

# *Welcome to today's* FDA/CDRH Webinar

*Thank you for your patience while we register all  
of today's participants.*

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# Final Guidance: Factors to Consider Regarding Benefit-Risk in Medical Device Product Availability, Compliance and Enforcement Decisions

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# Benefit-Risk

and what you need to know about it.

## Focuses on patients

- OC strives to make compliance and enforcement decisions that put the patient first and honor CDRH's mission to protect and promote public health. We do this by considering the relationship between potential benefits and risks.

## Promotes Consistency

- Though we already assess benefit and risk, this guidance provides us with a framework to consistently and systematically apply these principles to our decision making, within the Center and in the field. This consistency will help improve our work.



# Benefit-Risk

and what you need to know about it.

## Interfaces with Industry

- Benefit-risk allows us to engage firms with a risk-based and situational approach. Externally, it facilitates the conversation and changes the focus from sole compliance to quality, patient benefit, and consideration of patient preferences.

## Encourages New Thinking

- We will customize approaches to address issues, and use creative problem solving. This will require a culture change.

## Aligns CDRH

- Aligns CDRH with mutual support and a shared understanding across divisions, we can maximize patient benefit, reduce patient risks, and improve overall medical device quality.

# **Factors to Consider Regarding Benefit-Risk in Medical Device Product Availability, Compliance, and Enforcement Decisions**

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## **Guidance for Industry and Food and Drug Administration Staff**

**Document issued on December 27, 2016.**

**The draft of this document was issued on June 16, 2016**

For questions about this document regarding CDRH-regulated devices, contact the Office of Compliance at 301-796-5900.



U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Devices and Radiological Health



# Key Points from the Benefit-Risk in Medical Device Product Availability, Compliance and Enforcement Decisions Guidance

1. Complements the premarket Benefit-Risk Guidance documents
2. Overarching for a wide variety of decisions
3. Inform Compliance and Enforcement Decisions to Maximize Patient Benefit

# Guidance Contents

- I. Introduction
- II. Scope
- III. Patient Focused Benefit-Risk Assessments
- IV. Description of Factors to Consider
- V. How the FDA Considers Benefit-Risk
- VI. Examples

Appendix A: Intersection with International Organization for Standardization (ISO) 14971

Appendices B-D: Work Sheets

<http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm506679.pdf>

# I. Introduction

## Why?

- Provide clarity for FDA staff and industry regarding the benefit and risk factors
- Maximize medical device quality and patient safety

## How will the FDA implement?

- Pilots and other evaluation techniques
- Harmonize with premarket benefit-risk assessment
- Include a patient focus and use of Real World Evidence



## II. Scope

The FDA may consider benefit-risk factors during:

- Evaluation of device shortage situations
- Selection of the appropriate regulatory engagement mechanism
- Evaluation of recalls
- Petitions for variance from sections of Quality Systems (QS) regulation (21 CFR part 820) for which there were inspectional observations during a Premarket Approval (PMA) inspection.

This guidance:

- Applies to diagnostic and therapeutic devices
- Excludes CBER devices, combination products where CDRH is not the lead and Electronic Product Radiation Control products and other products regulated by FDA

# III. Patient Focused Benefit-Risk Assessment



The FDA has the authority to limit the availability of violative medical devices and to pursue other compliance and enforcement actions related to violative medical devices—

decisions regarding these actions should be made while focusing on the impact for patients

## IV. Description of Factors to Consider

- Factors for the Assessment of Medical Device Benefits
  - Type of benefit
  - Magnitude of benefit
  - Likelihood of patients experiencing one or more benefits
  - Duration of effect
  - Patient perspective on benefit
  - Benefit factors for healthcare professionals or caregivers
  - Medical necessity

## IV. Description of Factors to Consider

- Factors for the Assessment of Medical Device Risks
  - Severity of harm
  - Likelihood of risk
  - Distribution of nonconforming devices
  - Duration of exposure to population
  - False-positive or false-negative results
  - Patient tolerance on risk
  - Risk factors for healthcare professionals or caregivers

# IV. Description of Factors to Consider

- Additional Benefit-Risk Factors
  - Uncertainty
  - Mitigation
  - Detectability
  - Failure mode
  - Scope of the device issue
  - Patient impact
  - Preference for availability
  - Nature of violations or nonconforming product
  - Firm compliance history

## V. How the FDA Considers Benefit-Risk

- A Benefit-Risk evaluation is prompted by events that may lead the FDA to take regulatory action
- The FDA evaluates available benefit information from various sources
  - Manufacturers may provide information through the designated FDA point of contact (e.g. recall coordinator)
- The FDA evaluates risk information from various sources
- The FDA completes a benefit-risk assessment considering additional factors
- The FDA uses the outcome of a benefit-risk assessment to inform decisions

# V. How the FDA Considers Benefit-Risk

How might the FDA use benefit-risk to determine whether to take a regulatory or non-regulatory approach?

## High benefit, little risk

## Low benefit, high risk

Product  
Availability

Ensure patients have  
access to the device

Limit product availability

Compliance  
and  
Enforcement

Work with the  
manufacturer to  
address underlying  
issues

Take formal compliance  
or enforcement action

# VI. Examples

## Examples Related to Product Availability Decisions

Example 1: Recall and potential shortage of a high benefit implantable coated device with low additional risk

Example 2: Evaluation of a variance petition related to a high benefit drug delivery system for which risks posed by QS issues were sufficiently mitigated

Example 3: Continued access to nonconforming biological indicators with high benefit and mitigated additional risk

Example 4: Malfunction of a pregnancy test with low benefit and moderate additional risk

Example 5: Recall of a radiation therapy device with high benefit and increased risk for some patients

## Examples Related to Compliance and Enforcement Decisions

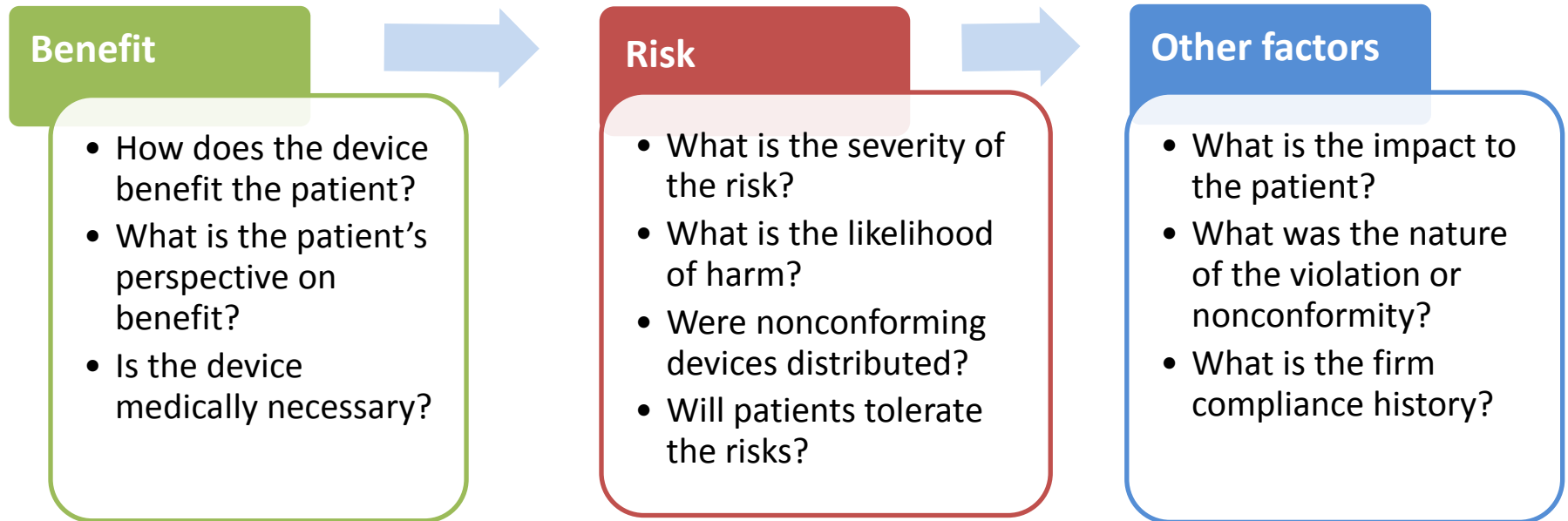
Example 1: Evaluating whether to send a Warning Letter or take an alternative approach for a low benefit, low additional risk aesthetic device

Example 2: Evaluation of potential actions following an inspection with observed QS deficiencies regarding a high benefit spinal fixation system



# Appendices B-D Worksheets

How is a benefit-risk assessment performed?



## Benefit

- **How does the device benefit the patient?**
  - Using real world data or other available data, what is the medical device's impact on clinical management and patient health?
  - Does the marketed product achieve the anticipated benefits?
  - Has real world practice led to new benefits?
  - Using real world data or other available data, what proportion of patients have been observed to benefit from the device?
- **What is the patient's perspective on benefit?**
  - What is the severity of the disease state?
  - Is this a chronic disease?
  - If chronic, can the illness be managed with other treatments or therapies?
  - How long do patients live with the disease?
  - Even if the benefit is in a small portion of the population, do those patients who would experience the benefit value it?

## Benefit

- **Is the device medically necessary?**
  - Is the device essential to the survival of patients?
  - Are alternative treatments available?
  - What other therapies are available for this condition?
  - How effective are the alternative treatments?

- **What is the severity of the risk?**
  - Do real world data or other available data show that medical device-related injuries have occurred at expected severity?
  - Are there any unanticipated injuries ?
  - Were there any changes in variations in serious adverse events among subpopulations?
  - Is the duration of harmful events longer than anticipated?
  - Is the harmful event reversible?
  - Has the type of intervention needed to address the harmful event changed?
  
- **What is the likelihood of harm?**
  - How frequently does this specific failure mode or defect occur?
  - What proportion of patients treated with or diagnosed by the nonconforming medical device is harmed?
  - How many patients were exposed to nonconforming devices?

## Risk

- **Were nonconforming devices distributed?**
  - What is the number of units on the market and market share?
- **Will patients tolerate the risks?**
  - What level of concern do patients have regarding the risks?
  - Even if the risk is in a small portion of the population, do those patients who would experience the risk understand it?
  - Are patients willing to take the risk of this treatment to achieve the benefit?

## Other Factors

- **How much uncertainty exists?**
  - What information does FDA have to assess benefit and risk?
  - What is the quality of the information FDA is using (for example, MDRs, literature, registry or clinical trial data, limited case studies, inspectional data etc.)? Is the quality of information a reliable source for making an objective and unbiased benefit or risk decision?
- **What is the impact on the patient?**
  - What are the risks to patients if the device is not available?
  - Are patients better off if the device is available?
- **What is the potential impact on patients related to the inspectional observation or regulatory non-compliance?**

## Other Factors

- **What is the nature of the violation or nonconformity?**
- **What is the firm's compliance history?**
  - Has the same or a similar inspectional observation or regulatory violation been observed at the manufacturer in the past 2 years? In the past 5 years? In the past 10 years?
  - Is the regulatory non-compliance significant enough that FDA would take regulatory action?
  - When did the firm report the harm to the FDA?
  - Would providing notice to the firm assist in informing the firm of its legal responsibilities?

# Questions?

Division of Industry and Consumer Education:  
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Slide Presentation, Transcript and Webinar Recording  
will be available at:

<http://www.fda.gov/training/cdrhlearn>

Under the heading: Postmarket Activities;

Sub-heading: General Policy Heading