May 31, 2018

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


To Whom It May Concern:

The Advanced Medical Technology Association (“AdvaMed”) appreciates the opportunity to provide input on the Food and Drug Administration’s (“FDA” or “Agency”) Digital Health Software Precertification (“Precert”) Program Working Model v0.1.1. AdvaMed represents manufacturers of digital health technologies, medical devices, and diagnostic products that are transforming health care through earlier disease detection, less invasive procedures, and more effective treatment. Our members range from the smallest to the largest medical technology innovators and companies.

We commend FDA for its ongoing efforts to create a Precert Program. If properly developed and implemented, the Precert Program has the potential to reduce pre- and post-market burdens for both software developers and FDA, and enable streamlined changes and modifications to software. Moreover, patients and consumers will benefit under the Precert program, as these important technologies will be available in a more timely manner.

AdvaMed is pleased to provide the following comments to the challenge questions contained in Section 3 of the Working Model. We anticipate submitting comments on sections 1, 2 and 4 shortly. We note that these comments represent our current thinking on this topic. As the Working Model and the broader precertification program are further developed, explained, and analyzed, our views may change and/or evolve. We also recommend that any future versions of the Working Model released for public comment include track changes to expedite review.

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AdvaMed would like to thank the FDA for its consideration of these comments and looks forward to continuing to work with the Agency on this important issue. Please do not hesitate to contact me at 202-434-7224 or zrothstein@advamed.org if you have any questions.

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Respectfully submitted,

/s/

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Attachment
3.1.1. What specific elements of review could be shifted to the company-specific excellence appraisal (as opposed to the product-specific review)?

We propose that all capabilities, commitments, practices, protocols, processes, and risk management approaches be assessed during the company-specific excellence appraisal.

Only product-specific information should be reviewed during the streamlined review, when streamlined review is required.

For example, during the excellence review, FDA can review a manufacturer’s approach to requirements planning, traceability, verification and validation (with an emphasis on V&V of the SaMD analytical performance and clinical performance as explored through beta testing), change management, and cybersecurity considerations both to software design and maintenance. Use of fit-for-purpose software tools and software engineering best practices can also be reviewed. Such elements can then be excluded from device reviews.

3.1.2. What are the features of a SaMD product that need to be assessed during device review?

When review is required, we believe that only product-specific information should be reviewed during the streamlined review. There are essentially three central product-specific questions that should be addressed during FDA review of SaMD:

1) How does the SaMD work?
2) How does the SaMD work for its intended use and intended user?
3) What is the risk analysis for the specific SaMD product?

We believe these questions can be answered in two ways – in a Description of Software and through an interactive demonstration of the performance of the SaMD with FDA.

Description of Software. The majority of the information needed for review can be captured in a modernized, high-level, robust “Description of Software,” which could be provided as a template that developers could easily complete. Within the Description, developers would provide:

- **SaMD Definition Statement** (as described in IMDRF SaMD N12 Section 6.0), which includes:
  - The significance of the information provided by the SaMD to the healthcare decision;
  - The state of the healthcare situation or condition; and
  - A description of the SaMD’s core functionality.

Review By Demo. In addition to the Description of Software, the FDA review could include a “review by demo” to demonstrate the SaMD’s performance as applicable given the SaMD description and risk analysis rather than a traditional paper review. As part of the review by demo, a decision summary could be compiled by the sponsor and FDA, which could include evidence of:

- **Analytical Validation**, such as:
  - Declaration of conformity to standards;
  - Summary of automated verification testing; and/or
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- Summary of development KPIs.

- **Clinical Validation**, such as:
  - Summary of product specific beta testing/clinical validation protocol and results (if needed); and/or
  - Summary Clinical Evaluation Report based on risk of SaMD (not always required).

If a streamlined review of SaMD is required, the process should allow such review through a demo, such as by challenging the software with real world source files or input, rather than through a traditional “paper” review. This would enable FDA to evaluate how the software performs. Due to the nature of these technologies, it is not appropriate to conduct a paper review of SaMD when an interactive demonstration can more readily address questions reviewers have and allow for real-time responses and demonstration of logic from developers.

Depending on the novelty of the SaMD, the software developer/manufacturer should have the flexibility to engage with FDA in interactive review by demo at various stages of SaMD development – from early in the development process to when the SaMD is more fully formed. Early engagement should not be required, but it can be a helpful option for novel products. For example, a developer could:

- Bring in an initial wireframe to demonstrate the intended use; and/or
- Conduct an interactive demo of an intended use case.

### 3.1.3. What product-specific content would be expected to be reviewed premarket?

See answer to 3.1.2.

### 3.1.4. What specific post-market real world data could be collected to support the assurance of safety and effectiveness for each product if an element is not reviewed premarket?

AdvaMed continues to work towards developing a response to this challenge question.

### 3.1.5. What updates should FDA require, and at what interval, to provide continuous assurance of safety and effectiveness?

FDA has asked for specific real world performance data, which should provide ongoing and up-to-date information about product performance and whether the SaMD can do what it claims it is intended to do.

Companies should collect complaints, perform trending, and conduct signal searches as well as utilize other best practices to continuously monitor the performance of their products. FDA has inspection authority and can continue to use this authority to determine whether companies are adequately tracking and monitoring their SaMD.

### 3.1.6. Should there be a phased market authorization, where some elements are reviewed premarket and other elements are gathered through real world evidence to support full market authorization? What should happen to products that receive
“preliminary” market authorization but fail to provide adequate evidence in the agreed upon timeframe?

If by phased-in market approach FDA is referring to the shift of certain performance data from the premarket to the postmarket, we agree. We would not agree with FDA use of a “conditional approval.” Instead, we would support an approval in which the benefit-risk balance enables collection of data postmarket.

3.2. Beyond number of days, what are additional key factors important for a successful streamlined review?

To be an attractive option for software developers, a streamlined review should be time-sensitive to facilitate rapid innovation and have a high level of predictability for participating companies. The following factors are important for a successful streamlined review:

- Interactive review (no hold letters or need to have submission issue meetings)
- Limited or no documentation requirements/expectations, especially as compared to typical 510(k)s or PMAs, other than the Description of Software by the company
- Hands on evaluation (i.e. review by demo) through demonstration and challenge of software by FDA software experts in collaboration with the developer
- Under current regulation, some type of decision summary, which should be developed as part of the review by demo

3.3. Once a review decision is made:

3.3.1. How should the FDA share that information with the company? With the public?

AdvaMed continues to work towards developing a response to this challenge question.

3.3.2. Should the public know that a product comes from a precertified company and if so, what is the best way to share that information?

AdvaMed continues to work towards developing a response to this challenge question.

3.4. Imagining that there is an initial, automated part of the review – what information can be provided so an initial automated review can add value?

We support a predefined template for the Description of Software, as described in 3.1.2.

3.5. A key element for streamlined review will be the communication between precertified companies and FDA. What technologies can be leveraged to support bi-directional communication?

E-mail, instant messaging, web conferences, and teleconferences could be leveraged to support communication. It will also be very important to have a portal of some type for applications, specifically to allow for interactive review and challenges of the software, as needed.

3.6. How should FDA handle an organization that submits an unsuccessful submission for premarket review? Should there be a limit on the number of unsuccessful
submissions a precertified organization can submit before their precertification status is affected?

There should not be a predefined limit, but FDA should understand the deficiencies associated with the unsuccessful submissions and use these to inform their periodic review of the organization’s Pre-Certification status. In addition, FDA should also reach out to the company to make sure that the advice and guidance is clear to the submitter, since many software developers may not be familiar with FDA review processes. Furthermore, if FDA is considering the use of a submission portal of some type, there may also be technical reasons for unsuccessful submissions which may not correlate to a compromised product or quality status (e.g., not actually being received).

3.7. Could FDA conduct a premarket review without requiring a premarket submission and if so, how, e.g., by accessing and interactively reviewing information internal to the precertified organization about the SaMD?

Yes. This could be achieved by having manufacturers submit required review information to an FDA website or portal or by a manufacturer granting FDA electronic access to certain documents. It is important to note that, under current regulation, it may be difficult for FDA to utilize a process that does not involve at least a short notification or submission, so changes to the existing law may be required.

3.7.1. What are possible methods to facilitate FDA access to necessary information?

See response to 3.5.

3.7.2. Is there information other than risk management, technical evaluation, and clinical evaluation necessary for such a review to assure safety and effectiveness of the SaMD?

We believe information on the risk management process can be shifted to the excellence appraisal. The review of product specific information for SaMD should include the Description of Software. The review by demo should ideally be able to address most other requirements, such as analytical and clinical validation.

3.7.3. How should the reviewed information relevant to the marketing authorization decision be documented for administrative purposes?

A summary of that information could be shared using a decision summary compiled during the review by demo.

3.8. Is premarket clinical performance necessary to assess SaMD safety and effectiveness? Please explain your answer and provide your rationale.

The level of clinical evaluation and importance of independent review should be commensurate with the risk posed by the SaMD. If clinical claims are made, then supporting information is required. It is important to note that there is a wide range of evidence (including beta testing) that may support clinical claims, and as emphasized in the FDA SaMD Clinical Evaluation Guidance, independent review varies in its importance based on the risk of the SaMD.
3.9. Should FDA be informed about new products, major changes, and minor changes from precertified organizations that do not undergo premarket review, and how?

FDA should be informed of major changes only, and only if a review is required for the initial product.