December 16, 2019

Division of Dockets Management Staff (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

Re:  Docket No. FDA-2012-N-1021; Medical Device User Fee and Modernization Act; Notice to Public of Web Site Location of Fiscal Year 2020 Proposed Guidance Development

Dear Sir or Madam:

The Advanced Medical Technology Association (“AdvaMed”) appreciates the opportunity to comment on the Center for Devices and Radiological Health’s ("CDRH’s") Fiscal Year 2020 ("FY 2020") Proposed Guidance Development.

AdvaMed is the world’s largest association representing manufacturers of medical devices, diagnostic products, and medical technology. AdvaMed’s member companies range from the largest to the smallest medical product innovators and manufacturers, with nearly 70 percent of our members generating less than $100 million in annual sales. AdvaMed's member companies produce innovations that transform health care through earlier disease detection, less invasive procedures, and more effective treatments.

We appreciate the Food and Drug Administration’s (“FDA’s” or “Agency’s”) efforts to promote transparency into its guidance priorities and to provide an opportunity for public input. Provided below is our feedback on the prioritization of the proposed FDA CDRH FY 2020 guidance documents to be developed, along with our recommendations for guidance documents that we believe should be, but were not, included in CDRH’s FY 2020 plans, and our recommendations for guidance documents that should be updated or withdrawn.

We prioritized the documents contained in FDA’s “A-List” and “B-List” according to whether they were a “high,” “medium,” or “low” priority to our member companies. As FDA can appreciate, AdvaMed’s membership comprises a breadth of manufacturers of medical devices, and we hope that our comments and additional guidance recommendations will be meaningfully considered in finalization of FDA’s guidance development priorities.¹

¹ We will not comment on guidance documents that already have been issued since the CDRH FY 2020 Priority List was published.
Part 1: FY 2020 Lists of Prioritized Medical Device Guidance Documents

Final Guidance Documents

As a general note, we recommend that FDA finalize several of the draft guidances issued in recent years. AdvaMed has submitted comments on these docket priorities and requests that FDA refer to those comments, which provide critical feedback and support meaningful implementation.

Of those final guidance documents on the “A-List,” the ones that are of highest priority to our members are:

- **Select Updates for Recommendations for Clinical Laboratory Improvement Amendments of 1988 (“CLIA”) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices:** Point-of-care (“POC”)
  diagnostics are an incredibly important aspect of today’s health care. With the increasing need for timely POC diagnostics from emerging infectious diseases to antibiotic resistance, this is a priority public health matter for physicians to have these critical tests as part of today’s modern health care system. We appreciate FDA’s reissuance of these draft guidances to support appropriate and flexible study designs and to improve the review process to support innovation and the public health. We encourage FDA to prioritize finalization on the “A-List.”

- **Recommendations for Dual 510(k) and Clinical Laboratory Improvement Amendments Waiver by Application Studies:** Point-of-care (“POC”) diagnostics are an incredibly important aspect of today’s health care. With the increasing need for timely POC diagnostics from emerging infectious disease to antibiotic resistance, this is a priority public health matter for physicians to have these critical tests as part of today’s modern health care system. We appreciate FDA’s reissuance of these draft guidances to support appropriate and flexible study designs and to improve the review process to support innovation and the public health. We encourage FDA to prioritize finalization on the “A-List.”

- **Clinical Decision Support Software:** We appreciate FDA’s reissuance of the Clinical Decision Support Software (“CDS”) Draft Guidance and encourage FDA to prioritize finalization. The draft guidance takes an important step in clarifying the types of software that are, or are not, subject to FDA’s regulatory oversight.

- **Safer Technologies Program for Medical Devices:** We support FDA’s efforts to establish a voluntary program to expedite the availability of medical devices that demonstrate significant safety improvements.

- **Device-Specific Criteria Guidance(s) for Safety and Performance Based Pathway Implementation:** We support FDA’s efforts to provide safety and performance guidance for specific device types pursuant to the Safety and Performance Based Pathway. The current 510(k) pathways (Traditional, Special and Abbreviated) have served patients and industry
well. Through legislation and changes in FDA policy, the 510(k) processes have evolved as innovation and technology have changed. FDA holds companies to high standards by ensuring that new devices meet current safety and performance expectations. Industry is committed to producing devices that meet the highest standards. This new pathway complements the current 510(k) pathways, all of which assure that patients have timely access to safe, effective and high-quality medical devices. Finalization of the existing draft guidance documents would be beneficial to facilitate use and understanding of the pathway. In finalizing the guidances, FDA should attend to the issues and proposed solutions raised in AdvaMed’s comments in response to the draft guidances.

- **Nonbinding Feedback After Certain FDA Inspections of Device Establishments:**
  Publication of this guidance is a requirement in FDARA section 702. Establishment operators face significant sanctions if they do not correct observations identified during FDA inspections. Consequently, they often invest considerable time and resources in corrections without confidence that these measures meet FDA expectations. The nonbinding feedback mechanisms better assures that proposed corrections align with FDA’s view of the remediation that should occur. The mechanism also offers establishment operators the benefit of FDA’s experience. In finalizing the guidance, FDA should attend to the issues and proposed solutions raised in AdvaMed’s comments in response to the draft guidance.

- **Multiple Function Device Products: Policy and Considerations:** We appreciate FDA’s decision to apply the policies espoused in the draft guidance to all medical devices with multiple functions, regardless of whether they contain software. In finalizing this guidance, FDA should attend to the issues and proposed solutions raised in AdvaMed’s comments in response to the draft guidance.

Of those final guidance documents on the “A-List,” we have also identified ones that were identified as “medium priority” by our members. While we support the inclusion of these on the “A-List,” they are of somewhat lower priority to our members. Those final guidances include:

- **510(k) Third-Party Review Program:** FDA should make all efforts to best leverage an effective program for all interested innovators in a manner that supports high-quality medical devices, including diagnostics, under the program.

- **Guidance on an Accreditation Scheme for Conformity Assessment of Medical Devices to FDA-Recognized Consensus Standards (“ASCA”):** FDARA requires FDA to issue final guidance to implement the pilot program. We support the Agency’s use of international voluntary consensus standards to meet regulatory requirements, which will further efforts to harmonize global medical technology regulations.
• **Recognition and/or Withdrawal of Voluntary Consensus Standards:** We support updated standards guidance to reflect the process for requesting recognition of standards, response process, and principles to consider, outlined in Sec. 3053, “Recognition of Standards,” of the 21st Century Cures Act to facilitate implementation and training.

Furthermore, we recommend moving the issuance of the following final guidances from the “B-List” to the “A-List”:

• **Replacement Reagent and Instrument Family Policy for In Vitro Diagnostic Devices:** Clear and consistent application of the FDA Replacement Reagent and Instrument Family Policy supports diagnostic innovation. This policy is not only important, but a core policy critical to advances and evolution of modern instrumentation, which are a cornerstone of patient care and promote an effective and transparent regulatory process. We greatly appreciate FDA’s issuance of the draft guidance and thoughtful consideration of policy refinement. We seek finalization of the draft guidance as soon as possible.

• **Blood Glucose Monitoring Test Systems for Prescription Point-of-Care Use:** We appreciate FDA’s reissuance as draft for comment two guidances that outline the Agency’s premarket notification expectations for blood glucose monitors to support accuracy and reliability of blood glucose monitoring test systems while also providing for innovation and continued investment in new technology. We seek prompt finalization of these guidances.

• **Self-Monitoring Blood Glucose Test Systems for Over-the-Counter Use:** We appreciate FDA’s reissuance as draft for comment two guidances that outline the Agency’s premarket notification expectations for blood glucose monitors to support accuracy and reliability of blood glucose monitoring test systems while also providing for innovation and continued investment in new technology. We seek prompt finalization of these guidances.

• **Unique Device Identification System: Form and Content of the Unique Device Identifier (UDI):** This draft guidance, issued in July 2016, is now four years old and has yet to be finalized. This guidance is needed for full implementation of the UDI system.

In addition, we have identified draft guidances for which we believe issuance of a final version should be included on the “A-List,” but final versions are not included on either the “A-List” or “B-List”:

• **Investigational IVDs Used in Clinical Investigations of Therapeutic Products:** This draft guidance helpfully outlines practical principles and key considerations for sponsors of clinical investigations of therapeutic products that also include investigational *in vitro* diagnostics (“IVDs”) and Institutional Review Boards (“IRBs”) that review these investigations.
• Developing and Labeling In Vitro Companion Diagnostic Devices for a Specific Group or Class of Oncology Therapeutic Products: AdvaMed supports FDA’s outlining in this draft guidance of considerations for the development and labeling of in vitro companion diagnostic devices to support the indicated uses of multiple drug or biologic oncology products, when appropriate.

Draft Guidance Documents

Of those draft guidance documents on the “A-List,” the ones that are of highest priority to our members are:

• Content of Premarket Submissions for Management of Cybersecurity in Medical Devices: Cybersecurity is an increasing concern for all connected medical devices. We believe it is important to understand FDA’s expectations for premarket submissions for these devices so that industry can provide adequate information for FDA review and, in partnership with FDA, help protect patients from cybersecurity threats.

• Distinguishing between Medical Device Servicing and Remanufacturing: AdvaMed continues to advocate for regulatory requirements for third-party servicers and remarketers in the interest of public health and safety. FDA indicated in its May 2018 report to Congress that it does regulate device remanufacturers and that it would issue guidance to distinguish between the two entities.

• Device-Specific Criteria Guidance(s) for Safety and Performance Based Pathway Implementation: We support FDA’s efforts to provide safety and performance guidance for specific device types pursuant to the Safety and Performance Based Pathway. The current 510(k) pathways (Traditional, Special and Abbreviated) have served patients and industry well. Through legislation and changes in FDA policy, the 510(k) processes have evolved as innovation and technology have changed. FDA holds companies to high standards by ensuring that new devices meet current safety and performance expectations. Industry is committed to producing devices that meet the highest standards. This new pathway complements the current 510(k) pathways, all of which assure that patients have timely access to safe, effective and high-quality medical devices. We support issuance of additional draft guidances addressing added device types under this pathway, including ones for in vitro diagnostics. Development and issuance of additional device-specific guidances would facilitate use and understanding of the program.

Of those draft guidance documents on the “A-List,” we have also identified ones that are of medium priority to our members. While we support the inclusion of these on the “A-List,” they are of somewhat lower priority. Those draft guidances include:

• Computer Software Assurance for Manufacturing, Operations, and Quality System Software: Programmable and automated manufacturing, operations, and quality system tools are increasingly deployed in industry and can provide overall improvement in quality systems and product quality. Guidance about the proper verification, validation,
and quality control of computer software and the Quality System Regulation would provide helpful clarity.

- **Procedures for Handling Post-Approval Studies Imposed by PMA Order (revision):** We support updating this guidance, including consideration of appropriate timelines for post-approval studies in light of lag for reimbursement, product training, patient and physician recruitment/enrollment issues and other delays in uptake of the device.

- **Postmarket Surveillance Under Section 522 of the Federal Food, Drug, and Cosmetic Act (revision):** We believe updating this guidance will provide helpful clarity regarding FDA expectations for postmarket surveillance plans and reports.

- **Unique Device Identification: Policy on Enforcement of GUDID Submission Requirements for Certain Class I Devices:** We believe issuance of this draft guidance will provide helpful clarity.

- **Pragmatic Generation of Validity Evidence for Patient-Reported Outcome Measures Used in Medical Device Submissions:** AdvaMed strongly supports FDA’s efforts to include the insights, understanding and experiences of patients and others, such as healthy patients, caregivers, and health care providers (who may themselves be patients), to assist the Agency, Sponsors and other stakeholders in improving the design of clinical trials. We believe these important stakeholders can provide invaluable input into such matters as: inclusion/exclusion criteria, endpoint identification and prioritization, the frequency and number of follow-up visits, outcomes that matter most to patients (including patient-reported outcomes), patient education materials, informed consent documents and all aspects of patient interaction/experience in a clinical trial. With patient input into these and other aspects of clinical trials, we believe we can truly partner with the patient community to improve recruitment, retention and completion of trials. We also believe this information will assist both reviewers and sponsors in better understanding the benefits and risks patients and others may associate with specific devices.

In addition, we have identified documents for which we would recommend that FDA move the issuance of a draft guidance from the “B-List” to the “A-List”:

- **Risk Categorization for Software as a Medical Device: FDA Interpretation, Policy and Considerations:** Software devices continue to be a complex area for industry to navigate and therefore any clarification FDA provides is welcomed.

Moreover, we have identified draft guidances for which we believe issuance of a draft should be included on the “A” list, but drafts are not included on either the “A-List” or “B-List”:

- **Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices:** The current guidance document is over 13 years old (2005) and software
practices have changed significantly since that time. Updating this guidance document would reflect current software development life cycle practices and documentation. Given that updating this draft guidance is a MDUFA IV commitment for which FDA already has missed the deadline, this guidance should be on the A-List.

- Leveraging Artificial Intelligence ("AI") and/or Machine Learning ("ML") in medical devices. We seek guidance on FDA thinking regarding how to leverage artificial intelligence and/or machine learning in medical devices, particularly regarding how to manage post-deployment dynamic or periodic updates to the algorithm based on new data. We request FDA’s risk-based guidance on submission content and design control evidence needed for using AI and/or ML in a medical device.

Part 2: Retrospective Review Guidances

We support FDA’s retrospective review of targeted guidances. We believe it would facilitate our development of future comments if, in future CDRH Priority lists, FDA could organize the guidances subject to the retrospective review by topic. If FDA continues to organize the retrospective review by year, we believe it would be helpful to do so in chronological order. Nonetheless, for purposes of these comments, we will generally continue to organize our input to the targeted retrospective review by year as organized by FDA.

❖ 1990

AdvaMed recommends that the following guidance document be withdrawn:

- Implantable Pacemaker Testing Guidance: This testing guidance is outdated and can be replaced by state-of-the-art, consensus ISO standards for active implantable devices that the FDA recognizes specified below. In addition, FDA also recognizes the clinical investigation consensus ISO standard for medical devices (ISO 14155).
  
  o ISO 14708-1 Implants for surgery — Active implantable medical devices: Part 1- General requirements for safety, marking and for information to be provided by the manufacturer;

  o ISO 14708-2 Implants for surgery — Active implantable medical devices: Part 2: Cardiac pacemakers; and

  o ISO 14708-6 Implants for surgery — Active implantable medical devices: Part 6: Particular requirements for active implantable medical devices intended to treat tachyarrhythmia (including implantable defibrillators).
❖ 2000

AdvaMed recommends that the following guidance documents be updated/revised:

- **Guidance Document for the Preparation of IDEs for Spinal Systems** - *Guidance for Industry and/or FDA Staff*: With the onset of additional data collection approaches, such as Real-World Data and use of registries, this guidance should be updated to incorporate these aspects. Additionally, this guidance is almost 20 years old and IDEs are prevalent in the world of spinal systems.

- **Guidance Document for Premarket Notification Submissions for Nitric Oxide Delivery Apparatus, Nitric Oxide Analyzer and Nitrogen Dioxide Analyzer**: *Guidance for Industry and for FDA Reviewers*

- **Guidance on Section 216 (six-year rule) of the Food and Drug Administration Modernization Act of 1997** - *Guidance for Industry and for FDA Reviewers*

- **Labeling for Electronic Anti-Theft Systems**: *Guidance for Industry*

- **Guidance Document for Dura Substitute Devices** - *Guidance for Industry*

❖ 2010

AdvaMed recommends that the following guidance documents be updated/revised:

- **Guidance for the Use of Bayesian Statistics in Medical Device Clinical Trials**: *Guidance for Industry and FDA Staff*: We believe this may warrant a review and update to ensure it is still up to date in light of the advances regarding *in silico* trials.

- **Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems**: *Guidance for Industry and FDA Staff*: Although there was an update in 2015, the labeling section remained the same. An update would be appropriate to address labeling and new information, such as Magnetic Resonance.

- **In Vitro Diagnostic (IVD) Device Studies - Frequently Asked Questions**: *Guidance for Industry and FDA Staff*

- **Guidance for the Non-Clinical and Clinical Investigation of Devices Used for the Treatment of Benign Prostatic Hyperplasia (BPH)**: *Guidance for Industry and Food and Drug Administration Staff*

- **Addition of URLs to Electronic Product Labeling**: *Guidance for Industry and FDA Staff*
❖ Other

AdvaMed recommends that the following guidance document be updated/revised:

- General/Specific Intended Use: Guidance for Industry: This guidance continues to be an essential document for industry and would benefit from review/revision with industry feedback, including addition of examples from the last 20 years since FDA released the guidance.

Thank you for the opportunity to submit these comments.

Respectfully Submitted,

/s/

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