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Quarterly Medical Device Warning Letters Update: January – March 2024

June 11, 2024

Medical Devices and Diagnostics

This client alert is the first in a series of alerts summarizing trends and otherwise notable allegations in publicly available FDA warning letters relating to medical devices. This alert summarizes trends in the warning letters issued in the first quarter of 2024 (January through March).[1]

As of June 11, 2024, FDA issued fourteen warning letters alleging violations of the Food, Drug, and Cosmetic Act (FDCA) related to medical devices.[2] Key trends and otherwise notable allegations in the warning letters this quarter include:

1. **Most Commonly Cited Violations**: Ten of the fourteen letters allege violations of the quality system regulations (QSR), eight of which specifically allege violations of design controls, with a particular focus on risk analyses under 21 CFR 820.30(g) and design changes under 21 CFR 820.30(i) (four letters each). For example, FDA alleges that Exactech failed to ensure that all applicable or potential failure mode codes were selected when calculating health risk and analyzing complaint data for design validation in violation of 21 CFR 820.30(g). FDA also issued five letters alleging violations of corrective and preventive action (CAPA) requirements under 21 CFR 820.100.

2. **Violations for Observations Not Included in Form 483:** In the Augustine warning letter, FDA alleges several violations of medical device report (MDR) requirements that were not included as inspectional observations in the Form 483 that preceded the warning letter. Specifically, FDA alleges that the company's MDR procedures were inadequate because, among other things, they did not include key definitions, and that the company failed to submit an MDR after a healthcare provider reported a second degree burn that required debridement and a skin graft. FDA concludes that the

[1] This alert summarizes some of the allegations contained in FDA's letters. It does not contain any analyses, opinions, characterizations, or conclusions by Covington & Burling LLP. The information presented herein does not necessarily reflect the views of Covington & Burling LLP or any of its clients.

[2] These warning letters include only those that were publicly posted by FDA as of the date listed, including: CMS #671249 (Jan. 4, 2024), CMS #667193 (Jan. 8, 2024), CMS #669904 (Jan. 19, 2024), CMS #673465 (Jan. 26, 2024), CMS #675069 (Jan. 29, 2024), CMS #657073 (Jan. 31, 2024), CMS #673150 (Feb. 7, 2024), CMS #676605 (Feb. 23, 2024), CMS #678042 (Mar. 15, 2024), CMS #677524 (Mar. 18, 2024), CMS #677753 (Mar. 18, 2024), CMS #677545 (Mar. 18, 2024), CMS #665159 (Mar. 21, 2024), and CMS #671243 (Mar. 21, 2024). Late posted letters will be addressed in a future client alert.

company's responses were "not adequate" because they did not address these observations, even though FDA acknowledges that the observations were "not included in the FDA Form 483."

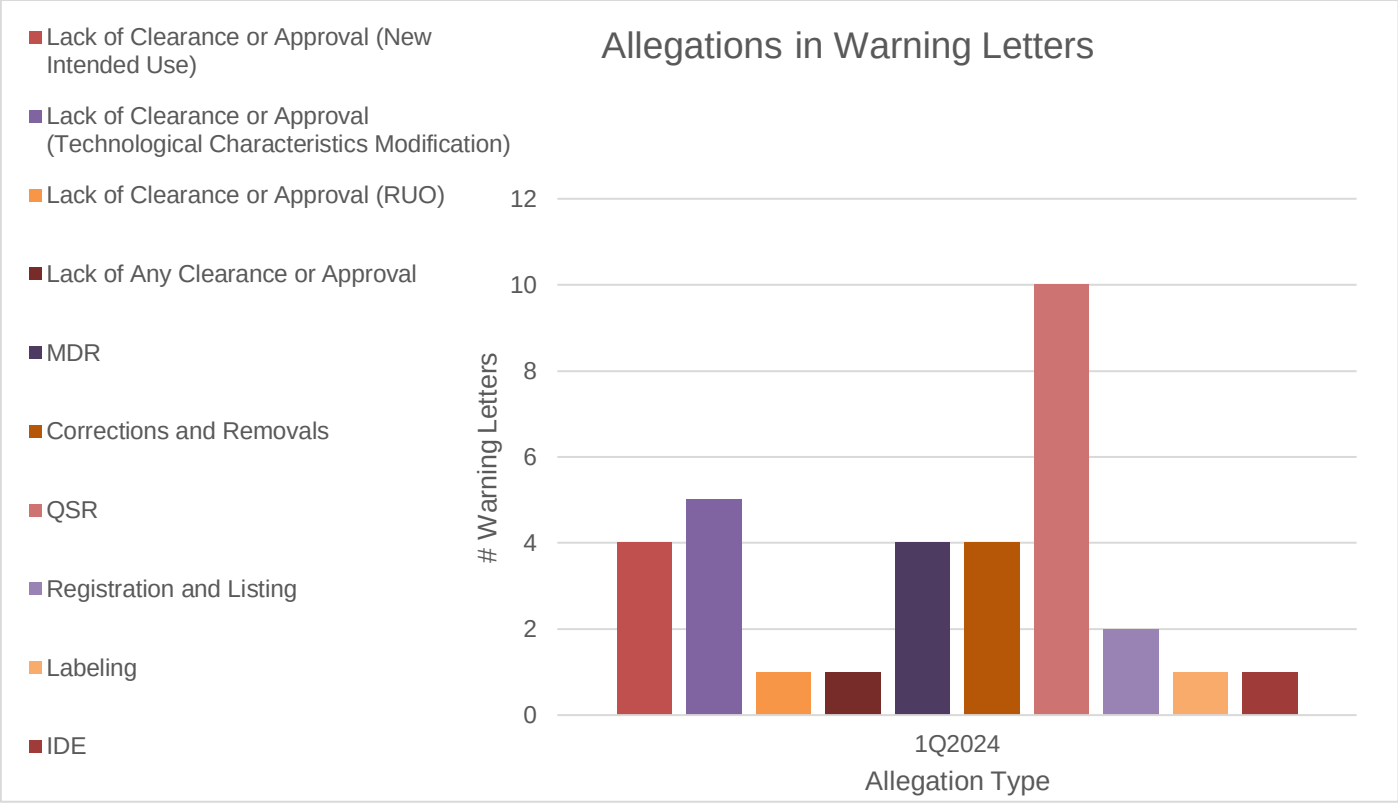
3. **Lack of Clearance or Approval for Research Use Only (RUO) Product:** In the Agena Biosciences letter, FDA alleges that the company was marketing a new device that lacked clearance or approval, and that the device was not for "research use only" (RUO), as the company claimed. Specifically, FDA alleges that the company's iPLEX HS Colon Panel intended for use with the MassARRAY4 System (MA4) (together, iPLEX on MA4) is either a new device that lacks clearance or approval or a significantly modified version of the firm's Impact DX™ Factor V Leiden and Factor II Genotyping Test on the IMPACT Dx™ System (IMPACT Dx), cleared under K132978. FDA states that although Agena claims the iPLEX HS Panel and MA4 are labeled as RUO, such "disclaimers ... are inconsistent with the evidence obtained during [FDA's] inspection and statements identified on [Agena's] website." FDA asserts that evidence of clinical use of the iPLEX on MA4 includes: verbal statements made to the FDA investigator during the inspection that the IMPACT Dx has been replaced with the MA4 system; distribution records and customer lists indicating shipment to clinical testing laboratories; a customer notification alerting customers to an increase in false negative results; the iPLEX HS Colon Panel user guide with instructions for interpreting reports; website statements making clinical claims; and customer stories on the website discussing clinical use.

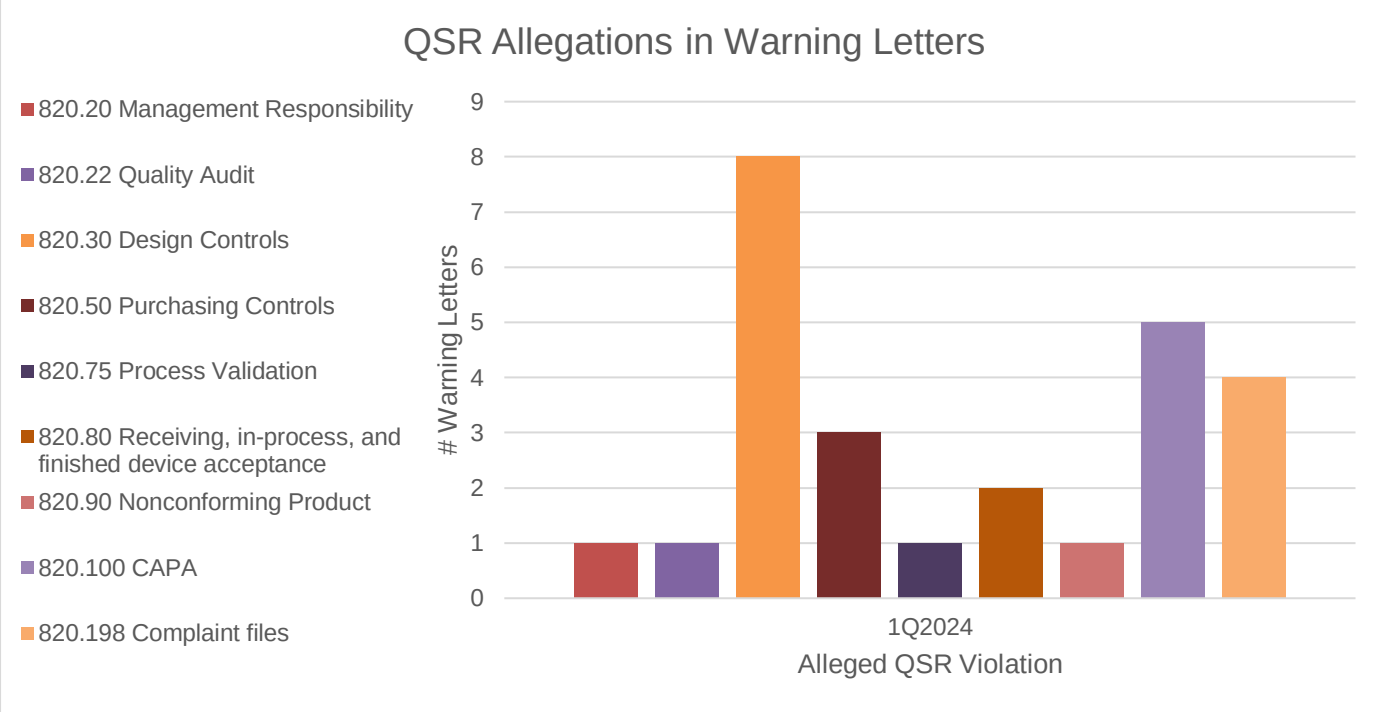
4. **Warning Letters for Modified Syringes from China:** This quarter, FDA issued three warning letters related to the Agency's ongoing concerns with plastic syringes manufactured in China. In November 2023, FDA issued a safety communication to consumers, health care providers, and health care facilities noting quality issues associated with several Chinese manufacturers of syringes. On March 18, 2024, FDA issued three warning letters associated with plastic syringes manufactured in China, alleging, among other things, that the syringes were significantly modified without clearance or approval. Two of the letters also allege violations of the QSR.

5. **Registration & Listing Violations**: Two warning letters allege violations of the FDCA's registration and listing requirements. The Sol-Millenium letter alleges failure to register three manufacturing establishments: one that performs complaint handling, and two that perform specification development. FDA also alleges that Sol-Millenium's devices are misbranded to the extent they are labeled with the address of a former headquarters, rather than the actual location of manufacturing, packing, or distribution or the principal place of business.

6. **Violations of Investigational Device Exemption (IDE) Requirements:** The warning letter issued to Nobles Medical Technology II, Inc. alleges that the company violated IDE requirements in the conduct of their significant risk clinical study of the device NobleStitch EL. Specifically, FDA alleges that Nobles failed to provide investigators with necessary information, to ensure that investigators were qualified, to obtain signed investigator agreements, and to provide financial disclosure records for sites. FDA states that similar observations were found at another clinical trial site and notes that "discrepant and unclear information has been provided regarding fundamental aspects of [the] study ... as well as safety and effectiveness information" in annual reports for the IDE.

The allegations in the warning letters sent this quarter can be grouped into the following categories:





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