

New FDA Draft Guidance on Benefit-Risk Factors Affecting Medical Device Compliance and Enforcement

In June, the U.S. Food and Drug Administration released draft guidance to clarify the benefit and risk factors it may consider in compliance and enforcement actions involving medical devices.¹

Medical device manufacturers are probably already aware that the FDA has issued a benefit-risk framework for assessing medical device premarket approvals and de novo classifications. This new draft guidance seeks to complement and build upon that existing benefit-risk framework in an effort to improve consistency in the FDA's decision-making across the total product life cycle. Notably, now manufacturers will be privy to the factors used by the FDA in considering post-market actions.

The framework in the draft guidance is meant to be applicable to both manufacturer and FDA decisions. For example, a device manufacturer may want to consider the benefit-risk factors when evaluating an appropriate response to nonconforming product or regulatory compliance issues. In other words, the factors would apply to a device manufacturer when deciding whether to issue a corrective action, up to a full-scale product recall, which can be one of the most significant regulatory dilemmas that a company can face.

The framework correspondingly applies to the FDA, which, of course, has the authority to limit the availability of violative medical devices and to pursue other compliance and enforcement actions in response to violative devices. The purpose of the benefit-risk factors in this arena is to address any nonconforming products while focusing on the impact on patients.

The draft guidance identifies the following factors for the assessment of medical device benefits when prioritizing compliance and enforcement efforts:

- Type of benefit(s): e.g., the effect of the device on patient treatment plans and quality or impact on survival;
- Magnitude of benefit(s): the degree to which patients experience the treatment benefit or effectiveness of the medical device;
- Likelihood of patients experiencing one or more benefits;
- Duration of effects;
- Patient preference on benefit;
- Benefit factors for health care professionals or caregivers: i.e., whether the device improves patient outcomes or improves clinical practice; and
- Medical necessity: i.e., the availability of other similar devices.

With respect to the risk factors, the FDA notes that changes in risk may occur due to, for example, observed unanticipated harm to patients exposed to the device, changes in the medical device use environment, device nonconformities, and design or manufacturing issues. Likewise, device nonconformities may increase risk or introduce new risks via failure to comply with applicable statutes or regulations. Risks may be revealed through post-market data even if the device conforms with regulations. The FDA indicated it will consider the following risk factors:

- Risk severity: (1) medical device-related deaths and serious injuries; (2) medical device-related non-serious adverse events; (3) medical device-related events without reported harm; and/or (4) duration of harm to patient;
- Likelihood of risk: (1) likelihood of medical device nonconformity; (2) likelihood of a harmful event given exposure to a nonconforming device; and/or (3) number of patients exposed;
- Nonconforming product risks: whether a nonconforming product has been distributed and how many are on the market;



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- Duration of exposure to population;
- False-positive or false-negative results: whether diagnostic devices are accurate;
- Patient tolerance of risk: the patients' concern regarding harm or potential harm; and
- Risk factors for health care professionals or caregivers: an adverse effect on the clinician or caregiver.

Both benefit and risk factors, when relevant, will be considered in the aggregate.

The draft guidance includes a number of other factors the FDA may consider related to product availability, compliance, and enforcement decisions:

- Uncertainty: of risks or benefits;
- Mitigations: actions taken by the manufacturer, FDA, or other stakeholders;
- Detectability: whether a nonconformity could be identified prior to use;
- Failure mode: whether the nonconformance is related to manufacturing, design, use conditions, or environment;
- Scope of the device issue;
- Patient impact: the effect of a compliance or enforcement action, or availability;
- Preference for availability;
- Nature of violations/Nonconforming product; and
- Firm compliance history: the manufacturer's regulatory history and initiative in identifying and correcting issues or the repetitiveness of such issues.

The benefit-risk factors often focus on patient perspective, and therefore, patient preferences are referenced as a source of data available to the FDA. Specifically, the draft guidance states, "FDA considers relevant and reliable evidence and data available to the agency at the time of a decision — including reliable patient preference information from a representative sample — on a case-by-case basis[.]" This aligns with the FDA's recent draft guidance stating that real-world evidence may be used to support the FDA's regulatory decision-making for medical devices. While patient preferences can provide useful information, manufacturers may have significant concerns about the reliability of this evidence, when one considers the likelihood of overly subjective and/or biased opinions and variability among individuals.

Providing further insight to device companies with potentially violative products, the draft guidance outlines how the FDA would use these benefit-risk factors to make informed decisions, especially following events such as a product recall, variance petition, safety signal, or medical device nonconformity. The draft guidance includes examples demonstrating how the FDA would conduct a benefit-risk assessment for medical devices, including: (1) a recall and shortage of an implantable coated device, (2) an evaluation of a variance petition for a drug delivery system, and (3) continued access to a nonconforming product. Other examples include evaluating whether to send a Warning Letter or take an alternative approach and evaluation of potential actions following an inspection with observed Quality System deficiencies. The FDA is, in a sense, telling manufacturers what steps should be taken when facing corrective action to best deter adverse scrutiny. There are others not delineated in this guidance document, and best practices should incorporate these and other industry and specific business considerations.

The draft guidance is open for comments from the industry until September 14, 2016.

While the draft guidance supplies insight into the FDA's decision-making process, the factors identified may be too vague to provide usefulness to medical device manufacturers. Moreover, the examples set forth in the draft guidance may not apply to many manufacturers and thus may not be helpful in making real-world decisions. Medical device manufacturers should familiarize themselves with the draft guidance, and carefully consider whether to submit comments before the September 14 deadline.

Cozen O'Connor's Products Liability attorneys are available to provide counsel and guidance on the issues discussed in this Alert.

¹ U. S. Food and Drug Administration, "Factors to Consider Regarding Benefit-Risk in Medical Device Product Availability, Compliance, and Enforcement Decisions."

