Inspections, Compliance, Enforcement, and Criminal Investigations

Mindray DS USA, Inc. d.b.a. Mindray North America 11/29/12

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Central Region
Waterview Corporate Center
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054
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November 29, 2012

WARNING LETTER

VIA UNITED PARCEL SERVICE

David A. Gibson
President & CEO
Mindray DS USA, Inc.
800 MacArthur Blvd
Mahwah, New Jersey 07430

13-NWJ-03

Dear Mr. Gibson:

During an inspection of your firm located in Mahwah, New Jersey, on June 11, 2012 through August 02, 2012, an investigator from the United States Food and Drug Administration (FDA) determined that your firm manufactures Class II medical devices such as patient monitors, chemistry analyzers and ultrasound systems. Under Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. § 321(h), these products are devices because they are intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or are intended to affect the structure or function of the body.

The inspection revealed that the devices are adulterated within the meaning of section 501(h) of the Act [21 U.S.C. § 351(h)] in that the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformity with the Current Good Manufacturing Practice (cGMP) requirements of the Quality System (QS) regulation found at Title 21, Code of Federal Regulations (CFR), Part 820.

We received a response from Mr. Russell Olsen, Vice President, Quality and Regulatory Affairs dated August 23, 2012, concerning our investigator's observations noted on the Form FDA 483 (FDA 483) that was issued to your firm. We address this response below, in relation to each of the noted violations.
These violations include, but are not limited to, the following:

1. Failure to adequately establish procedures for corrective and preventive action, pursuant to 21 CFR 820.100(a). For example:

A. Your firm replaced at least 17 units of the V-Series monitors with failed touch screens between 11/19/2011 through 06/08/2012, which caused the user interface to be inoperable. Recent examples of V-Series (V21) Monitoring Systems with failed touch screens include EG-06000182, EG-06000183, EG-06000190, and EG-06000191. Your firm had not completed any corrective or preventive actions and had not evaluated the effectiveness of your supplier's corrective actions.

B. Your firm released at least 103 units of DPM 6/Beneview T5 Patient Monitors, which had cracked bezels. Your firm had not completed any corrective or preventive actions for this issue, in which the DPM 6 monitor supplier attributed to the material used for manufacturing the front housing of the device after finding that the plastic studs on the front housing frequently rupture or break during manufacturing.

C. Your firm failed to conduct adequate CAPA investigations for failed NIBP modules of Spectrum, Passport V, and Passport 2 Monitors. For example, your firm had at least 12 Discrepant Material Reports, generated between 08/2010 and 03/2012, which involved a failed NIBP module of the Spectrum and Passport 2 devices; at least 69 Service Work Orders, completed between 07/08/2011 and 06/07/2012, which involved a failed NIBP module of the Spectrum device; and at least 14 Service Work Orders, completed between 06/2011 and 06/2012, which involved a failed NIBP module of the Passport V device.

D. Your firm failed to conduct adequate CAPA investigations for released units of Panorama Monitor with failed disclosure drives. For example, your firm had at least 53 Service Work Orders, completed between 07/01/2011 and 06/13/2012, which involved a replacement of a failed disclosure drive for a Panorama device.

E. Failure Investigation and Corrective/Preventive Action Form No. 497, dated 08/02/2011, stated that DPM Central Station had a software anomaly which caused the trend data for a patient to be replaced by another patient. On 05/12/2011, your firm released a product correction letter to the field to correct the issue via a software upgrade. The CAPA effectiveness verification method was identified as verifying that all documents in the corrective action have been modified. However, your firm was not able to provide any documentation to demonstrate that the CAPA has been verified for effectiveness and that it does not adversely affect the finished device.

F. Failure Investigation and Corrective/Preventive Action Form No. 476, dated 09/03/2010, stated that DPM 6/7 Monitor failed to contain the disclosure and calculator functions following a software upgrade, and your firm attributed the failures to an inaccurate software upgrading procedure. On 08/11/2010, your firm released a product correction letter to the field to correct the issue via a software upgrade. However, your CAPA effectiveness verification method was indicated as "not applicable" and there was lack of documentation to indicate that the CAPA has been verified for effectiveness and that it does not adversely affect the finished device.

We reviewed your firm's response and conclude that it is not adequate. Your response states that you will implement appropriate corrective actions based on root causes and conduct risk analysis, where appropriate. You have not provided this data for our review.

2. Failure to review, evaluate, and investigated complaints involving the possible failure of a device, labeling, and packaging to meet any of its specifications, pursuant to 21 CFR 820.198(c). For example:

A. Your written procedures for complaint handling do not require that complaints involving possible failure of a device, labeling, or packaging be reviewed, evaluated and investigated.

B. A written complaint investigation had not been conducted for 15 units of the O_2, Auto ID, Multi-Gas Module, Part No. 6800-30-50502, which is part of the DPM 6/Beneview T5 Monitor, in which the software could not be upgraded.

C. A written complaint investigation had not been conducted for the Spectrum Monitor, Serial No. MS131938F8, which had the following failed components: U7, cooling fan, motor pump,

and V2.

We reviewed your firm's response and conclude that it is not adequate. Your response stated that you have opened a CAPA for investigating the cause of the failure to upgrade 15 multi-gas units for O2, Auto ID, Multi-Gas Modules, however, you have not provided the CAPA report or details of the investigation. Further, your response states that you have recommended a labeling update for the **(b)(4)** component as part of the investigation for the Spectrum Monitor, however, the details of this labeling update were not included in the investigation report.

3. Failure to adequately establish procedures to control product that does not conform to specified requirements, pursuant to 21 CFR 820.90(a). For example, Document No. 0002-04-0004, NCMR Procedure, Rev. R, released 10/07/2010, does not require that non-conforming products be evaluated for the need for an investigation.

Your firm's response to this observation appears to be adequate. Your firm has updated your NCMR Procedure, Section 9.0, which defines the specific criteria for initiating an investigation of nonconforming product. We will verify the implementation of this corrective action during a future inspection.

4. Failure to validate device software, pursuant to 21 CFR 820.30(g). For example:

A. Your firm conducted a field correction after discovering software anomalies of the V Series Monitor, including software versions below 2.2.0.41 that caused the V Patient Server synchronization failures. Your firm released software version 2.0.0.29, which included the synchronization capabilities, however, the partial and full verification studies that were completed did not test the VPS synchronization capability for the following: NIBP, arrhythmia, and heart rate algorithms; departmental default settings for different patient sizes. Further, your firm failed to conduct a full integration performance verification study as required by Protocol 0088-00-0334-0833.

B. Your firm conducted a field correction after discovering software anomalies in the released software versions below 2.2.0.19 that caused the system to reset and reboot resulting in incorrect or no alarm settings if a patient discharge is followed by a patient admission within a 4 second time period and incorrect alarm and patient settings and no display of patient data if a dialog is opened within a 10 second time period after VPS is selected in the patient ID mismatch dialog for attaching the VPS module. Your firm released Software Version 2.2.0.1.9 to include a fix for the timing issue, in which CAPA Report, No. 500, dated 01/10/12, attributed the timing issue to the software discharge function. Your firm failed to conduct a full integration performance verification study as required by Protocol 0088-00-0334-0833.

The adequacy of your firm's response cannot be determined at this time. As part of your correction you have committed to the following: enhancing the Software Development Process EOP 2001 to require a definition of a minimum set of testing to be performed on every final software version prior to release to production and to add detail to the software design sections; changing the SRB process SOP 0002-06-6819 to require justification of testing chosen for each software change; enhancing the Test and Validation Protocol SOP 0002-09-0004 to detail how to handle test amendme.nts, Change Verification Forms, and reviewer responsibilities; conduct training for generating verification protocol; and creating a System Level Regression Test to verify the essential performance of the V Series Monitor, which will be executed prior to each release of software to the field. Please provide this information as it is completed so" that it can be reviewed.

5. Failure to correctly translate the device design into production specifications, pursuant to 21 CFR 820.30(h). Specifically, your firm lacks a written procedure to ensure that device designs are correctly translated into production specifications. For example:

A. The DPM 6/7 Monitor failed to contain the disclosure and calculator functions following a software upgrade which was completed to update the firm's logo for released units, as well as finished units, pending distribution. Your firm attributed these failures to an inaccurate software upgrading procedure. There is no assurance that a design transfer procedure has been adequately established for DPM 6/7 Monitor to allow a verification of the proper functioning of the software following each software upgrading or device reconfiguration

process to ensure an accurate translation of the device design and conformance to predefined user needs and intended uses.

B. Your firm had 22 units of Masimo SPO_2 Module, Part No. 6100-30-86412, used for Passport V Monitor, Part No. 6100-F-PA00291; which had a defective **(b)(4)** the interface board after a 1500V hi-pot test during a rework/reconfiguration process for the Passport V Monitor. The supplier of the **(b)(4)** had approved faulty labeling material and the placement position for the individually packaged **(b)(4)** Module. The affected module was not validated during design rework/reconfiguration for each V Monitor. There is no assurance that design transfer procedures have been adequately established for each rework/reconfiguration process of Passport V Monitor to ensure an accurate translation of the device design.

The adequacy of your firm's response cannot be determined at this time. As part of your corrective action, you state that you will draft a design transfer protocol for each product that identifies and validates the essential performance requirements. Your response also states that you will complete a validation of all active manufacturing procedures using the design transfer protocol. Please provide this information as it is completed so that it can be reviewed.

6. Failure to adequately establish procedures to ensure equipment is routinely calibrated, inspected, checked, and maintained, pursuant to 21 CFR 820.72(a). Specifically, there is lack of adequate written procedures for testing equipment for patient monitors. For example:

A. The **(b)(4)** Non-Invasive Blood Pressure (NIBP) Analyzer's manufacturer's operation manual requires that calibration tests include visual inspections, a battery test, board tests, and system tests. However, your firm was not able to provide calibration test results for this piece of equipment.

B. The **(b)(4)** Patient Simulator's manufacturer's operation manual requires that calibration test specifications include temperature, cardiac output, respiration, ECG artifact, blood pressure artifact, and instructions to complete a performance check and a complete calibration test. However, your firm was not able to provide calibration test results except for temperature and humidity.

We reviewed your firm's response and conclude that it is not adequate. Your response states that you have created calibration procedures for the **(b)(4)** analyzer and the **(b)(4)** Simulator, however, you did not provide any calibration testing results for these pieces of equipment to demonstrate how these procedures are effective and have been implemented.

Our inspection also revealed that your firm's DPM 6/7 Monitor and the DPM Central Station devices are misbranded under Section 502(t)(2) of the Act, 21 U.S.C. § 352(t)(2), in that your firm failed or refused to furnish material or information. respecting the device that is required by or under Section 519 of the Act, 21 U.S.C. § 360i, and 21 CFR Part 806 - Medical Devices; Reports of Corrections and Removals.
Significant violations include, but are not limited to, the following:

7. Failure to submit a written report to FDA of any correction or removal of a device to remedy a violation of the act caused by the device, which may present a risk to health, unless the information had already been provided as set forth in 21 CFR 806.10(f) or the correction or removal action is exempt from the reporting requirements under 806.1(b), as required by 21 CFR 806.10(a)(2). For example:

A. The DPM 6/7 Monitor failed to contain disclosure and calculator functions following a software upgrade for updating the firm's logo. The failures were attributed to an inaccurate software upgrading procedure. On 08/11/2010, your firm issued a correction letter to hospital administrators and informed the users of the software anomalies, and requested that the users contact your firm for a software upgrade to restore the missing functions, including full disclosure and drug, hemodynamic, renal, oxygenation, and ventilation calculations.

B. The DPM Central Station had a software anomaly which caused the trend data for a patient to be replaced by another patient's data, causing possible documentation errors in diagnosis

and treatment plan development. On May 12, 2011, your firm issued a correction letter to hospital administrators and informed the users of the software anomaly and the field correction to the issue which was a software upgrade.

Your firm's response to this observation appears to be adequate. Your firm submitted field Correction and Removal Reports for each event, dated August 23, 2012, for the DPM 6/7 Monitor and the DPM Central Station Monitoring System. FDA will review the information you submitted and classify these field corrections as a recall. Your firm also revised the Product Corrections and Removals procedure, #0002-00-0051, to ensure the evaluation of a correction or removal for reportability. The revised procedure includes an analysis of both the risk to health and violation of the Act.

Our inspection also revealed that the devices are misbranded under Section 502(t)(2) of the Act, 21 U.S.C. § 352(t)(2), in that your firm failed or refused to furnish material or information regarding the devices that is required by or under Section 519 of the Act, 21 U.S.C. § 360i, and 21 CFR Part 803 - Medical Device Reporting. Significant violations include, but are not limited to, the following:

8. Failure of your firm to adequately develop, maintain and implement written Medical Device Report (MDR) procedures, as required by 21 CFR 803.17. After reviewing your firm's MDR procedure titled "Medical Device Reporting Procedure", Document No: 0002-01-0024, revision AD, the following issues were noted:

1. Your firm's MDR procedure does not establish internal systems that provide for timely and effective identification, communication, and evaluation of events that may be subject to MDR requirements. For example:

- There are no definitions of what your firm will consider to be a reportable event under 21 CFR Part 803. To facilitate the correct interpretation of reportable events and to assure the quality of MDR submissions, the procedure should include definitions based on 21 CFR 803.3 for the terms "become aware", "MDR reportable event", "caused or contributed," "malfunction," and "serious injury," and definitions for the terms "reasonably known" and " reasonably suggests," found respectively in 21 CFR 803.SO(b) and 803.20(c)(1).

2. Your firm's MDR procedure does not establish internal systems that provide for timely transmission of complete medical device reports. Specifically, the following are not addressed: The circumstances under which your firm must submit supplemental or follow-up report and the requirements for such reports;

- The procedure does not include the address for where to submit MDR reports. The address is: Food and Drug Administration (FDA), Center for Devices and Radiological Health (CDRH), Medical Device Reporting, P. O. Box 3002, Rockville, MD 20847-3002.

3. Your firm's MDR procedure does not describe how it will address documentation and record-keeping requirements, including:

- Information that was evaluated to determine if an event was reportable.

We reviewed your firm's response dated August 23, 2012, and conclude that it is not adequate. Your firm included in its response a revised MDR procedure titled "Medical Device Reporting Procedure," Document.#0002-01-0024, Revision AF. A review of your firm's revised procedure was conducted. Your firm's revised MDR procedure still does not meet the requirements of 21 CFR 803.17. The following issues were noted:

4. Your firm's MDR procedure does not establish internal systems that provide for timely and effective identification, communication, and evaluation of events that may be subject to MDR requirements. For example:

- There are no definitions of what your firm will consider to be a reportable event under 21 CFR Part 803. To facilitate the correct interpretation of reportable events and to assure the quality of MDR submissions, the procedure should include definitions based on 21 CFR 803.3 for the terms "become aware", "caused or contributed," "malfunction," and "serious injury," and definitions for the terms "reasonably known" and "reasonably suggests," found

respectively in 21 CFR 803.50(b) and 803.20(c)(1).

5. Your firm's MDR procedure does not establish internal systems that provide for timely transmission of complete medical device reports. Specifically, the following are not addressed:

- The circumstances under which your firm must submit supplemental or follow-up report and the requirements for such reports.
- The procedure does not include the address for where to submit MDR reports. The address is: FDA, CDRH, Medical Device Reporting, P.O. Box 3002, Rockville, MD 20847-3002.

If your firm wishes to submit MDR reports via electronic submission it can follow the directions stated at the following URL:

http://www.fda.gov/ForInduSTry/FDAeSubmitter/ucm107903.htm[1]

If your firm wishes to discuss MDR reportability criteria or to schedule further communications, it may contact the MDR Policy Branch by email at ReportabilityReviewTeam@fda.hhs.gov.

Our inspection also revealed that the V Series Patient Monitor/Endeavour Monitoring System device is adulterated under Section 501(f)(1)(B) of the Act, 21 U.S.C. § 351(f)(1)(B), because your firm does not have an approved application for premarket approval (PMA) in effect pursuant to Section 515(a) of the Act, 21 U.S.C. § 360e(a), or an approved application for an investigational device exemption under Section 520(g) of the Act, 21 U.S.C. § 360j(g). The device is also misbranded under Section 502(o) the Act, 21 U.S.C. § 352(o), because your firm did not notify the agency of its intent to introduce the devices into commercial distribution, as required by Section 510(k) of the Act, 21 U.S.C. § 360(k). For a device requiring premarket approval, the notification required by Section 510(k) is deemed satisfied when a PMA is pending before the agency. [21 CFR 807.81(b)] The type of information that your firm needs to submit in order to obtain approval or clearance for the device is described on the Internet at http://www.fda.gov/cdrh/devadvice/3122.html[2]. The FDA will evaluate the information that your firm submits and decide whether the product may be legally marketed.

Specifically, your firm modified the V Series Patient Monitor/Endeavour Monitoring System in the following ways: 1) adding four remote connections of desktop computers allowing clinicians to view other applications while monitoring patients vital signs; 2) enabling a simultaneous display of data from two patients on a single host monitor; and 3) enabling the monitor to be notified of an alarm condition where clinicians can observe specified parameters for another networked monitor from a remote location. These modifications could significantly affect the safety or effectiveness of the device, therefore, these changes require a new premarket notification submission, as required by 21 CFR Part 807.81(a)(3)(i).

A follow up inspection will be required to assure that correction and/or corrective actions are adequate. Your firm should take prompt action to correct the violations addressed in this letter. Failure to promptly correct these violations may result in regulatory action being initiated by the FDA without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil money penalties. Also, federal agencies may be advised of the issuance of Warning Letters about devices so that they may take this information into account when considering the awarding of contracts. Additionally, premarket approval applications for Class III devices to which the Quality System regulation violations are reasonably related will not be. approved until the violations have been corrected.

Please notify this office in writing within fifteen business days from the date you receive this letter of the specific steps your firm has taken to correct the noted violations, as well as an explanation of how your firm plans to prevent these violations, or similar violations, from occurring again. Include documentation of the corrections and/or corrective actions (including any systemic corrective actions) that your firm has taken. If your firm's planned corrections and/or corrective actions will occur over time, please include a timetable for implementation of those activities. If corrections and/or corrective actions cannot be completed within fifteen business days, state the reason for the delay and the time within which these activities will be completed. Your firm's response should be comprehensive and address all violations included in this Warning Letter.

Your firm's response to this letter should be sent to: U.S. Food and Drug Administration, 10 Waterview Blvd, 3rd Floor, Parsippany, New Jersey 07054. If you have any questions about the contents of this letter, please contact Stephanie Durso, Compliance Officer, at 1-973-331-4911 (phone) or 1-973-331-4969 (fax).

Finally, you should know that this letter is not intended to be an all-inclusive list of the violations at your firm's facility. It is your firm's responsibility to ensure compliance with applicable laws and regulations administered by FDA. The specific violations noted in this letter and in the Inspectional Observations, FDA 483, issued at the close of the inspection may be symptomatic of serious problems in your firm's manufacturing and quality management systems.

Your firm should investigate and determine the causes of the violations, and take prompt actions to correct the violations and bring the products into compliance.

Sincerely yours,
/S/
Diana Amador-Toro
District Director
New Jersey District

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Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.

Links on this page:

1. http://www.fda.gov/ForInduSTry/FDAeSubmitter/ucm107903.htm
2. http://www.fda.gov/cdrh/devadvice/3122.html