July 12, 2023

Mr. Richard M. Karcich
[redacted]

Re: Citizen Petition – Docket Number FDA-2013-P-0199

Dear Mr. Karcich:

This letter responds to your petition, received on February 15, 2013, by the Food and Drug Administration (FDA or the Agency).

I. Actions Requested

In the petition, you request "the Commissioner of Food and Drugs to issue new regulations or amend existing regulations covering measurement of the safety and reliability of the software in medical devices." You specifically ask FDA to issue or amend their regulations to "[adopt] measurement of code change activity and test activity as a basis for improving software fault management in medical device software." You state that "manufacturers will then develop an approach that predictably meets release schedules with known safety and reliability and focus on the organization's business objectives while improving patient outcomes."

In support of your petition, you incorporate by reference various pieces of information. Specifically, you direct FDA to information located at two web links at https://www.linkedin.com and https://dropbox.com. FDA was not able to access the information you reference. Further, incorporation by reference of this kind is not accepted as support for a petition under 21 CFR Part 10.20(c). However, FDA has reviewed and considered all the statements provided in your petition.

In accordance with 21 CFR 10.30(e), and for the reasons described below, we are denying your petition.

II. Statutory and Regulatory Background

FDA has long regulated software that meets the definition of a device in section 201(h)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act),[1] also referred to as a device software function.

[1] 21 U.S.C. 321(h)(1).

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Device software functions are subject to, among other requirements in the FD&C Act and its implementing regulations, the requirements of the Quality System regulation (QS regulation). [2] The QS regulation requires manufacturers of finished medical devices to review and approve changes to device design and production[3], and document changes and approvals in the device master record.[4] Any process whose results cannot be fully verified by subsequent inspection and testing must be validated,[5] and changes to the process require review, evaluation, and revalidation of the process where appropriate.[6] Software validation requires the establishment, maintenance, and/or documentation of validation protocols and validation records for software and software changes. When computers or automated data processing systems are used as part of production or the quality system, manufacturers must validate computer software for its intended use according to an established protocol.[7] All software changes must be validated before approval and issuance, and validation activities must be documented.[8] In addition, the Corrective and Preventive Action (CAPA) requirement in the QS regulation[9] requires manufacturers to analyze information, identify and investigate product and quality problems, and take appropriate and effective corrective and/or preventive action to prevent their recurrence.

Software modifications are considered design changes under the QS regulation.[10] The design control requirements[11] apply to all classes of devices automated with computer software. There are specific design controls requirements focused on the proper specification, risk management, verification and validation of a device and its software.[12] The QS regulation requires manufacturers to manage risks that may be associated with the use of their device software functions.

In addition to the above regulatory requirements, there are also a number of FDA guidance documents relating to software that provide the digital health industry with recommendations on a variety of topics.[13]

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[2] See 21 CFR Part 820.
[3] 21 CFR 820.30 and 820.70.
[4] 21 CFR 820.181.
[5] 21 CFR 820.75.
[6] 21 CFR 820.75(c).
[7] 21 CFR 820.70(i).
[8] *Id.*
[9] 21 CFR 820.100.
[10] Some design changes may require submission of a new 510(k) premarket notification to the Agency. For additional information, see *Deciding When to Submit a 510(k) for a Software Change to an Existing Device*, *Guidance for Industry and FDA Staff* (October 2017) available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/deciding-when-submit-510k-software-change-existing-device.
[11] 21 CFR 820.30.
[12] 21 CFR 820.30.
[13] These include, but are not limited to, the information sponsors should include in their premarket submissions for device software functions, clinical evaluation of software, cybersecurity, and policy considerations for multiple function software products. These FDA guidances, and others with digital health content, are available at https://www.fda.gov/medical-devices/digital-health-center-excellence/guidances-digital-health-content.

III. Discussion

A. FDA regulatory requirements address the safety and effectiveness of device software functions, including requirements for management of change activities

In your petition, you state that you analyzed a Class 1 recall of a medical device and posit how "1) measurement of change activity in the static domain, 2) measurement of test activity in the dynamic domain, and 3) measurement of the size and character of software faults could supplement/complement the discovery (prior to release) of the software faults…" You further suggest "that unexamined code permitted the software faults to remain" and that "static analysis would provide direct information on where code problems are likely to be." You say that measurement of change activity would allow a manufacturer to be "able to isolate the precise version where the faulty code responsible for the software failure was introduced." You propose that isolating root cause of failure would be easier if we knew in which version the fault causing software failure occurred.

FDA's existing regulations help ensure the safety and effectiveness of software device functions, including management of change activity and testing. In particular, the QS regulation [14] requires manufacturers to establish and follow a quality system to help ensure their devices, including device software functions, meet quality and safety requirements. The QS regulation also requires that manufacturers develop and follow procedures that are appropriate for a given device and its risks, which may include change management procedures for software device functions. It also allows for flexibility in the application of appropriate controls and risk management. In so doing, this allows FDA to keep pace with the industry, evolving technology, and clinical applications. [15]

It is the responsibility of each manufacturer to establish methods and procedures to design, produce, and distribute devices that meet the requirements of the QS regulation, [16] including those relating to design controls. As described in "Design Control guidance for Medical Device Manufacturers," (published in 1997) [17] "[d]esign control applies to all changes to the device or manufacturing process design, including those occurring long after a device has been introduced to the market." Changes are part of a continuous, ongoing effort to design and develop a device that meets the needs of the user and/or patient, such that the design control process is revisited throughout the life of a product.

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[14] 21 CFR Part 820.

[15] As noted in its Preamble, the QS regulation intends to provide "the flexibility necessary to allow manufacturers to adopt advances in technology, as well as new manufacturing and quality system procedures, as they become available." Medical Devices; Current Good Manufacturing Practice (CGMP) Final Rule; Quality System Regulation, 61 FR 52602, 52605 (October 7, 1996). Further, "FDA attempted to write the current regulation with at least the same degree of flexibility, if not more, to allow manufacturers to design a quality system that is appropriate for their devices and operations and that is not overly burdensome." See id. At 52607.

[16] 21 CFR Part 820.

[17] *Design Control guidance for Medical Device Manufacturers* (March 1997) available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/design-control-guidance-medical-device-manufacturers.

One way FDA addresses the management of change activity is through the corrective and preventive action, or CAPA, requirement.[18] The CAPA requirement specifically requires the following:

- Investigation of the cause of nonconformities relating to product, processes, and the quality system;
- Identification of the action(s) needed to correct and prevent recurrence of nonconforming product and other quality problems;
- Verification or validation of the corrective and preventive action to ensure that such action is effective and does not adversely affect the finished device;
- Implementation and recording of changes in methods and procedures needed to correct and prevent identified quality problems; and
- Employment of appropriate statistical methodology where necessary to detect recurring quality problems

B. FDA has issued recommendations in guidance regarding the content of premarket submissions for device software functions addressing management of change activity

FDA guidance titled "Content of Premarket Submissions for Device Software Functions" (June 2023),[19] discusses the recommended documentation sponsors should include in premarket submissions for review of the safety and effectiveness of device software functions, while recognizing changes to the FD&C Act as amended by the 21st Century Cures Act. In particular, the guidance recommends that sponsors include information in their premarket submissions on change management procedures. The guidance describes configuration or change management as an important aspect of software development. Specifically, the guidance recommends manufacturers include information regarding processes and procedures to manage the software life cycle development, software configuration and change management, and software maintenance, such as risk assessment of software changes, initial testing that evaluates the correctness of the implemented software change(s), and regression analysis and testing.

C. FDA's comprehensive approach to verification and validation of device software functions includes and goes beyond measurement of test activity

In the petition, you recommend adopting measurement of test activity to improve software medical device fault management. Typically, testing alone cannot fully verify that software is complete and correct. Rather, software testing is one of several verification activities intended to confirm that the software development output meets its input requirements. Software verification

[18] 21 CFR 820.100.
[19] *Content of Premarket Submissions for Device Software Functions* (June 2023) available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/content-premarket-submissions-device-software-functions.

involves evaluating the "consistency, completeness, and correctness of the software and its supporting documentation, as it is being developed, and provides support for a subsequent conclusion that software is validated." [20] FDA guidance on "General Principles of Software Validation" (January 2002) further clarifies that "verification activities include various static and dynamic analyses, code and document inspections, walkthroughs, and other techniques." The guidance also notes that most "software problems are traceable to errors made during the design and development process."[21] In the guidance, FDA addresses this issue and describes its approach to evaluating a software system and its interpretation of how certain provisions of the QS regulation apply to software. As the guidance notes, testing, planning, verification, traceability, configuration management, and many other aspects of good software engineering help to support a final conclusion that software is validated.[22] Further, while this guidance does not recommend any specific life cycle model or any specific technique or method, it does recommend that software validation and verification activities be conducted throughout the entire software life cycle.

IV. Conclusion

FDA's existing regulations and guidance, noted above, help ensure the safety and effectiveness of software medical devices, including reliability and management of change activity and testing. Therefore, FDA is not at this time issuing specific new regulations or amending existing regulations in this area.

For the reasons outlined in this response, FDA denies your Petition. If you have any questions about this response, please contact Samantha Collado of our Office of Policy at 240-402-6607 or by email at Samantha.LohCollado@fda.hhs.gov.

Sincerely,

Ellen J. Flannery -S Digitally signed by Ellen J. Flannery -S Date: 2023.07.12 14:07:39 -04'00'

Ellen J. Flannery, JD
Deputy Center Director for Policy
Director, Office of Policy
Center for Devices and Radiological Health

[20] Section 3.3 of *General Principles of Software Validation; Final Guidance for Industry and FDA Staff* (January 2002) available at https://www fda.gov/regulatory-information/search-fda-guidance-documents/general-principles-software-validation.
[21] Section 3.3 of *General Principles of Software Validation; Final Guidance for Industry and FDA Staff* (January 2002) available at https://www fda.gov/regulatory-information/search-fda-guidance-documents/general-principles-software-validation.
[22] *General Principles of Software Validation; Final Guidance for Industry and FDA Staff* (January 2002) available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/general-principles-software-validation.