

Comments and suggestions regarding the Draft Guidance for Industry and FDA Staff: Functional Indications for Implantable Cardioverter Defibrillators. Docket No. 2005D-0391. Electronic comments: www.fda.gov/dockets/ecomments; written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. 0208 6 JAN -9 A9:45

These comments and suggestions to the **Draft Guidance for Industry and FDA Staff: Functional Indications for Implantable Cardioverter Defibrillators [Docket No. 2005D-0391]** are provided by Cameron Health, Inc. ("Cameron Health").¹

Cameron Health appreciates the FDA's decision to create a Draft Guidance for Industry on functional indication for Implantable Cardioverter Defibrillators (ICDs). Cameron Health would like to comment that the present draft appears to focus too much on ICD features and not on the most salient attributes of the ICD: its clinical safety, efficacy and overall patient benefit.

The proposed draft guidance document regularly discusses specific ICD features and design attributes. As an example, a feature that is frequently discussed is antitachycardia pacing (ATP). Cameron Health believes that features such as ATP can be beneficial in the appropriate patient population. However, it is also believed that narrowing the functional indication to be inclusive of any particular feature may result in patients being excluded from improvements in patient care. By way of example, would it be reasonable to exclude a functional indication for a device that lacked ATP, but improved patient safety and/or clinical efficacy?

The language of the present draft of the Guidance Document also appears to exclude novel technologies that may improve patient co-morbidities and other patient benefits. Specifically, a novel ICD may be declined a functional indication merely because it does not resemble a "historic" ICD. Again, by way of example, would it be reasonable to exclude a functional indication for a device that utilized a new waveform that substantially reduced defibrillation thresholds and improved patient safety?

To resolve the above issues, it may be more appropriate that the primary criteria for receiving a functional indication should be the safety and clinical efficacy of the ICD device. By making safety and efficacy the benchmark for a functional indication, the Draft Guidance will be aligned with the primary endpoints of the defining trials for ICDs (e.g., AVID, MUSTT, MADIT I & II, SCD-HeFT). All of these mortality trials were based on the ability of the ICD to prevent sudden cardiac death in at risk patients using high energy defibrillation shocks. Of note, although ATP was allowed in a subset of these trials, no clinical endpoint addressed the safety and efficacy of ATP.

The following are suggested language changes from various sections of the Draft Guidance Document. These suggested changes are proposed to focus the Draft Guidance document on the clinical safety, efficacy and patient benefits of ICD therapy rather than design characteristics and features:

¹ Cameron Health is a privately-held development stage medical device company located in San Clemente, CA. With over 60 employees, Cameron Health is developing an implantable cardioverter defibrillator (ICD) that challenges the historic model in favor of one based on simplicity.

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1. On page 2, lines 31-32, the Guidance Document reads:

“The ICD is intended to provide ventricular antitachycardia pacing and ventricular defibrillation for automated treatment of life-threatening ventricular arrhythmias.”

This sentence limits functional indications to only ICDs possessing tiered-therapy. Historically, the fundamental premise for every ICD has been to provide high energy shock therapy to defibrillate life-threatening ventricular arrhythmias. The premise of delivering high energy shocks remains the single common function of ICDs throughout their evolutionary development. Furthermore, clinical efficacy of ICDs is based on high energy defibrillation shocks and not ATP therapy for terminating ventricular arrhythmias. In fact, to Cameron Health’s knowledge, ATP has never been evaluated as a primary endpoint in any published PMA. Cameron Health believes that exclusion of all ICDs that lack antitachycardia pacing (ATP) is an unnecessary limitation.

The following suggested language resolves the issues presented above:

“The ICD is intended to provide ventricular defibrillation, with or without antitachycardia pacing for automated treatment of life-threatening ventricular arrhythmias.”

By using more inclusive language regarding the antitachycardia pacing feature, the wording of the sentence is now in concert with the primary intention of the ICD – defibrillation. As such, the sentence is no longer exclusionary to ICDs lacking ATP.

2. In the Defibrillators Appropriate for ICD Functional Indications Section on page 3, lines 28-32, the Guidance Document reads:

“While different model ICDs may offer different features and functions, the life-saving attributes of most ICD models are based on similar concepts of sensing, detecting, classifying, and treating ventricular arrhythmias using pacing therapy (antitachycardia pacing) and/or high energy shocks (defibrillation).”

This sentence implies that high energy defibrillation shocks are the secondary modality for treating ventricular arrhythmias.

The following suggested language resolves the issues presented above:

“While different model ICDs may offer different features and functions, the life-saving attributes of most ICD models are based on similar concepts of sensing, detecting, classifying, and treating ventricular arrhythmias using high energy shocks (defibrillation) and/or pacing therapy (antitachycardia pacing).”

By using more inclusive language regarding the antitachycardia pacing feature, the wording of the sentence is now consistent with the fundamental design intent of all ICDs. More specifically, the ICD’s primary purpose is to prevent sudden cardiac death in patients with

lethal ventricular tachyarrhythmias by providing high energy defibrillation shocks (defibrillation).

3. On page 4, starting at line 2, the Guidance Document reads:

“FDA agrees with this determination and believes that ICDs are appropriate for a functional indication when, by virtue of their similar design and characteristics, they would be expected to demonstrate the same level of safety and effectiveness as the ICDs represented in the literature summary that was reviewed at the June 2000 Panel Meeting.”

This sentence places an emphasis on the similar design and characteristics of the ICDs. The primary concern should be based on the safety and clinical effectiveness of the ICD. This broader interpretation would allow innovative ICD technologies that bring important clinical and patient benefits the ability to obtain a functional indication based on the safety and effectiveness of the device; even if the design and characteristics are a departure from conventional ICD technology.

The following suggested language resolves the issues presented above:

“FDA agrees with this determination and believes that ICDs are appropriate for a functional indication when they would be expected to demonstrate the same level of safety and effectiveness as the ICDs represented in the literature summary that was reviewed at the June 2000 Panel meeting.”

Scientific literature shows that the clinical efficacy of ICDs in providing mortality benefit has not changed since the introduction of the first approved ICDs. However, there have been significant design changes in ICDs during the last 20 years (device configuration, lead design and placement, waveforms, etc.), and these changes have significantly impacted the clinical co-morbidities associated with the implant of ICDs (e.g., the shift from epicardial patches implanted via a thoracotomy to an ICD with a transvenous lead system). Rather than focus on the design and device configurations in determining whether or not an ICD system is considered for a functional indication, the critical factor should be that any new technology must demonstrate the appropriate level of safety and effectiveness as present ICDs with a functional indication.

4. On page 4, lines 12 -16 of the Guidance Document read:

“The defibrillators that FDA does not consider appropriate for functional indications include external defibrillators, wearable defibrillators, de-featured implantable defibrillators where the risk-benefit profile suggests the need for a more narrow intended patient population, or defibrillators that use radically different detection algorithms, shock waveforms, or electrode configurations than those under discussion at the June 2000 Panel meeting.”

This statement makes an assumption that unless new ICD designs are similar to conventional ICD technology in terms of its detection algorithms, shock waveforms, or electrode configurations, the new ICDs are not appropriate for a functional indication.

The following suggested language resolves the issues presented above:

“The defibrillators that FDA does not consider appropriate for functional indications include external defibrillators, wearable defibrillators, de-featured implantable defibrillators where the risk-benefit profile suggests the need for a more narrow intended patient population.”

The critical factor for obtaining a functional indication should be that any new implantable defibrillator technology must demonstrate the appropriate level of safety and effectiveness. The detection algorithms, shock waveforms or device configurations should be irrelevant in determining whether or not an ICD system is considered for a functional indication. It seems to be unreasonable to exclude a functional indication for a device that utilized a new waveform that substantially reduced defibrillation thresholds and improved patient safety merely because it did not resemble the historic representation of an ICD.

5. On page 4, paragraph 3 reads:

“Any PMA submission in which a manufacturer seeks a functional indication statement for its ICD should include data demonstrating that the particular ICD has the ability to sense, detect, classify, and treat life-threatening ventricular arrhythmias using antitachycardia pacing and defibrillation, and that the ICD has a favorable risk-benefit profile.”

This statement assumes that all ICDs are tiered-therapy devices that use antitachycardia pacing and defibrillation to treat life-threatening ventricular arrhythmias.

The following suggested language resolves the issues presented above:

“Any PMA submission in which a manufacturer seeks a functional indication statement for its ICD should include data demonstrating that the particular ICD has the ability to sense, detect, classify, and treat life-threatening ventricular arrhythmias using defibrillation and/or antitachycardia pacing, that the ICD has a favorable risk-benefit profile.”

The statement is now consistent with the fundamental design intent of all ICDs – preventing sudden cardiac death by providing high energy defibrillation shocks (defibrillation). This change allows a novel technology lacking ATP to be considered for a functional indication if the device provided comparable safety and efficacy to current devices.

In conclusion, Cameron Health believes that the primary criteria for receiving a functional indication should be the safety and clinical efficacy of the ICD device and not on any particular ICD feature. It would be unfortunate if a byproduct of this Guidance Document limited functional indications for ICDs to existing technology and design characteristics without considering novel technologies that would result in improved patient benefit.