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June 16, 2014

Margaret A. Hamburg, MD
FDA Commissioner
Food and Drug Administration (FDA)
10903 New Hampshire Ave.
Silver Spring, MD 20993

Dear Dr. Hamburg:

On behalf of more than 18,000 board-certified orthopaedic surgeons, the American Academy of Orthopaedic Surgeons, with the support of the Musculoskeletal Tumor Society and the Pediatric Orthopaedic Society of North America, hereafter "we" or "the societies," welcomes the opportunity to offer comments on the Food and Drug Administration's (FDA) request for feedback on the draft guidance "Humanitarian Device Exemption (HDE): Questions and Answers."

General Comments

We appreciate the agency's efforts to address commonly raised questions, clarify definitions, and provide greater transparency to the HDE pathway. Overall, we find the document to be clear and informative. The flowchart is a useful tool to enhance stakeholder understanding of the decision points in the selection of the appropriate regulatory pathway for a product.

The societies are supportive of the changes which allow manufacturers to realize a profit on Humanitarian Use Devices (HUDs). These modifications to the HDE program provide additional incentive for manufacturers to engage in the development and production of devices for underserved populations.

Specific Comments

Question 4

The definition of "use," for the purpose of this document, does not encompass off-label applications, such as those for compassionate use. Further clarification in this area is important, either in additional language in this guidance or as a stand-alone guidance on compassionate use, to facilitate patient access to HUDs when no therapeutic alternative exists. While the answers to questions 60 and 61 provide some additional

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detail, our surgeon members continue to report varying interpretations among manufacturers and hospitals/healthcare systems as to when and how IRBs are involved in the decision to use devices. We look forward to additional guidance from the agency to support the optimal function of these critical regulatory pathways.

Question 7

The definition of comparable devices is helpful, but examples would greatly contribute to clinicians' understanding of how the FDA applies the considerations outlined in the document.

Question 14

Benefit-risk balance is important when evaluating treatment options for patients. As demonstrated in the many presentations by stakeholders during the FDA's Patient Preference Workshop in September 2013, different patient populations will have drastically different assessments of what constitutes acceptable risk. We believe it is critical for sponsors to clearly describe the intended patient population, current treatment options, and reasoning behind the acceptability of greater risk. Surgeons must assess individual patient's risk tolerance before using HUD products and clearly communicate with the patient the possible risks and benefits, in light of HUDs' exemption from requirements of establishing a reasonable assurance of effectiveness.

Question 17

As discussed above, we are supportive of the profit mechanism included in this guidance as a means to encourage manufacturers to pursue the development and production of devices for underserved populations.

Question 18

The societies appreciate the examples provided in this answer. We find that they clarify the reasons that a traditional approval or clearance pathway is not functional for the types of devices made available under this exemption.

Questions 21-24

Given their potential role in the assessment of the annual distribution number (ADN), it is imperative that end users (surgeons and hospitals) need to be made aware of how the FDA defines the ADN and the impact of distribution practices on a device's eligibility for HDE. We encourage manufacturers to facilitate the return of unused devices by hospitals and surgeons, to reduce the risk of artificially inflated ADNs negatively impacting the availability of HUDs.

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Question 25

We encourage the FDA to work with the undersigned societies and other stakeholders to refine the definition of "pediatric population" to include elements such as radiographic measurement of skeletal development, to augment the classification of patients.

Question 31

The societies encourage their members to submit adverse event reports, when appropriate, to contribute to the orthopaedic community's understanding of device performance and to assist FDA in the early identification of potential problems. We believe there is a great need to redesign the reporting interface, to improve the accessibility and function of this important tool, thereby facilitating reporting.

Conclusion

We thank the FDA for considering our suggestions and hearing our concerns. The societies look forward to working with the FDA and other stakeholders to continue to advance the science of orthopaedic care and continuously improve patient safety and outcomes.

Sincerely,

Frederick M. Azar, MD
President, American Academy of Orthopaedic Surgeons

Kristy Weber, MD
President, Musculoskeletal Tumor Society

Gregory A. Mencio, MD
President, Pediatric Orthopaedic Society of North America