ACRP Regulatory Affairs Committee (RAC) Review of FDA Draft Guidance

Public Notification of Emerging Postmarket Medical Device Signals ("Emerging Signals")

What is the guidance?
This draft guidance document presents the FDA's current thinking on the policy for notifying the public about medical device "emerging signals" which are defined as "new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."

The guidance proposes that the public be informed about emerging signals that the Agency is monitoring or analyzing, even if the information has not been fully analyzed, validated or confirmed, and for which the Agency does not yet have specific recommendations.

Who does it impact & how?
This has the potential to impact health care providers, patients and consumers in addition to medical device manufacturers by having information about potential "emerging signals" publicly available before full analysis, validation or confirmation of the information.

What did ACRP RAC have to say about it?
Overall, the RAC raised concerns with the draft guidance document as written as there is potential for public safety and health risks if beneficial devices are discontinued unnecessarily based on preliminary signals that are not analyzed, validated or confirmed.

When were the RAC's comments sent to the agency?
March 24, 2016

Where can I access this document?
http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm479248.pdf

Public Notification of Emerging Postmarket Medical Device Signals ("Emerging Signals")

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on December 31, 2015.

You should submit comments and suggestions regarding this draft document within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions about this document, contact the Office of Communication and Education, 301-796-5660 or the Office of Surveillance and Biometrics, 301-796-6006.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Office of Communication and Education
Office of Surveillance and Biometrics

Preface

Additional Copies

Additional copies are available from the Internet. You may also send an e-mail request to CDRH-Guidance@fda.hhs.gov to receive a copy of the guidance. Please use the document number 1500027 to identify the guidance you are requesting.

Public Notification of Emerging Postmarket Medical Device Signals ("Emerging Signals")

Draft Guidance for Industry and Food and Drug Administration Staff

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

I. Introduction

The Food and Drug Administration (FDA) is issuing this draft guidance to describe the Agency's policy for notifying the public about medical device "emerging signals." 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.

At the time a medical device is approved or cleared, it has a benefit-risk profile that health care providers, patients, and consumers use to make treatment decisions. Once a medical device is on the market, new information, including unanticipated problems, may change the benefit-risk profile of a device. Timely communication of emerging signals may help health care providers, patients, and consumers make informed treatment choices based on the most current available information. This draft guidance document proposes criteria, timeframes, a method of communication, and follow-up for FDA communications for emerging signals. This document does NOT address findings of postmarket safety or reduced benefit that are confirmed, or for which the Agency has specific recommendations for consumers, patients, health care providers, health care facilities, or industry.

Historically, the FDA has communicated important medical device postmarket information after having completed an analysis of available data and, in most cases, after having reached a

decision about relevant recommendations for the device user community and about whether further regulatory action is warranted. For such safety or effectiveness issues, FDA generally will provide new or amended advice or instructions for patients, practitioners, and/or consumers regarding the safe and effective use of the device, based on the new data. In these cases, the Agency uses a variety of mechanisms to communicate publicly, including recall notices, safety communications, and press releases.

However, in addition to these types of public communications, we believe there also is a need to notify the public about emerging signals that the Agency is monitoring or analyzing, even when the information has not been fully analyzed, validated or confirmed, and for which the Agency does not yet have specific recommendations.

Because of the evolving nature of this information, FDA would be sharing it with the public at an early stage of the Agency's assessment and evaluation of the signal. Further, in contrast to a device safety communication, 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.

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 to FDA. This may in turn assist the Agency in further understanding the emerging signal.

FDA's guidance documents, including this draft guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. Background

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.[1] 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

[1] *See* 21 U.S.C. 360c(a)(2) and 21 C.F.R. 860.7.

becomes available once the device is more widely distributed and used under real-world conditions of actual clinical practice.

The FDA strives to provide current information concerning the potential benefits and risks of marketed medical devices to health care providers, patients, and consumers so that they can make informed treatment choices based on all available information.[2] We also recognize the potential unintended consequences of public communication about emerging signals, prior to confirmation and full evaluation of the data, 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. This latter concern is particularly relevant when the Agency has not yet developed specific recommendations. However, FDA believes that when an emerging signal meets the criteria described in Section III, including that it is based on reliable data, the benefits of providing early information to the public outweigh these risks if communicated carefully and thoughtfully.

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. 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).

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 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.

III. Considerations for Determining When FDA Will Issue a Public Notification About an Emerging Signal

FDA considers many factors in the course of evaluating and communicating about medical device emerging signals. These factors may include, but are not limited to, the following:

- Seriousness of the adverse event(s) (e.g., severity and reversibility) relative to the known benefits of the device;

[2] FDA discloses such information pursuant to all applicable laws, regulations, and policies, including sections 301(j) and 520(c) of the Federal Food, Drug, and Cosmetic Act, the Trade Secrets Act, the Privacy Act, and FDA disclosure regulations.

- Magnitude of the risk (e.g., likelihood of occurrence);
- Magnitude of the benefit;
- Strength of the evidence of a causal relationship between the use of a device and the adverse event;
- Extent of patient exposure (e.g., how broadly is the device used, is the device still actively manufactured and distributed);
- Whether there is a disproportionate impact on vulnerable patient populations (e.g., children, pregnant women, elderly, cancer patients, chronically ill, at-home/unmonitored);
- Potential for preventing, identifying, monitoring or mitigating the risk;
- Availability of alternative therapies;
- Implications for similar or related devices (e.g., multiple models from multiple manufacturers);
- Anticipated time for completion of initial FDA assessment and development of recommendations;
- Accuracy and availability of information already in the public domain.

At times, the decision to communicate about a medical device emerging signal may be affected by information the public has received from sources other than FDA, such as in the mainstream or social media. In some cases, the safety of a particular medical device or type of device may be publicly questioned based on incorrect, incomplete, or misleading information. In such cases, FDA may issue a statement or engage in other methods of communication to clarify or correct information and respond to public interest.

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 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.

Whenever FDA discusses medical device safety, it should exercise judgment in determining whether and when to communicate and what to say. FDA staff should strongly consider public communication about an emerging signal when all of the following statements apply:

1. 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;
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.

FDA staff should conduct an initial assessment of the need to communicate about an emerging signal within 30 days of receiving the information.

If during the evaluation of a signal, a decision is made to NOT communicate, FDA staff should conduct an internal reassessment of the decision within 30 days of receiving new information, using the considerations described above.

IV. Content of Communication and Follow-up

FDA strives to keep all communications clear and understandable. We consider elements of human behavior in our decision to communicate and in the content of our communication. We realize that risk information provided without context may alarm patients, causing them to discontinue therapy with a beneficial device or to avoid a potentially beneficial therapy. In our communications on medical device emerging signals, whenever possible and appropriate, we will include specific information on the known benefits and risks of the device and its use, as well as information on the emerging signal.

To provide consistency, FDA proposes to communicate medical device emerging signals using the format and content described in Appendix A of this guidance. Once a medical device emerging signal is communicated, the Agency may provide updates that:

- Provide new information related to the emerging signal collected since the initial public notification;
- Update the public that no additional substantive information is available and/or that no known change in the benefit-risk profile of the device has occurred since the last posting;
- Notify the public of additional actions being taken or completed by FDA and/or the manufacturer(s).

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.

Appendix A: Format of Public Notification about a Medical Device Emerging Signal

Early Communication: FDA Evaluating [summary of issue]

This communication reflects FDA's current assessment of available information about [issue]. It is intended 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. Posting this information does not mean that FDA has concluded there is a causal relationship between the medical device and the emerging signal. Nor does it mean that the FDA is advising patients or health care professionals to discontinue or modify use of these products. The FDA will update this document when additional information or analyses become available.

Date:
Device (including known benefits and risks):
Summary of Emerging Signal:
Additional Information for Patients and Health Care Professionals (if any):
Ongoing FDA Actions:
How to Report Problems to the FDA:

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MISSION:
ACRP promotes excellence in clinical research.

99 Canal Center Plaza
Suite 200
Alexandria, VA 22314
USA

T | 703.254.8100
F | 703.254.8101

office@acrpnet.org
www.acrpnet.org

March 24, 2016

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

In reference to docket number: FDA-2015-D-4803

The Association of Clinical Research Professionals (ACRP) is the primary resource for clinical research professionals in the pharmaceutical, biotechnology and medical device industries, and those in hospital, academic medical centers and physician office settings. ACRP was founded in 1976 to address the educational and networking needs of research nurses and others who supported the work of clinical investigations. Some 40 years later, ACRP is a global association comprised of individuals dedicated to clinical research and development. Our mission is "ACRP promotes excellence in clinical research."

ACRP appreciates the opportunity to provide the FDA with our comments on the DRAFT Guidance document Public Notification of Emerging Postmarket Medical Device Signals ("Emerging Signals") as this issue has a significant impact on our membership. The attached document provides detailed comments/suggestions/recommendations on specific sections of the draft guidance.

While we support the Agency's initiative to further enhance public safety, we are deeply concerned about the process proposed in this DRAFT Guidance.

We believe that there is significant risk with publicly providing invalidated information too soon, and it is clear from this document that FDA shares those concerns. However, no risk mitigation considerations or plans are presented to address this risk.

Given the risk that users will limit their use of a beneficial device, the fact that the manufacturer(s) is the likely expert on the signal, and that signals can come from sources of varying reliability, we believe that FDA should consult with industry prior to issuing any public communication. Nowhere in the draft guidance does FDA indicate that it will consult with or obtain information from industry regarding the Emerging Signals.

Additionally, it would seem reasonable to have allowed more time for the Unique Device Identification requirements to become fully effected, and to utilize this tool as a way to oversee and track/report on post market signals rather than add this Guidance to the mix.

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99 Canal Center Plaza
Suite 200
Alexandria, VA 22314
USA

T | 703.254.8100
F | 703.254.8101

office@acrpnet.org
www.acrpnet.org

We applaud the FDA's efforts on this important issue and hope that our feedback helps improve the final version of the document. Please let me know if you have any questions regarding our comments, or if we may otherwise serve as a resource on issues related to clinical research.

Sincerely,

Jim Kremidas
Executive Director

FDA-2015-D-4803 : Public Notification of Emerging Postmarket Medical Device Signals ("Emerging Signals")		
Page Number	**Text Line**	**Comments**
5	124-128	**The Guidance States:** **"We also recognize the potential unintended consequences of public communication about emerging signals, prior to confirmation and full evaluation of the data, 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. This latter concern is particularly relevant when the Agency has not yet developed specific recommendations."** We believe finalizing this Guidance without having addressed these risks would be detrimental to patient health.
5	142-144	**The Guidance States:** **"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."** It is implied that this investigation would take place *before* any notice of Emerging Signals is communicated to the public. If that is not the case we are extremely concerned about the lack of certainty regarding potential impact on device use by providers and patients, due to the unknown timeframes noted.
6	199-200	**The Guidance States:** **FDA staff should conduct an initial assessment of the need to communicate about an emerging signal within 30 days of receiving the information.** This seems to directly contradict the section above by indicating a 30 day decision should be made. Please clarify.