

This guidance is intended to remain in effect until November 7, 2023, unless superseded by a revised final guidance before that date. For further information, refer to 88 FR 15417, March 13, 2023, available at <https://www.federalregister.gov/d/2023-05094>.

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Coagulation Systems for Measurement of Viscoelastic Properties: Enforcement Policy During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency (Revised)

Guidance for Industry and Food and Drug Administration Staff

**January 14, 2021
Updated January 28, 2021**

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health (CDRH)
Office of Product Evaluation and Quality (OPEQ)**

Preface

Public Comment

This guidance is being issued in response to the Coronavirus Disease 2019 (COVID-19) public health emergency. This guidance is being implemented without prior public comment because the Food and Drug Administration (FDA or the Agency) has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and 21 CFR 10.115 (g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices.

Comments may be submitted at any time for Agency consideration. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to <https://www.regulations.gov>. All comments should be identified with the docket number FDA-2020-D-1138 and complete title of the guidance in the request.

Additional Copies

Additional copies are available from the FDA webpage titled "COVID-19-Related Guidance Documents for Industry, FDA Staff, and Other Stakeholders," *available at* <https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders>, and the FDA webpage titled "Search for FDA Guidance Documents," *available at* <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>. You may also send an e-mail request to CDRH-Guidance@fda.hhs.gov to receive an additional copy of the guidance. Please include the document number 20041-R1 and complete title of the guidance in the request.

Questions

For questions about this document, contact Takeesha Taylor-Bell, Acting Deputy Director, Office of Health Technology 7, Division of Immunology and Hematology Devices, at 240-402-6566 or takeesha.taylor-bell@fda.hhs.gov.

Table of Contents

I.	Introduction.....	4
II.	Background.....	5
III.	Scope.....	6
IV.	Policy	6
	A. Modifications to Indications, Hardware and Software.....	7
	B. Labeling of Modified Devices.....	9

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Guidance for Industry and Food and Drug Administration Staff

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

I. Introduction

FDA plays a critical role in protecting the United States from threats such as emerging infectious diseases, including the Coronavirus Disease 2019 (COVID-19) pandemic. FDA is committed to providing timely guidance to support response efforts to this pandemic.

FDA is issuing this guidance to provide a policy to help expand the availability of coagulation systems for measurement of whole blood viscoelastic properties that are used to assess hemostasis, for the duration of the COVID-19 public health emergency. This document updates the guidance of the same title issued on January 14, 2021.

This policy is intended to remain in effect only for the duration of the public health emergency related to COVID-19 declared by the Secretary of Health and Human Services (HHS) on January 31, 2020, effective January 27, 2020, including any renewals made by the HHS Secretary in accordance with section 319(a)(2) of the Public Health Service Act (PHS Act) (42 U.S.C. 247d(a)(2)).

Given this public health emergency, and as discussed in the Notice in the *Federal Register* of March 25, 2020, titled "Process for Making Available Guidance Documents Related to Coronavirus Disease 2019," available at <https://www.govinfo.gov/content/pkg/FR-2020-03-25/pdf/2020->

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[06222.pdf](#), this guidance is being implemented without prior public comment because FDA has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 371(h)(1)(C)) and 21 CFR 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices.

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA guidance means that something is suggested or recommended, but not required.

II. Background

There is currently an outbreak of respiratory disease caused by a novel coronavirus. The virus has been named "SARS-CoV-2" and the disease it causes has been named "Coronavirus Disease 2019" (COVID-19). On January 31, 2020, HHS issued a declaration of a public health emergency related to COVID-19 and mobilized the Operating Divisions of HHS.¹ In addition, on March 13, 2020, there was a Presidential declaration of a national emergency in response to COVID-19.²

Hypercoagulability, an abnormally increased risk for blood clotting, has been observed in patients with COVID-19. Laboratory abnormalities commonly observed among hospitalized patients with COVID-19 associated coagulopathy include: mild thrombocytopenia, increased D-dimer levels, increased fibrin degradation products, and prolonged prothrombin time.³ Hypercoagulability has been most notably reported in COVID-19 patients with acute respiratory distress syndrome (ARDS).⁴ FDA believes the policy set forth in this guidance will help address these urgent public health concerns by helping to expand the availability and capability of coagulation systems for measurement of whole blood viscoelastic properties. Coagulation systems for measurement of whole blood viscoelastic properties can help identify changes in coagulation status and are used routinely as an aid in the assessment of hemostasis in the perioperative period of select surgical procedures and in the assessment of bleeding and thrombosis following a traumatic injury or event. Modified use of these devices in hospital patient healthcare settings may increase access to important examination of whole blood viscoelastic properties to facilitate patient management by healthcare providers during the COVID-19 public health emergency.

¹ Secretary of Health and Human Services, Determination that a Public Health Emergency Exists (originally issued Jan. 31, 2020, and subsequently renewed), *available at*

<https://www.phe.gov/emergency/news/healthactions/phe/Pages/default.aspx>.

² Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19) Outbreak (Mar. 13, 2020), *available at* <https://trumpwhitehouse.archives.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/>.

³ <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html>

⁴ Wu, Chaomin, MD, Chen, Xiaoyen, MD, and Cai, Yanping, MD. (2020) "Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China." *JAMA Intern Med.* 180(7):934-943. doi:10.1001/jamainternmed.2020.0994, *available at* <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2763184>.

III. Scope

The enforcement policy described in Section IV of this guidance applies to the legally marketed coagulation systems listed in Table 1 intended for use in measuring the dynamics of clot formation, firmness, and dissolution as affected by the kinetics of thrombin generation, platelet activation, fibrin generation, clot strength, clot stability, and inhibitory effects in whole blood, and that have been subsequently modified to facilitate patient management by healthcare providers during the COVID-19 public health emergency. The output for these coagulation systems consists of semi-quantitative results and a graphical display (e.g., tracing or curve) that demonstrates the kinetic changes of whole blood as it clots over time.

Table 1

Device Type	Classification Regulation	Product Code	Class
Multipurpose system for in vitro coagulation studies	21 CFR 864.5425	JPA ⁵	II
Coagulation system for the measurement of whole blood viscoelastic properties	21 CFR 864.5430 ⁶	QFR	II

IV. Policy

As hypercoagulability has been observed in patients with COVID-19, FDA recognizes the importance and utility of increased availability of devices to test for and manage coagulopathies in patients in hospitals and other healthcare facilities, which are experiencing increased patient load due to the COVID-19 public health emergency. In developing this policy, FDA's intent is to foster the continued availability of safe and effective medical devices while being flexible regarding certain modifications made to coagulation systems for measurement of whole blood viscoelastic properties to include use in hospital patient healthcare settings in response to the COVID-19 public health emergency. Currently, coagulation systems for measurement of whole blood viscoelastic properties have not been cleared or approved for use in hospital patient healthcare settings.

FDA recognizes that expanded use of coagulation systems for measurement of whole blood viscoelastic properties may help facilitate the assessment of hemostasis beyond the perioperative and trauma settings. Thus, FDA does not intend to object to limited modifications to the

⁵ This product code includes several different types of coagulation systems. This guidance specifically addresses devices with intended use(s) and technological characteristics described in Section III. Coagulation systems that do not have the intended use(s) and technological characteristics described in Section III are outside the scope of this guidance (e.g. coagulometers that perform coagulation screening and/or anticoagulation monitoring tests on plasma and/or whole blood using clotting, chromogenic, immunoturbidimetric, or chemiluminescent detection methods).

⁶ This classification regulation is subject to special controls, including general performance testing/validation requirements. See 21 CFR 864.5430. The special controls associated with this classification regulation remain in effect during the declared public health emergency, and the policy set forth in this guidance does not apply to compliance with those requirements. The special controls for this classification regulations can be found at <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/denovo.cfm?id=DEN180017>.

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indications, functionality, hardware, and/or software of the coagulation systems for measurement of whole blood viscoelastic properties that are within the scope of this guidance as identified in Section III, without prior submission of a premarket notification under section 510(k) of the FD&C Act and 21 CFR 807.81,⁷ where the modification does not create an undue risk to the patient in light of the public health emergency.⁸ This policy applies where a modification is made to the device that would typically require that a manufacturer submit a new 510(k) submission to FDA.

Manufacturers must document changes to their device in their device master record and change control records and make this information available to FDA, if requested, as required by 21 CFR 820.30 and 21 CFR 820.180.

This policy does not apply to compliance with other requirements, including reports of corrections and removals in 21 CFR Part 806, medical device reporting under 21 CFR Part 803, and *in vitro* diagnostics (IVD) labeling requirements under 21 CFR Parts 801 and 809, among others.

A. Modifications to Indications, Hardware and Software

Based on current information and experience, FDA believes the following hardware and software architecture modifications to the devices listed in Table 1 would not create an undue risk to the patient in light of the public health emergency:

- 1) Expansion of indications for use beyond the cleared indications (to assess coagulation status of perioperative and trauma patients) to include hospitalized patients suspected of a COVID-19 associated coagulopathy;
- 2) For viscoelastic devices previously cleared or approved only for use in hospital clinical laboratories, a change to the indication for use to include use in hospital patient healthcare settings by trained healthcare professionals; or
- 3) Hardware or software modifications that support relocation of these devices to not previously reviewed or cleared hospital patient healthcare settings with testing performed by trained healthcare professionals, or hardware or software modifications intended to reduce electromagnetic emissions in confined spaces in order to prevent electromagnetic interference with surrounding systems.

Based on current information and experience, FDA believes a modification would not create undue risk to the patient in the following scenario:

- 1) The device is intended for the purpose of supporting and providing adjunctive patient management recommendations to the healthcare professional about treatment of COVID-19

⁷ For further guidance on modifications that trigger the requirement that a manufacturer submit a new premarket notification (510(k)) to FDA, refer to “Deciding When to Submit a 510(k) for a Change to an Existing Device: Guidance for Industry and Food and Drug Administration Staff,” available at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/deciding-when-submit-510k-change-existing-device>.

⁸ Certain modifications to the indications, functionality, or hardware or software of the exempt devices in Table 1 may require premarket notification subject to the limitations of the exemption under 21 CFR 864.9.

Contains Nonbinding Recommendations

or co-existing conditions; and

- 2) The healthcare provider can independently review the basis for any diagnostic or treatment recommendations.

Based on current information and experience, the following are examples of modifications which FDA believes would create an undue risk to the patient:

- 1) Changes made to the hardware or software that directly affect the measuring capabilities and functionality of viscoelastic devices; or
- 2) The modified device is intended to be solely or primarily relied upon by the healthcare professional to make a clinical diagnosis or treatment decision pertaining to COVID-19 or co-existing conditions.

Quality System (QS) regulation design controls require manufacturers to conduct verification and validation (21 CFR 820.30(f) and (g)), including establishing and maintaining procedures to ensure that design outputs meet design input requirements and that devices conform to defined user needs and intended uses. Such verification and validation should be performed for all changes made under the enforcement policy described in this guidance document. In designing, evaluating, and validating changes made to the intended use setting, hardware, or software, FDA recommends considering the following FDA-recognized consensus standards for the specific device type, including (as applicable):⁹

- International Electrotechnical Commission (IEC) 60601-1-2– Medical Electrical Equipment Part 1-2: General Requirements for Basic Safety and Essential Performance – Collateral Standard: Electromagnetic Disturbances – Requirements and Tests
- IEC 61010-1 – Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 1: General requirements

In addition, for any such changes, manufacturers should ensure appropriate cybersecurity controls are in place to ensure device cybersecurity and maintain device functionality and safety. The following online resources may be helpful in developing and maintaining these cybersecurity controls:

- [Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices](#);¹⁰
- [Content of Premarket Submissions for Management of Cybersecurity in Medical Devices](#);¹¹
- [Postmarket Management of Cybersecurity in Medical Devices](#);¹²

⁹ For the current edition of the FDA-recognized consensus standard(s) referenced in this document, see the FDA Recognized Consensus Standards Database at

<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>.

¹⁰ Available at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-content-premarket-submissions-software-contained-medical-devices>.

¹¹ Available at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/content-premarket-submissions-management-cybersecurity-medical-devices-0>.

¹² Available at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/postmarket-management-cybersecurity-medical-devices>.

Contains Nonbinding Recommendations

- [FDA Fact Sheet: The FDA's Role in Medical Device Cybersecurity – Dispelling Myths and Understanding Facts.](#)¹³

B. Labeling of Modified Devices

Coagulation systems for measurement of viscoelastic properties are devices subject to the labeling requirements in 21 CFR Parts 801 and 809, and the labeling requirements in the special controls for these devices identified under 21 CFR 864.5430. Manufacturers should refer to those regulations for a complete list of labeling requirements for *in vitro* diagnostic devices. In addition, FDA recommends that the devices modified as described in this guidance use labeling that helps users better understand the device modifications. FDA recommends that the labeling include the following elements to help ensure that such devices do not create an undue risk to the patient and to help users understand the device modification(s) under this policy.

- 1) A detailed description of the changes to the device from the specifications that were cleared or granted marketing authorization by FDA, including:
 - a. a detailed explanation of which indications for use have been FDA-cleared or granted marketing authorization and which, if any, have not;
 - b. changes to functionality, if any;
 - c. changes to hardware, and/or software, if any;
 - d. information on the new specific performance characteristics and new risks to health; and
 - e. instructions for mitigating any known risks associated with these differences.
- 2) Adequate instructions for use for the intended user and indicated environment(s) of use, including, if appropriate, instructions specific to hospital patient healthcare settings.
- 3) The minimum installation and qualification testing to be performed during installation to ensure that the modified device will perform as intended after installation.
- 4) The minimum post-installation inspection, calibration, testing, and maintenance to be performed to provide reasonable assurance of proper installation and safe and effective operation of the modified product.
- 5) A prominent and clear statement that results generated by the devices are adjunctive (supporting) and should not be solely or primarily relied upon to diagnose or treat COVID-19 associated coagulopathy.
- 6) A prominent and clear statement that the device is not indicated for the diagnosis of COVID-19.
- 7) A prominent and clear statement that all results are intended to be interpreted by a licensed healthcare practitioner with the appropriate training.
- 8) For devices that require manual sample or reagent pipetting and where the pipette is not supplied with the device system, a prominent and clear statement to the user that only appropriately calibrated pipettes should be used per the instructions for use of the applicable device system.

¹³ Available at <https://www.fda.gov/media/123052/download>.

Contains Nonbinding Recommendations

- 9) A prominent and clear statement to highlight that the device has been evaluated for interfering substances that may potentially be relevant to the expanded patient population and hospital patient healthcare settings (e.g., antiphospholipid antibodies) and a list of interfering substances that have not been tested for, if any.