

FDANEWS

14TH ANNUAL

MEDICAL DEVICE QUALITY CONGRESS

Benefit-Risk Considerations for Medical Devices: A Panel Discussion

Tuesday, March 28, 2017 • 3:00 – 4:15 pm ET

Panel

- **Beverly Lorell, M.D. Moderator**
**Senior Medical & Policy Advisor, FDA & Life Sciences Group,
King & Spalding**
- **Robin Newman**
Director, Office of Compliance, CDRH, FDA
- **Ann Ferriter**
**Director, Division of Analysis and Program Operations, OC,
CDRH, FDA**
- **Nikki Willett**
**Global Strategy, Medical Device & Diagnostics Industry, Veeva
Systems**

Today's Focus

- FDA's new final guidance

Contains Nonbinding Recommendations

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

**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

Today's Agenda

- Perspectives and insights from Office of Compliance, CDRH, FDA
- Perspectives and insights from the Medical Device Community
 - Including a recent survey
- Questions and discussion!

And to Keep in Mind...



Discussion and Q&A



Questions – Understanding FDA’s Approach

- Is FDA changing its policies for medical device compliance and enforcement decisions?
- How and when should firms engage with FDA to share benefit-risk information?
 - When a *potential* postmarket signal trend develops?
 - When a firm is contemplating but *has not yet initiated a recall* (removal or correction)?
- How should user facilities engage with FDA to share benefit-risk information?
- How does FDA weight factors to drive consistency in its benefit-risk decisions?
- What pilots has FDA conducted? What was the outcome?

Questions – How might Firms Apply this Guidance

- How might this guidance build on applications of the “recalls vs. product enhancement” guidance?
- How might this guidance affect a firm’s internal escalation of an early post-market potential safety and/or product nonconformance signal?
- How might this guidance affect a firm’s internal conduct of a health hazard evaluation for a potential post-market safety signal?
- Does this guidance change industry’s understanding of what is a risk to health? A serious injury?
- What constitutes a reasonable patient survey? How diverse should the patient population be? How large? Are testimonials of benefit enough?

Questions – Estimating Risk and Benefit

- For PMA devices, a firm’s premarket pivotal trial usually allows a tight estimate of benefit: the “number of patient needed to treat (NNT)” for a single patient to achieve the benefit seen in a trial
 - How should firms consider NNT in estimating postmarket benefit?
- Because postmarket reporting is voluntary by patients and doctors, postmarket estimates of actual harm or “near misses” may have large under-reporting problems
 - How should firms consider “number needed to harm (NNH)” in the context of postmarket under-reporting or absence of an all-inclusive postmarket safety registry?

Questions – Emerging Issues

- How should a firm think about potential postmarket benefit-risk for a 510(k) device that is performing within specifications...
 - When there is a potential change in the natural history of the underlying condition of patients exposed to the device? (As example, the morcellator issue)
- How should a firm think about potential postmarket benefit-risk for either a 510(k) or PMA device when it is being used in practice of medicine outside the intended use?
 - In pediatric patients
 - In adult patients
- How is FDA applying this benefit-risk framework to rapidly developing new “hot off the press” data?
 - As example, new data about a marketed device product presented at a national scientific meeting

Thank You for Being a Great Audience!



Benefit-Risk Considerations for Medical Devices: Panel Discussion

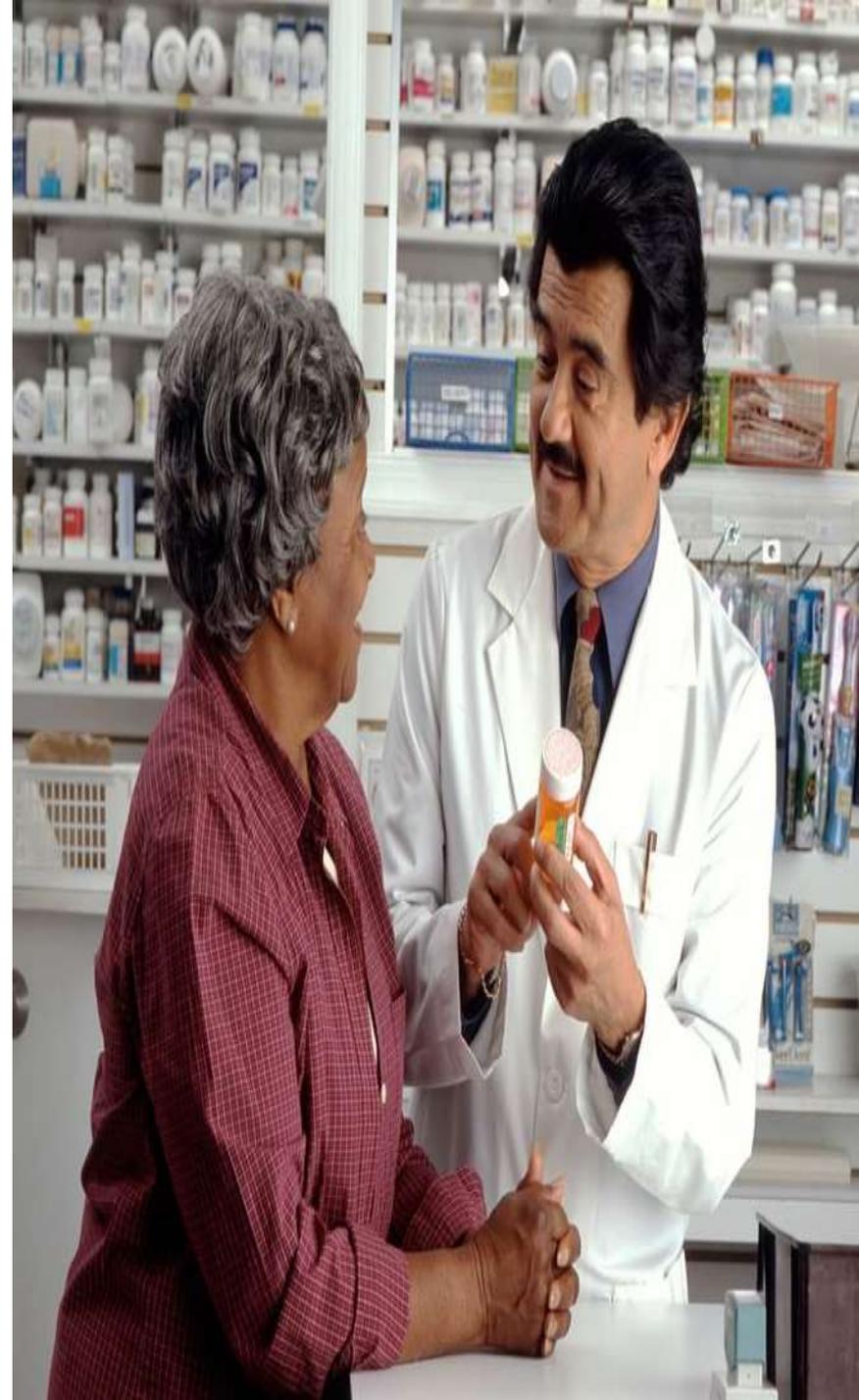
Robin W. Newman, Director, Office of Compliance CDRH
Ann Ferriter, Director, Div of Analysis & Program Ops, OC
Beverly Lorell, MD, Senior Medical and Policy Advisor,
FDA Life Sciences Team , King & Spalding LLP
Nikki Willit, Global Strategy, Medical Devices &
Diagnostics, Veeva Systems and Founder LinkedIn Quality
& Regulatory Network Group

2016-17 Office of Compliance Top Priorities

- Partnering with Patients
 - Benefit Risk
- Promoting a Culture of Quality
 - Quality in the Office
 - Case for Quality
- On the Horizon
 - Program Alignment
 - Total Product Life Cycle

Benefit Risk Vision

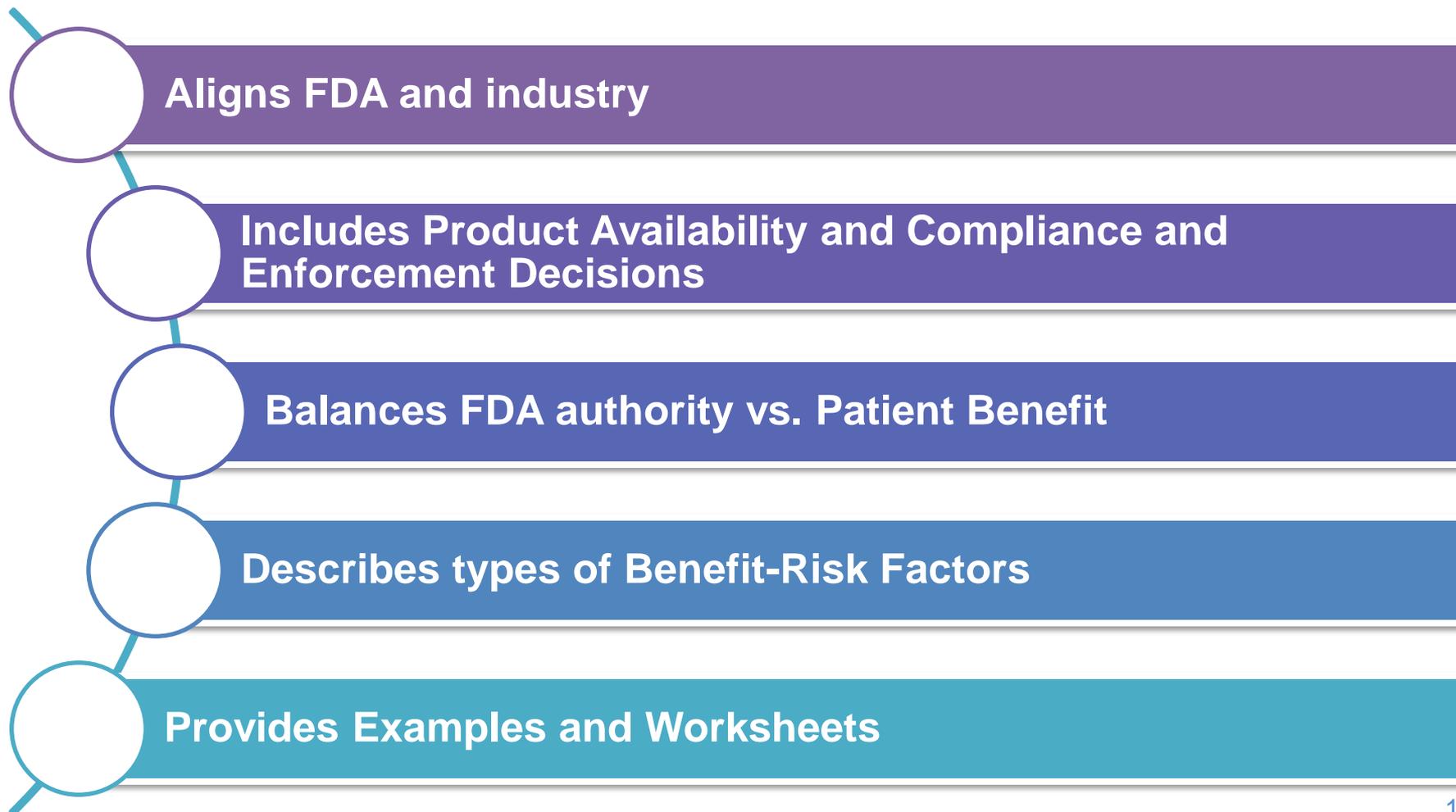
“We are undertaking these projects to enable CDRH, ORA, and industry to share the same framework for risk so that we can reach a better understanding more quickly and consistently thereby assuring a level playing field across medical device firms while also reducing the duration of public exposure to risk.”



Benefit Risk Guidance

- Passed as an official guidance document December 26, 2016.
- Focus is to now implement in routine practices of the Office of Compliance.

Points from the Draft Guidance



Introduction

Why?

- Clarify benefit and risk factors when prioritizing resources
- 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

Scope

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 (QS) regulation (21 CFR part 820) for which there were inspectional observations during a (PMA) inspection.

Patient Focused Benefit Risk Assessments

In situations with risk to patient harm, FDA can help maximize benefit and reduce risk to patients by:

Assessing the situation

Considering patients' perspectives

Evaluating any regulatory non-compliance or device nonconformity

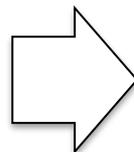
Factoring in alternatives, where available

Considering the benefit-risk tradeoffs for patients of each decision option and

Determining the most appropriate next steps.

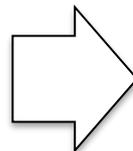
How FDA Considers Benefit Risk

BR Assessment indicates high benefits to patients with little risk



FDA works with manufacturer without enforcement action

BR Assessment indicates low benefits to patients with high risk



FDA takes compliance or enforcement action to address problem

Examples Related to Product Availability Decisions

Recall and shortage

Evaluation of a variance petition

Continued Access to Nonconforming Product

Examples Related to Compliance and Enforcement Decisions

Evaluation of whether to send an Warning Letter or take an alternative approach

Evaluation of potential actions following an inspection of a manufacturer with observed Quality System deficiencies

How is a benefit risk assessment performed?

Benefit

- How does the device benefit the patient?
- What is the patient's perspective on benefit?
- Is the device medically necessary?
- How do practitioners experience the device?

Risk

- What is the severity of the risk?
- What is the likelihood of harm?
- Were nonconforming devices distributed?
- Will patients tolerate the risks?
- Can the risk be sufficiently mitigated?

Other Factors

- What is the impact to the patient?
- What was the nature of the violation or nonconformity?
- What is the firm's compliance history?

Benefit

- **How does the device benefit the patient?**
 - Using real world 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?
 - 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 disease?
 - Even if the benefit is in a small portion of the population, do those patients who would experience the benefit value it?

Risk

- **What is the severity of the risk?**
 - Do real world or other available data show that medical device-related injuries have occurred at expected frequency/severity?
 - Are there any unanticipated injuries?
 - Were there any changes or 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?

Other Factors

- **How much uncertainty exists?**
 - What information does the FDA have to assess benefit and risk?
 - What is the quality of the information FDA is using (i.e. MDRs, literature, registry or clinical data, limited case studies, 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 of 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? 5 years? 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?

Thank You!



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MARCH 28-30, 2017

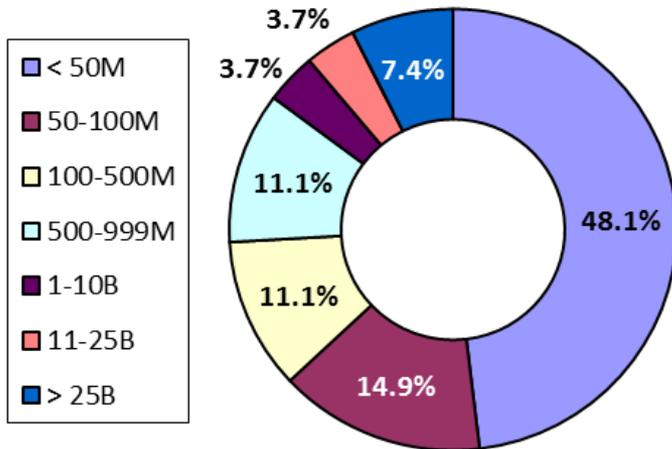
Guidance on Benefit-Risk Considerations for Medical Devices: Industry Survey

Nikki Willett, Global Strategy, Medical Devices and Diagnostics Industry, Veeva Systems
Founder LinkedIn Quality & Regulatory Network with more than 111k members globally

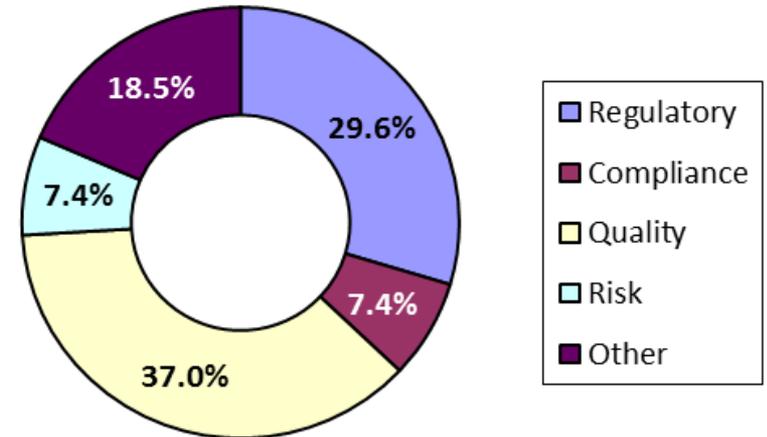
Source: LinkedIn, LinkedIn Quality & Regulatory Network Group, FDAnews

Demographics of Participants

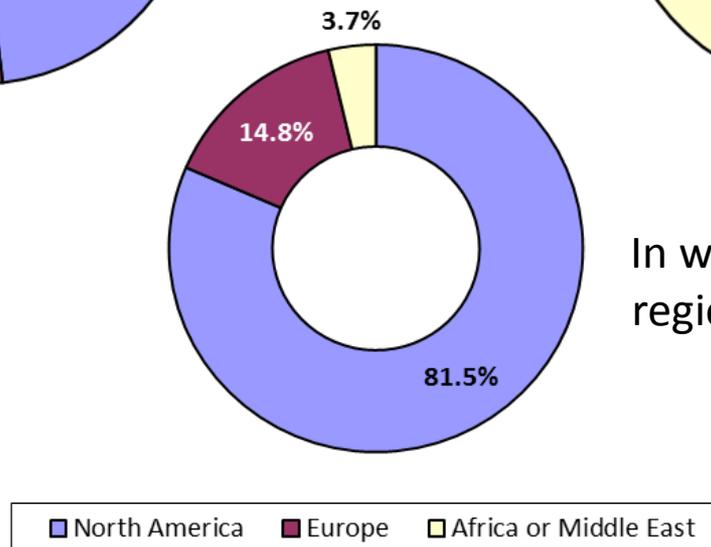
Annual Revenue
(M=Million, B=Billion)



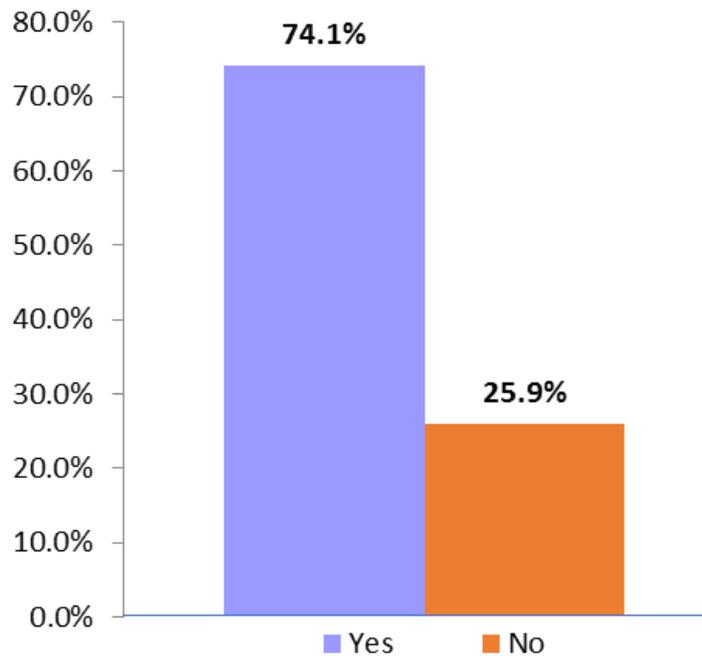
What part of the organization
do you represent?



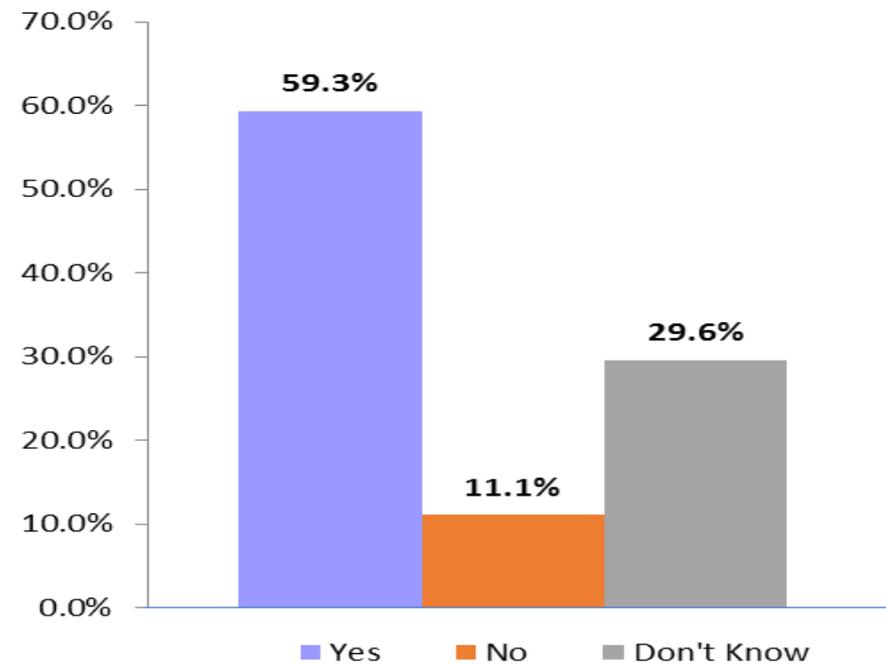
In which geographical
region do you reside?



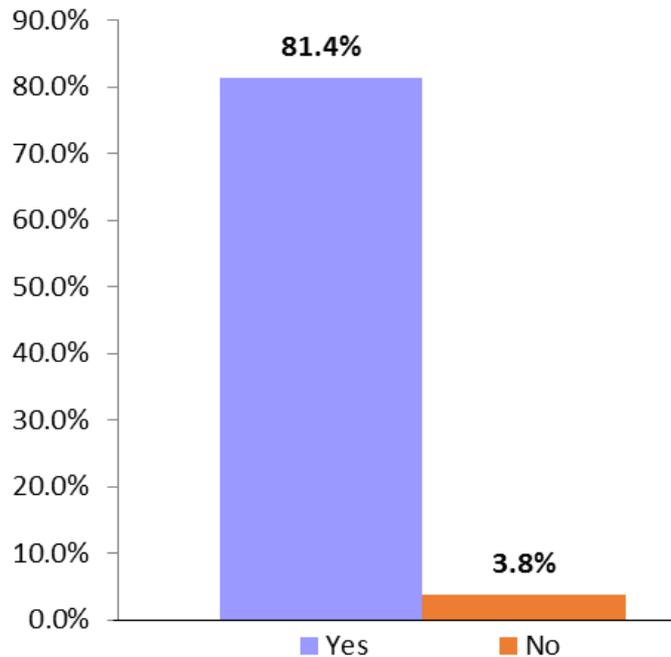
Have you read and understood the Guidance impact on your company?



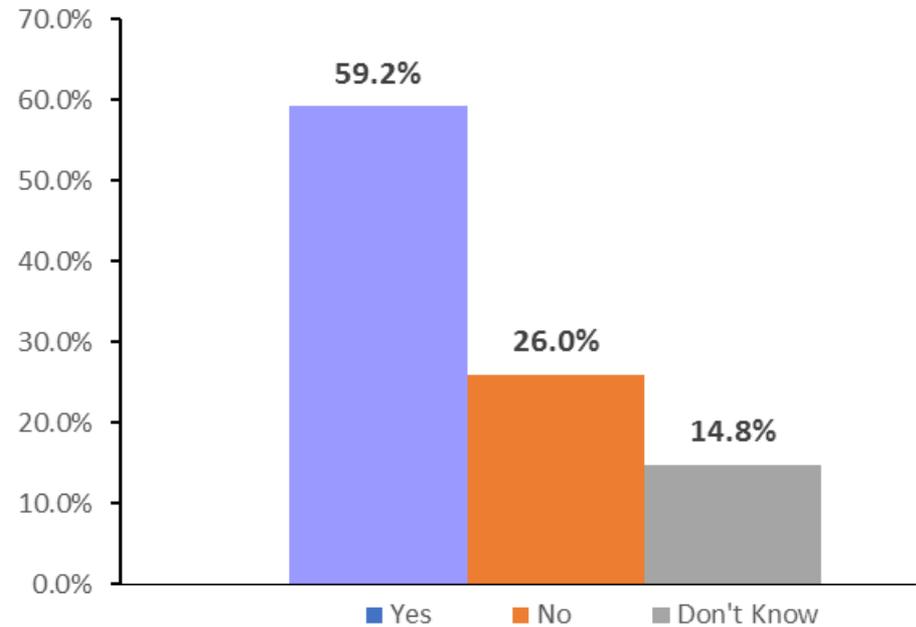
Are you incorporating the suggestions in the Guidance for benefit-risk analysis in your overall health hazard evaluation?



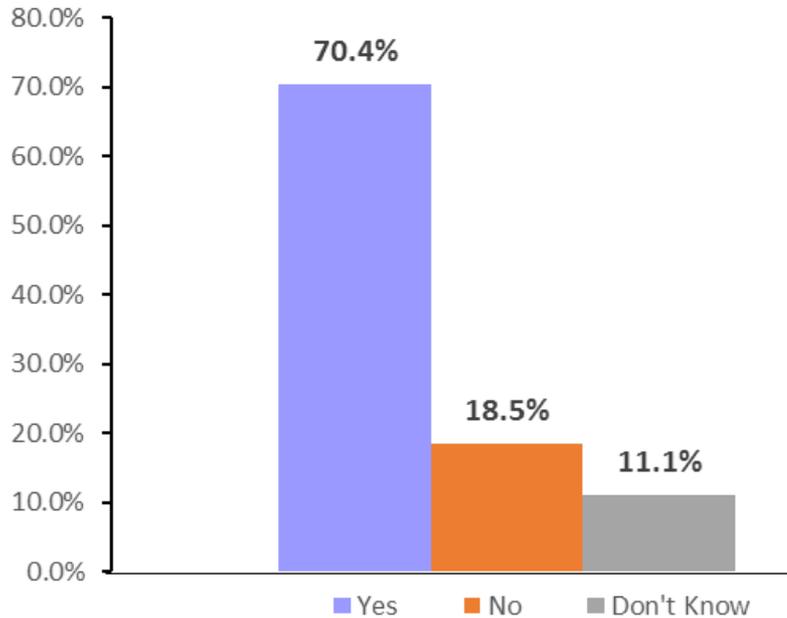
Do you believe the Guidance helps better align the actions and thinking of the FDA to those taken by Industry?



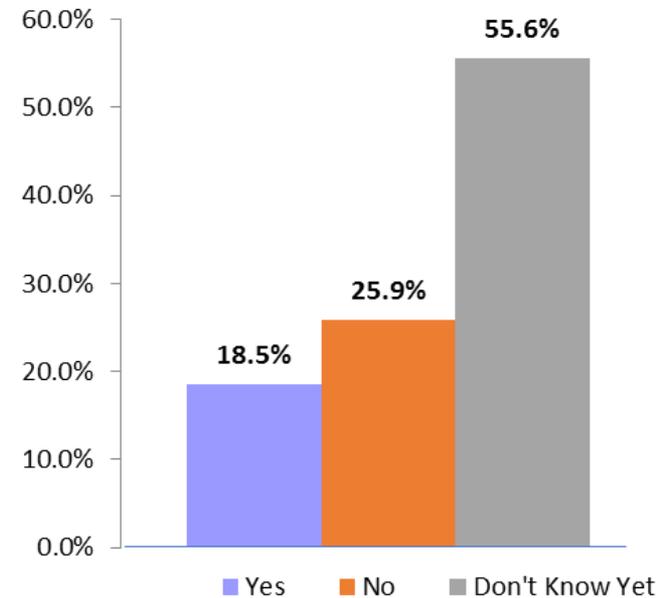
Do you believe that the three “factors” will help in the FDA's assessment when prioritizing compliance and enforcement efforts following an inspection?



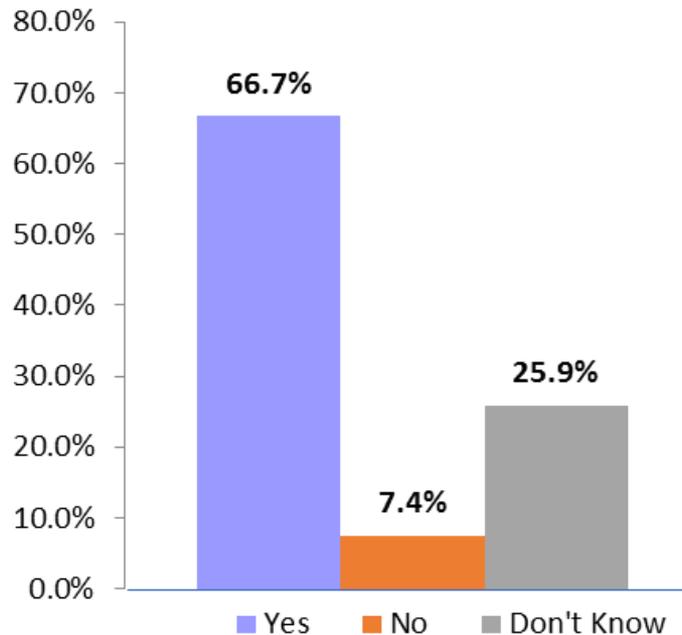
Do you believe the examples of Risk Factors being considered by the FDA are sufficient?



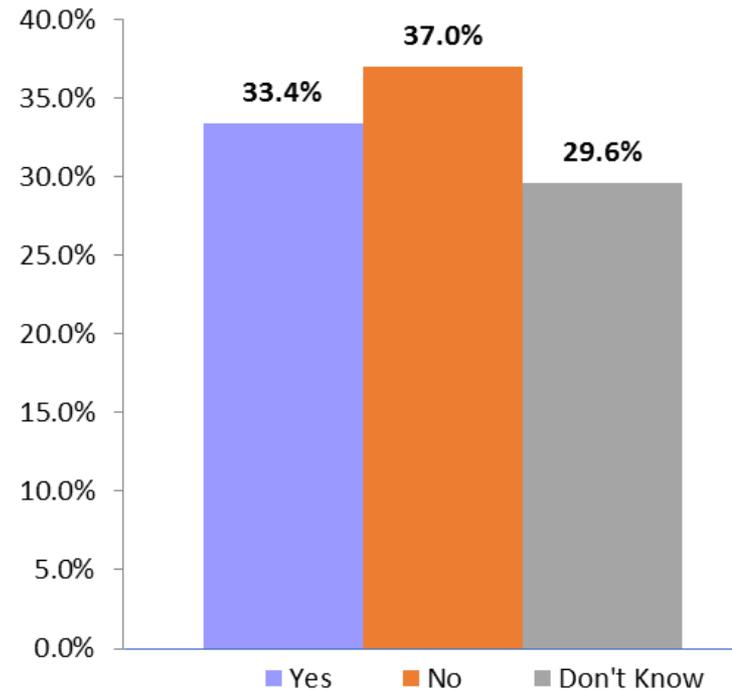
Will your company volunteer data to the FDA to help in making benefit-risk determinations?



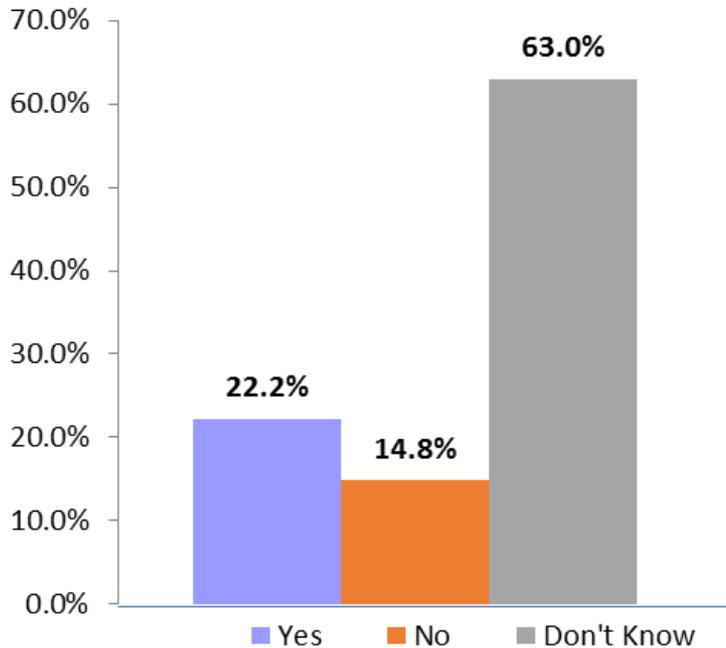
Do you believe that the publicly available summary of FDA's benefit-risk decision will help you have a better understanding of what factors were considered as part of favorable or enforcement decision following an inspection?



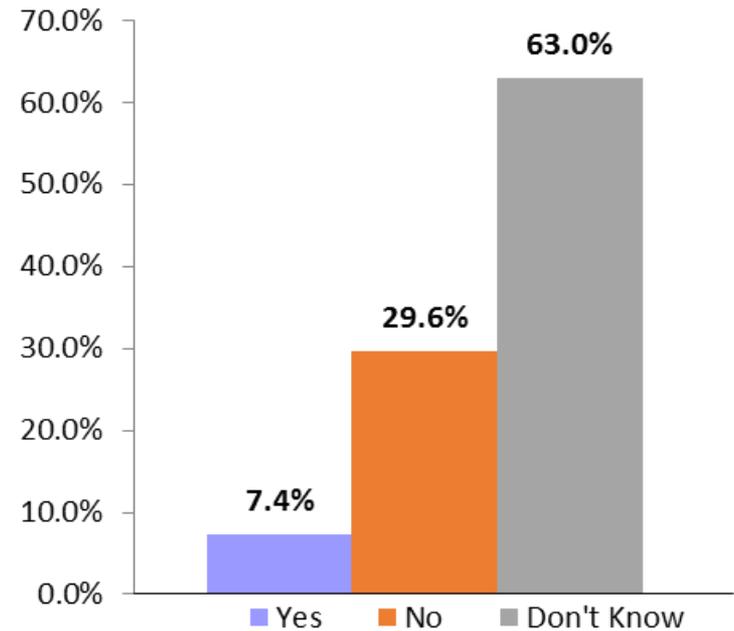
The FDA will consider any "relevant and reliable" information including patient preference (PPI), from a representative sample. Do you believe this data can be reliable without providing the FDA your device risk-benefit data and calculations?



Will your company contact the FDA with Benefit-Risk data and calculations to make a strong case for enforcement discretion based on this Guidance?



Is your company participating or willing to participate in FDA's Pilot, if available?



Sample Comments from Participants - Benefits

- When defining our 3.1 Ed Safety/Risk Procedure, this guidance was instrumental in defining proactive criterion of evaluation and control for new product and feature development. I know that is not what is intended.... but never-the-less useful
- It would be of benefit to the customers/patients who use/need the product.
- Depends on the results. If the results are favorable, then as long as statistically sound techniques were used, then it's reliable. If the results are negative, then a review of the manufacturer's data would reveal the assumptions made that may have been incorrect or the restrictions that were not considered when selecting patient samples.
- Yes, since the ultimate goal is providing safe and effective devices and having fair and consistent reviews.
- Essential to bring all experiences from all sources together in one processing function to facilitate best outcomes and future reactions/ adjustments/ refinements.
- Examples help verify that our current risk/benefit analysis approach is acceptable.
- I take information from everywhere and try to fit it to the need. The scope of the Guidance does not directly fit product development, but the values are well represented.

Sample Comments - Opportunity to Respond

1. Depends on the results. If the results are favorable, then as long as statistically sound techniques were used, then it's reliable. If the results are negative, then a review of the manufacturer's data would reveal the assumptions made that may have been incorrect or the restrictions that were not considered when selecting patient samples.
2. Patient preference is too subjective. Patients are typically uninformed.
3. Benefit-risk information is crucial but patient preference information provided by the company is marketing.
4. It's helpful to an extent but may give false pretenses to a similar company who might allow more regulatory risk in their product due to favorable decisions elsewhere.
5. Should include probability of harm if device is not used and probability of providing misdiagnosis.
6. Each aspect has differing acceptance criterion. We have named the classes but haven't defined their methods of evaluation.

Sample Comments - Opportunity to Respond (2)

7. Not sure if the risk concepts in 13485 & 14971 incorporated correctly. Need more details on how to use these factors.
8. Can sometimes be more academic than implementable. Broad prospect of devices. Need some guidance on priority and urgency.
9. Above are "reactive measures". Mandatory training for appropriately using medical devices by clinicians and para clinical staff will help reduce risks for patients. FDA and Health Canada needs to ensure appropriate training is mandatory for clinical and para clinical users.
10. Not sure how to align substantial equivalence with risk-benefit analysis and how certain product specification differences impact the risk-benefit analyses.
11. Yes, guidance definitely helps however different medical devices are a combination of engineering and computerized hardware and software. The guidance does not explain to help determine risks associated with few category products.

Summary

- Any risk guidance to improve decisions on device and patient outcome is good for the Industry
- Although every company has some level of benefit-risk analysis / management, examples provided in the Guidance helps gain insight into the FDA's thought process providing more alignment between the FDA and Industry
- Business need and success also needs to balance risk
- Uncertainty of whether it covers all diverse medical devices, technologies and situations
- Some other outside influence needs to be understood as a factor – operator usage and training; if the device is not used; and probability of providing misdiagnosis
- “Devil is in the Details” – broad implementation, many many small details

Thank You