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March 29, 2016

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

Re: Docket No. FDA-2015-D-4803: Public Notification of Emerging Postmarket Medical Device Signals ("Emerging Signals"); Draft Guidance for Industry and Food and Drug Administration Staff; Availability

To Whom It May Concern:

The Advanced Medical Technology Association ("AdvaMed") appreciates the opportunity to provide comment on the Food and Drug Administration's ("FDA" or "Agency") Draft Guidance for Industry and Food and Drug Administration Staff: Public Notification of Emerging Postmarket Medical Device Signals ("Draft Guidance").[1] AdvaMed represents manufacturers of medical devices, diagnostic products, and health information systems that are transforming health care through earlier disease detection, less invasive procedures, and more effective treatment. Our members range from the smallest to the largest medical technology innovators and companies.

Patient safety is the number one priority of the medical technology industry. However, as proposed, the Draft Guidance represents a significant departure from the Agency's current postmarket communication practices and may not, by FDA's own admission, be in the public interest. According to the Draft Guidance, "an emerging signal is new information about a medical device used in clinical practice: 1) that the Agency is monitoring or analyzing, 2) that has the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." *Draft Guidance* at p. 3. We believe this policy—and the stated goals of the Draft Guidance—raise numerous legal, regulatory, and policy concerns.

The Draft Guidance fails to articulate a reasonable basis to communicate emerging signals to the public. In fact, FDA acknowledges that the release of an emerging signal to the public may deter use of a safe and effective medical device. A scientifically-driven regulatory agency should define clearly the strength of evidence and uncertainty that has resulted in the public communication of information about previously cleared or approved devices.

[1] Public Notification of Emerging Postmarket Medical Device Signals ("Emerging Signals"); Draft Guidance for Industry and Food and Drug Administration Staff; Availability (Dec. 31, 2015), *available at* http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm479248.pdf.

Moreover, the release of information that might be, as FDA admits, incorrect, incomplete, or misleading will negatively impact the use of devices and patient wellbeing.

Indeed, the Agency already has statutory processes in place to communicate information about medical devices. These include medical device reporting, recalls and associated communications, safety communications and alerts, and press releases. Moreover, the Quality System Regulations require manufacturers to continually evaluate risks associated with their devices through postmarket monitoring activities and initiate corrective actions when necessary. Such corrective actions are communicated to healthcare providers and patients, and typically to FDA as well. This information is also made publicly available on FDA's website.

Below we provide a general summary of our concerns with the Draft Guidance. More specific comments can be found in the attached document.

1. FDA Lacks Statutory Authority to Communicate Emerging Signals

The emerging signals policies proposed by the Draft Guidance are not supported by the Federal Food, Drug and Cosmetics Act ("FDCA" or "Act"). FDA does not point to such authority either. Nevertheless, the Draft Guidance proposes sweeping changes to FDA's current postmarket communication policies. Such changes should be accomplished through notice and comment rulemaking pursuant to the Administrative Procedures Act ("APA"), rather than through guidance.

As an initial matter, communication of an emerging signal without any statutory or administrative process will undermine device labeling and associated regulations. To the extent use of a legally marketed device is avoided because of an emerging signal communication, the practical effect is a legally unsupported rescission of a premarket notification order or withdrawal of a PMA. FDA's action would also effectively determine that a device is misbranded because, based on this new information, existing cleared or approved labeling could be considered "false or misleading in any particular" under section 502(a) or violative of 501(c) of the Act if its quality or performance is not what is represented. As a result, FDA must address liability considerations that may arise due to emerging signal communications, including those for the device manufacturer(s) (*e.g.*, sale of a misbranded device) and healthcare practitioners (*e.g.*, medical malpractice), especially if they elect to continue using the device after the FDA's communication.

Furthermore, it appears that FDA is attempting to emulate drug practices, though it is doing so without the same legal authority the FDCA vests the Agency to regulate drugs. Section 921 of the Food and Drug Administration Amendments Act of 2007 ("FDAAA"), among other things, requires FDA to "conduct regular, bi-weekly screening of the Adverse Event Reporting System database and post a quarterly report . . . of any new safety information or *potential signals* of a *serious risk* identified by the Adverse Event Reporting System within the last quarter." 21 U.S.C. § 533(k)(5) (emphasis added) (later referred to as "FAERS"). This Section of the Act applies only to drugs; it is not extended to devices. There is no

parallel provision in the Act that provides a foundation for such communications for medical devices. In addition, while the FDCA's drug provisions permit the agency to undertake labeling changes based on postmarket studies, adverse event reports or other information after a statutorily mandated process (*i.e.*, discussions with the drug sponsor prior to an order and dispute resolution and appeals processes after the order is released), device provisions of the FDCA do not have a similar analog.

In fact, the Draft Guidance does not even provide complete information concerning FDA's proposed policy, making it impossible for stakeholders to fully comment on the proposal. For example, FDA does not explain a number of fields in the proposed Appendix A, including a sample "summary of emerging signal," "additional information for patients and health care professionals," and "ongoing FDA action." And as discussed below, FDA fails to identify the data sources it will use and statistical methodologies it will employ. Without complete information, we are not fully informed of FDA's proposal and cannot provide comprehensive comments in response to the Draft Guidance. The failure to provide all relevant information runs afoul of FDA's Good Guidance Practices. 21 C.F.R. § 10.115. Regardless, though, because the proposed policy described in the Draft Guidance represents a significant departure from the Agency's current practices and is not supported by statute, FDA should proceed through notice and comment rulemaking pursuant to the APA.

Even if the FDA can identify a statutory foundation for this policy, the Agency's decision making process described in the Draft Guidance would likely lead to actions that are arbitrary and capricious. The U.S. Supreme Court has held that when dealing with a private party, an administrative agency must have "examine[d] the relevant data and articulate[d] a satisfactory explanation for its action including a rational connection between the facts found and the choice made." *Motor Veh. Mrs. Ass'n v. State Farm Ins.*, 463 US 29, 43 (1983). The Draft Guidance states that the Agency will issue an emerging signal communication if it "believes" there is a need to notify the public. *Draft Guidance* at p. 4. The Agency, more importantly, fails to provide guidance to patients and health professionals on how to act until further information is gathered and the signal is either confirmed or ruled out.

2. Emerging Signals Will be Confusing and Misleading

We are profoundly concerned that emerging signal communications issued prior to the Agency having adequate, fully analyzed, validated and confirmed evidence, and without appropriate instructive recommendations, will create unnecessary confusion for healthcare providers and patients and could have unintended consequences including an adverse impact on public health[2] and long-lasting reputational damage to valuable devices. This confusion

[2] *See, e.g.*, Gould and Krahn, *Complications Associated with Implantable Cardioverter-Defibrillator Replacement in Response to Device Advisories*, JAMA, 2006: 295(16): 1907-11 (Concluding that implantable cardioverter-defibrillator (ICD) "generator replacement in patients with advisory devices is associated with a substantial rate of complications, including death. These complications need to be considered in the development of guidelines determining the appropriate treatment of patients with advisory devices."); Sengupta et al., *Implantable Cardioverter-Defibrillator FDA Safety Advisories: Impact on Patient Mortality and Morbidity*, Heart Rhythm, 2012: 9(10): 1619-26 (concluding that ICD patients within scope of an advisory experienced statistically similar outcomes as those not within scope).

is likely to extend beyond the specific device in question, reaching to all similar devices with the same intended use. Furthermore, premature FDA announcements of unconfirmed potential device risks may also lead to frivolous litigation, class action lawsuits and other legal actions. Although FDA acknowledges such potential unintended consequences in the Draft Guidance, the Agency does not explain how it will address negative impacts to patients, the healthcare community, and device manufacturers. *See, e.g., Draft Guidance* at p. 5 ("We also recognize the potential unintended consequences of public communication about emerging signals . . . including the possibility that a beneficial device's use may be avoided or inappropriately stopped because of uncertain or unproven risks or uncertainty around the benefits.).

In addition to creating unnecessary confusion, FDA openly acknowledges that "[i]n some cases, the safety of a particular medical device or type of device may be publicly questioned based on *incorrect*, *incomplete*, or *misleading* information." *Draft Guidance* at p. 6 (emphasis added). The public health relies on the communication of accurate and reliable information from public health agencies. Public reliance on information from FDA that turns out to be incorrect, incomplete, or misleading will undermine public confidence,[3] is highly unlikely to promote the public health, and will likely lead to inappropriate changes in medical care. Even if the limitations and weaknesses in the available information could be effectively communicated, there would be no way to put it into a rational clinical or scientific context or know what the benefit of such qualified, unconfirmed information means and what change in patient care should result.

Should FDA proceed with the types of policies described in the Draft Guidance, the Agency must put in place safeguards to minimize these concerns. At a minimum, an emerging signal communication should include information concerning the impact and risk associated with a patient or healthcare provider or facility deciding to no longer use, either fully or partially, the device in question. For example, the communication should explain that the device continues to be safe and effective, the potential benefits the device provides that would be lost should the user cease use of the product, and the risks the patient might assume under alternate therapies. Appropriate disclaimers advising any changes in device use should be done so in consultation with the treating physician. Including impact and risk information will better balance the communication and provide a more complete discussion of the issue. Further, appropriate organization of the information should be considered for all intended audiences.

Moreover, FDA should update emerging signal communications on a basis more frequently than "at least twice per year." *Draft Guidance* at p. 7. FDA should publish updates on at least a quarterly basis until the investigation is closed, and if appropriate, updates may

[3] We note that FDA is one of the most widely recognized and influential government agencies that advocates on behalf of the public health. Consumers are likely to perceive any publications by the FDA as a warning and would react by limiting their use of the device in question. As a result, FDA should evaluate whether the issuance of an emerging signal communication is subject to the peer review guidelines outlined in the Office of Management and Budget's Bulletin M-05-03, *Final Information Quality Bulletin for Peer Review* (Dec. 16, 2004).

indicate that no new information is available. Immediate notifications should be provided to the public when either FDA has (1) determined that there is not a causal relationship between the issue and device, or (2) closed out the emerging signal investigation.

Lastly, we recommend that, if FDA proceeds with a version of this policy, a pilot should be utilized to further evaluate the best communication methods, the actual value of emerging signal communications, and a better understanding of the unintended consequences that will occur.

3. The Device Manufacturer(s) Must Be Included in FDA's Process

Should FDA proceed with a version of this policy, the Agency must establish clear and reasonable administrative processes that include input and communications with the medical device manufacturer(s). We believe that in most, if not all, cases the device manufacturer(s) will have valuable information concerning the emerging signal. Manufacturers may have information in their quality records and risk management files that are relevant to the emerging signal. These records use appropriate statistical techniques and trending methods (*e.g.*, survival curves and Statistical Process Control, appropriate denominators and groupings across product platforms or types, relevant manufacturing information, and use conditions and demographics) that could better explain the data. Engaging with the manufacturer(s) at appropriate times in the process will help prevent the premature communication of unfounded information, allow for a thorough analysis of the issue, and potentially identify corrective actions if necessary.

In particular, we believe that the manufacturer(s) should be directly engaged by FDA when: (1) The emerging signal is first identified and the data is first evaluated, (2) before any public communication of an emerging signal is issued, (3) before any public communications are updated, and (4) before FDA closes out any public communications. During each of these phases the device manufacturer(s) should be consulted and provided at least 30 days to respond to any Agency communication concerning an emerging signal, and any response provided by the manufacturer(s) should be included in any public announcement issued by the Agency. (In fact, such a process would be consistent with the FAERS system, which requires notification to pharmaceutical companies prior to the publication of information).

It is also unclear what obligations exist for manufacturers in response to an emerging signal communication. For example, the Draft Guidance does not address whether the manufacturer is expected to reassess the quality and safety management steps it has already taken (*e.g.*, initiate a new investigation or revisit its health hazard assessment, or contact user facilities with its own communication to supplement that of the Agency). Additional clarification in this regard is needed.

4. FDA Must Better Define the Data and Evaluation Mechanisms

FDA fails to explain the type of data that will be used and the statistical methodologies the Agency will employ to generate an emerging signal communication. The datasets and

applied methodologies to their assessments must be clearly defined. Otherwise, this policy may lead to subjective decision-making that is supported by neither the data nor scientific rationale. Considering the potential ramifications of issuing an emerging signal communication, FDA, at a minimum, must utilize data that shows (1) a serious problem (2) that is causally related to the device. Indeed, drug communications emanating from information gathered by the FAERS database is limited to this degree to ensure patient risk (in both using and not using a product) is of paramount concern.

Limiting emerging signal communications to only those that might be based on causally related data (the level of evidence supporting a causal association should be defined) and that represent a serious risk to patient health will also ensure consistency with FDA's medical device regulations. For example, FDA requires device manufacturers to report corrections and removals when there is a "risk to health posed by the device." 21 C.F.R. § 806.10(a)(1). A device poses a risk to health if there is "a reasonable probability that use of, or exposure to the product will cause serious adverse consequences or the use may cause temporary or medically reversible adverse health consequences, or outcomes where probability of serious health consequences is remote." 21 C.F.R. § 806.2. Similarly, 21 C.F.R. § 803.3 defines MDR reportable events as adverse events and malfunctions for which evidence reasonably suggests there may be a causal connection to a death or serious injury. While existing regulations clearly consider both the seriousness of the issue and the causal link with the product, the Draft Guidance fails to mention these basic concepts.

Furthermore, FDA must clearly explain the data sets it intends to utilize and address basic questions concerning data veracity, such as how it will ensure the data is not the result of off-label use of the device and whether the data source can be trusted (*e.g.*, social media). In this regard, we would expect FDA to provide the following information concerning the data: (1) Whether FDA has sufficient information about the product and its use conditions to appropriately assess the data; (2) whether FDA has access to accurate denominator data; (3) how FDA calculates the probability of an occurrence; (4) whether the data is differentiated so that acute and chronic monitoring signals are analyzed with an appropriate statistical methodology and applied to the correct type of denominator (*e.g.*, if trending device longevity on a model that is no longer manufactured, trending by sales in that time period would provide a denominator of zero); (5) whether FDA has access to demographic and use condition information that places the data into context; (6) whether FDA understands the key influencing factors, such as information from the device's Design History File that could influence the interpretation of the perceived issue; and (7) the statistical methodology FDA will use to determine that a risk profile has changed for a device.

Regarding the last item, statistical methodologies, we note that when a manufacturer seeks clearance or approval for a device, FDA requires detailed statistical evidence regarding the benefit(s) of the device. We believe FDA should employ similar methodologies for its postmarket communications concerning the same product. The Draft Guidance does not explain a mechanism that ensures the benefit-risk profile established by the Office of Device Evaluation during the device's premarket review will be translated and applied consistently by the Office of Surveillance and Biometrics when reviewing an emerging signal.

Lastly, the Draft Guidance refers to "FDA staff" making determinations about whether an emerging signal communication is appropriate. The Draft Guidance should specifically define the FDA staff that will review information relating to a potential emerging signal and make a determination about whether a public communication will be issued. Senior staff within FDA should be required to sign off on all early communications to ensure that decisions to issue such communications are consistent and scientifically appropriate. In particular, all decisions relating to early public communications—including the determination that an initial communication is warranted and what each public communication will say—should require concurrence by both the Director of CDRH's Office of Surveillance and Biometrics and CDRH's Chief Scientist, with review by the Center Director prior to public notification. Defining the reviewers who will take part in each investigation and make final decisions about public communications will help maintain consistency across different cases and ensure appropriate considerations will be taken into account.

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AdvaMed would like to thank the FDA for its consideration of these comments. Please do not hesitate to contact me at 202-434-7224 or zrothstein@advamed.org if you have any questions.

Respectfully submitted,

/s/

Zachary A. Rothstein, J.D.
Associate Vice President
Technology and Regulatory Affairs

Attachment

AdvaMed Comments

Date: **March 29, 2016**

Document Title: **Public Notification of Emerging Postmarket Medical Device Signals; Draft Guidance for Industry and Food and Drug Administration Staff**

Submitters Name: **Zachary A. Rothstein, J.D.**

Company: **Advanced Medical Technology Association (AdvaMed)**

#	Page/ Section/ Paragraph/ Line	Comment/Proposed Change	Rationale
1	General	FDA should thoroughly assess and determine what it can learn from the early communication program that already exists for drugs. For example, of the early signals identified and communicated in the drug program, how many of those ultimately were confirmed as issues requiring a recall or safety notification? Those learnings should be used to better shape this proposal and should be described to inform the public's understanding of why a similar program should be established for devices.	FDA should provide additional information about whether the benefits of an emerging signal communication warrant the stated public health risks of such a program.
2	General	FDA should seek feedback and allow comments from the manufacturer both throughout the process of determining whether an emerging signal exists and after a public communication has been issued. The manufacturer will likely have valuable insights as to the information giving rise to the potential issue, and therefore, the Draft Guidance should clarify how and when the manufacturer will be consulted by FDA. In particular, we believe that the manufacturer should be directly engaged by FDA when (1) the emerging signal is first identified and the data is being evaluated, (2) before any public communication of an emerging signal is issued, (3) before any public communications are updated, and (4) before FDA closes out any public communications. During each of the above phases, the manufacturer of the device should be consulted and provided with an opportunity to comment. Furthermore, we believe the manufacturer should be provided at least 30 days to respond to any Agency communication concerning an emerging signal, and any response provided by the manufacturer should be included in any public announcement issued by the Agency concerning the emerging signal.	Engaging with the manufacturer at these critical junctures will ensure that the information to which FDA has access is comprehensive. Participation in this process will also allow manufacturers to be better prepared for handling questions about emerging signals from healthcare professionals and patients.

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3	General	FDA should state in the Draft Guidance that it will not communicate information about emerging signals to foreign regulatory authorities. Should FDA determine that it will share emerging signals with foreign regulatory authorities, the Agency should explain to what extent and how the Agency plans to communicate such information, particularly for cases involving a manufacturer that is based outside of the U.S. In this case, FDA should notify the manufacturer before the Agency has communications with a foreign regulatory authority and provide the manufacturer with an opportunity to comment.	FDA does not address this issue in the Draft Guidance.
4	Line 60	We recommend clarifying the terms "new" and "clinical practice."	Additional clarity will help explain FDA's intent. Furthermore, it is not clear whether clinical practice refers only to institutional healthcare or whether homecare is also included.
5	Lines 61-64	Clarify that all four conditions must be met.	It is unclear whether FDA will consider some or all of the four factors when determining whether to issue an emerging signal communication.
6	Lines 62-63	Reconsider the following criteria: "that has not yet been fully validated or confirmed"	As explained in our cover letter, we are concerned that patients and healthcare professionals may avoid safe and effective devices due to communications based on information that is neither validated nor confirmed.
7	Lines 95-96, 130, 134, 157, 158, 195, and 197	The Draft Guidance uses a number of key terms that are not defined. We suggest the following terms be defined, ideally in a glossary appended to the main text of the Draft Guidance, consistent with FDA's existing regulations and policies: • "reliable" • "newly recognized type of adverse event" • "increased rate or severity of the event"	Without clear definitions for these terms, the use of this language introduces ambiguity into how FDA and stakeholders should interpret the Draft Guidance. Providing specific definitions is necessary to clarify the scope of the Draft Guidance as well as the criteria that FDA will apply in analyzing a potential emerging signal.

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		• "sufficient strength of evidence" and • "significantly alter" As an example, we recommend that FDA interpret the term "newly recognized type of adverse event" using principles and criteria drawn from the Agency's definitions set forth in 21 C.F.R. § 812.3 (for "unanticipated adverse device effects") and 21 C.F.R. § 814.39(o) (for "newly acquired information"). Definitions of the other terms could similarly draw from existing regulatory concepts and definitions.	
8	Lines 103-104	This sentence discusses the potential that an emerging signal communication may promote enhanced vigilance and increase reporting to FDA. However, the Draft Guidance neither acknowledges nor discusses how such enhanced reporting would introduce a level of bias into the ongoing analysis of signals that are not validated or confirmed. A large influx of unreliable data may diminish FDA's ability to properly analyze the data and may ultimately taint any conclusions.	FDA should consider and explain in the Draft Guidance how the Agency will account for introduced bias.
9	Lines 134-137	FDA should provide additional detail concerning how the Agency will identify an emerging signal based on reported device malfunctions. It appears the Agency will focus on newly identified types of adverse events, rather than what may be an increase in reported device malfunctions. Furthermore, we believe FDA should consider relevant product information previously submitted to the Agency, such as human factors studies in support of a 510(k) clearance, before issuing an emerging signal communication.	A manufacturer's understanding of a particular device malfunction may change over time.
10	Lines 137-140	The Draft Guidance currently states that "[a] medical device emerging signal may be associated with one product from one manufacturer, one type of product or similar products from multiple manufacturers, or multiple different product types from multiple different manufacturers (*e.g.*, materials issues)." We recommend that FDA clarify how the Agency will consider data in each of these situations.	The way in which data and information is analyzed for one device can be different than how it is evaluated for a category of devices. Manufacturers would benefit from better understanding how FDA will assess each type of situation and the Agency's method for determining whether an emerging signal—and for which devices this emerging signal may be

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		For example, the Draft Guidance does not address the circumstances under which the data for one device will be considered by FDA to be applicable to a class of devices, which may be marketed by different manufacturers. We also suggest that FDA explain the circumstances under which it will pool data for devices from multiple manufacturers into a single analysis.	relevant—exists in each case.
11	Lines 144-147	The Draft Guidance states that "in certain circumstances, the FDA may . . . elect to seek recommendations from one of its Advisory Committees to assist in evaluating available information pertaining to a signal." We agree that such an approach may be warranted in some cases. We also recommend that the Agency establish mechanisms by which manufacturers who disagree with FDA's decisions regarding an emerging signal and/or public communication can raise their concerns on an expedited basis to an external group that can provide impartial input. As part of this dispute resolution process, FDA could seek input from an independent advisory panel of clinical experts.	The Draft Guidance does not currently define a process by which a manufacturer can challenge FDA's decisions regarding an emerging signal communication. Moreover, the Agency suggests only that it will confer internally on such decisions, but input from independent, third-party experts may sometimes be warranted.
12	Lines 147-149	We recommend revising or deleting the following sentence: "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."	The Draft Guidance defines an emerging signal as information "that has not yet been fully validated or confirmed, and for which the Agency does not yet have specific recommendations." *See Draft Guidance,* Lines 62-64. Based on this definition, it is unclear how FDA could utilize an emerging signal to issue a specific recommendation and/or take regulatory action as proposed in this sentence.
13	Lines 155-172	The Draft Guidance outlines certain factors that FDA may consider when it evaluates and communicates about an emerging signal. FDA should elaborate on these factors to make them more specific, concrete, and transparent. At a minimum, the following factors should be further defined: • Magnitude of the risk, • Magnitude of the benefit,	The factors currently listed in the Draft Guidance are vague and subjective. As a result, they do not provide stakeholders with meaningful information about how FDA will interpret them and may result in inconsistent and unpredictable determinations.

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		• Strength of the evidence of a causal relationship between the use of a device and the adverse event, • Availability of alternative therapies, • Implications for similar or related devices, and • Accuracy and availability of information already in the public domain. For example, we suggest that FDA provide further information about how it would assess the "[m]agnitude of the benefit" of a device as it considers whether to issue an emerging signal communication. FDA could state that a device's benefits could include considerations such as the device's impact on clinical management, patient health, patient satisfaction, quality of life, probability of survival, improvement of patient function, prevention of loss of function, and relief from symptoms. For diagnostic devices, the benefits of a device should be assessed against its ability to identify a specific disease, provide diagnosis at different stages of a disease, predict future disease onset, and/or identify patients more likely to respond to a given therapy and therefore enable treatment of the disease or reduce/prevent its spread. Similarly, it is not clear how FDA can evaluate the magnitude of risk if, by definition, information leading to an emerging signal is not widespread.	
14	Line 172-173	Add the following items: • Potential for triggering subsequent, incorrect, incomplete, or misleading information, • Potential for unintended consequences that would expose patients to additional hazards, • Source and veracity of data, and	We believe these items will help improve the quality of an emerging signal communication.

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		• Ability for the issue to be detected by a healthcare provider or patient.	
15	Lines 174-179	Delete reference to "mainstream or social media."	We do not believe it is appropriate for FDA to communicate about an emerging signal based on data gathered from mainstream or social media sources. FDA is a scientifically driven agency. Relying on unsubstantiated and unverified information is inappropriate. Furthermore, this policy could allow nefarious actors to harm the reputation and use of safe and effective medical devices.
16	Lines 183-186	We recommend clarifying how FDA intends to prevent healthcare providers and patients from limiting use of an otherwise safe and effective device upon announcement of an emerging signal. Furthermore, FDA should specify how it will communicate corrections to such announcements, particularly if it is determined that the emerging signal does not raise patient concerns. FDA should rapidly investigate the data to assess whether the signal is supported. The Agency should also state the timelines and process it will follow to perform such investigations.	While FDA states its intention for issuing an emerging signal communication is to not limit use of a particular device, the Draft Guidance admits that such results are likely to occur. Such cases are likely to damage the reputation of the device and manufacturer. It is imperative, therefore, that FDA lay out an adequate process that will correct any announcements that are later deemed unnecessary.
17	Line 192	Replace "potentially" with "very likely"	We believe the word, "potentially," is too vague and will include many events that are not causally related to the device.
18	Lines 195-197	Conflicts of interest may affect the information that is provided to FDA with respect to the device's 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 the information that is used as evidence to support an emerging signal communication should be made publicly available.
19	Lines 199-200	FDA should explain what triggers the 30-day timeline. The Draft Guidance simply states the time begins when the Agency "receiv[es] the information." This is not clear. Moreover, lines 142-143 state that "[t]he gathering and interpretation of the additional data needed to fully characterize an emerging signal can be complex, and it may take weeks	It will be helpful to understand FDA's thinking concerning the type and amount of information that is sufficient to warrant an emerging signal communication, and how quickly FDA intends to act on that information.

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		or months to conduct the analyses . . . ." This statement seems to contradict the 30-day timeline stated in lines 199-200.	
20	Line 206-207	Define: "elements of human behavior"	It is unclear what this phrase is intended to explain.
21	Line 216	"[t]he Agency ~~may~~will provide updates that:"	It is incumbent upon the Agency to provide all relevant updates regarding an emerging signal communication in a timely manner.
22	Lines 216, 223, 225-229, 249	Updates must occur more frequently than "at least twice per year." FDA should issue updates on at least a quarterly basis until the investigation is closed. If appropriate, an update can indicate that no new information is available. In cases where FDA determines that an emerging signal does not pose a risk, a communication should be issued within 24 hours. We also recommend that FDA add a fourth bullet after Line 223 indicating that the Agency will promptly notify the public when it has (i) ruled out a potential causal relationship between the adverse event and the device(s) or (ii) has closed out an emerging signal investigation.	Timely updates, particularly when new information is available or an investigation has been closed, are important to prevent the miscommunication (or misinterpretation) of an emerging signal communication.
23	Lines 225-226	The Draft Guidance states that updates to emerging signal communications will be posted to the FDA website. The Agency should clarify in which portion of its website these communications will be located and what background information will be provided to explain to the public what an emerging signal communication means. Furthermore, when the update acknowledges that there is no specific issue with the device, a simple post to the Agency's website is insufficient. The same methods and communication mechanisms used to announce the earlier communication should be utilized when issuing an update. We recommend that the webpage for emerging signals be located under, "Device Postmarket Surveillance," within the, "Medical Device Safety," section of the FDA's website. The communications should be organized in a chart similar to the one used by CDRH to inform stakeholders on the progress of each post-approval study (*available at* http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm).	This information will help stakeholders locate the communications and their updates. The presentation of this information (*e.g.*, the use of a chart and a general introduction to emerging signals) is important to provide the necessary context and ensure transparency of FDA's investigation of an emerging signal.

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		The columns for the chart should list the manufacturer's name, the device name, the device's medical specialty, the title of the communication, the emerging signal's status (*e.g.*, "Review ongoing" or "Closed"), any updates to the original emerging signal communication, and the date on which the next update is expected. We suggest that the top of the webpage include the following background information about an emerging signal: "An emerging signal is new information about a medical device used in clinical practice that the Agency is monitoring or analyzing, that has not yet been validated or confirmed, and for which the Agency does not yet have specific recommendations."	
24	Lines 236-242	Appendix A of the Draft Guidance proposes standard language to be included in each public communication about an emerging signal. We propose the following revisions: Posting this information does not mean FDA has concluded thatthere is a causal relationship exists between the medical device and the emerging signal. Nor does it mean FDA is advising patients or health care professionals to limit, discontinue, or modify use of these products. This communication reflects FDA's current assessment of available information about [issue]. FDA has not reached any conclusions about the matters discussed in this communication, and the device continues to be legally marketed. ItThis communication is intended solely to highlight this information at an early stage in the FDA's review before the FDA has completed a full investigation or determined whether this information warrants regulatory action. FDA does not intend for this communication to suggest, or be used as evidence that, the manufacturer has failed to comply with any legal obligations, including legal obligations relating to public	The language proposed by FDA in the Draft Guidance is vague and could be misinterpreted by the general public to suggest that an emerging signal confirms a device has a safety issue or the manufacturer has engaged in wrongdoing. These revisions aim to clarify FDA's position with respect to emerging signals and prevent the misinterpretation and misuse of these communications.

#	Page/ Section/ Paragraph/ Line	Comment/Proposed Change	Rationale
		disclosure or legal duties to patients or health care professionals. The FDA will update this document when additional information or analyses become available. FDA expects that it will publish the next update on [date]. Add contact information (manufacturer and FDA) Add a disclaimer: FDA is not requiring or recommending further action based on the information contained in this notice. In addition, if the emerging signal communication does not specifically recommend a labeling change, the notification should expressly state this fact. Below is an example of such a statement: "FDA does not believe there is sufficient information available at this time to support a label change for this device." Furthermore, if the notification addresses a situation where the device is being used under conditions that are not described in its labeling, a statement to this effect should also be included. For example: "FDA believes that [device] continues to be safe and effective when used in accordance with its Instructions for Use."	
25	Lines 236-242	To the extent FDA decides it is appropriate to target such communications directly to patients, the Agency should use a different communication template for patients than what is provided in the Draft Guidance. For example, a communication intended for receipt by a patient should encourage the patient to consult with their physician should they have any questions.	Different audiences are likely to interpret and react to these communications in different ways.