issue and identify corrective actions if necessary.
225-229	Updates to the communication should be posted to the FDA website at least twice per year, or more often as necessary and appropriate, until either the Agency issues a more formal "Safety Communication" containing specific recommendations for patients, health care providers, and/or health care facilities, or until the signal evaluation is otherwise completed and the public is notified of the Agency's conclusions.	MITA is concerned that quick communication of emerging signals to the public will occur but that correction of miscommunication or inaccurate information will not be updated in a timely manner. This contradicts the intention described in line 182: "…give health care providers, patients and consumers access to the most current information…" Therefore the information should be updated immediately if new information is available.

In conclusion, MITA urges the FDA to consider the post market tools currently at the Agency's disposal and consider how these existing tools and communication channels could be enhanced to better meet the gaps FDA intends to address with this draft guidance. This will help ensure the public continues to access important safety and risk information through existing channels. Should the Agency decide to move forward with this guidance, MITA believes clarification on the many open questions raised in this letter is an affirmative government responsibility. MITA also

requests that the FDA provide detailed clarification to the various sections of the guidance outlined above.

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MITA Member companies consider themselves partners with FDA in achieving effective and safe outcomes for patients. As such, we count on your careful consideration of this response and look forward to further engaged dialog with us leading to an outcome that meets all stakeholder expectations. If you have any questions, please contact Megan Hayes, Director, Regulatory and Standards Strategy at 703-841-3285 (mhayes@medicalimaging.org) or me at 703-841-3235 (phope@medicalimaging.org).

Respectfully,

Patrick Hope
Executive Director

MITA is the collective voice of medical imaging equipment and radiopharmaceutical manufacturers, innovators and product developers. It represents companies whose sales comprise more than 90 percent of the global market for medical imaging technology. These technologies include: magnetic resonance imaging (MRI), medical X-Ray equipment, computed tomography (CT) scanners, ultrasound, nuclear imaging, radiopharmaceuticals, and imaging information systems. Advancements in medical imaging are transforming health care through earlier disease detection, less invasive procedures and more effective treatments. The industry is extremely important to American healthcare and noted for its continual drive for innovation, fast-as-possible product introduction cycles, complex technologies, and multifaceted supply chains. Individually and collectively, these attributes result in unique concerns as the industry strives toward the goal of providing patients with the safest, most advanced medical imaging currently available.