

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

UNITED STATES OF AMERICA)	Criminal No.
)	
v.)	<u>Counts One and Two:</u>
)	Introduction of Misbranded Medical Devices
MAGELLAN DIAGNOSTICS, INC.,)	into Interstate Commerce
)	(21 U.S.C. §§ 331(a), 333(a)(1))
)	
Defendant)	<u>Forfeiture Allegation:</u>
)	(18 U.S.C. § 982(a)(7))
)	

INFORMATION

The Acting United States Attorney (the “United States Attorney”) alleges that, at all times relevant to this Information:

General Allegations

1. MAGELLAN DIAGNOSTICS, INC., headquartered in Billerica, MA, was a medical device company that sold products for detecting lead levels in the blood of children and adults.
2. MAGELLAN did not timely notify the FDA about a malfunction that tended to cause its lead-testing devices to produce inaccurate blood lead level results or about MAGELLAN’s subsequent corrective change in the devices’ instructions for use.

MAGELLAN’s Lead-Testing Devices

3. MAGELLAN produced a family of instruments for blood lead analysis using a method called anodic stripping voltammetry. Those devices included, but were not limited to, LeadCare II and LeadCare Ultra (collectively the “LeadCare Devices”).

4. LeadCare II was released in 2006 and was the only point-of-care lead testing device, which means it was cleared by the United States Food and Drug Administration (FDA) for use in non-laboratory settings such as doctors' offices and clinics. The LeadCare II device could be used to test blood samples drawn from a vein ("venous" samples) and samples drawn from a fingerstick. Most LeadCare II tests were conducted on fingerstick samples; MAGELLAN estimated that approximately 5–8% of LeadCare II users conducted testing with venous blood samples. In 2017, MAGELLAN estimated that LeadCare II devices were used to conduct 2.5 million blood lead tests per year—accounting for more than half of all lead tests conducted in the United States.

5. LeadCare Ultra was released in 2013 and was designed for use at medium and large hospitals and reference labs. LeadCare Ultra could be used to test both fingerstick blood samples and venous blood samples but was predominantly used for venous blood samples. In 2017, MAGELLAN estimated that LeadCare Ultra devices were used to conduct 420,000 blood lead tests per year.

6. MAGELLAN sold its LeadCare Devices to customers located throughout the United States and in foreign countries.

FDA and FDCA

7. FDA was responsible for protecting the health and safety of the American public by ensuring, among other things, that medical devices—including diagnostic testing devices—were safe and effective. Under its statutory mandate, FDA regulated the manufacture, processing, packing, labeling, and shipment in interstate commerce of medical devices.

8. The federal Food, Drug, and Cosmetic Act (FDCA), among other things, governed the manufacture and interstate distribution of medical devices for human use, as codified at 21 U.S.C. §§ 301 et seq.

9. The FDCA and its implementing regulations required device manufacturers to submit pre-market notifications to the FDA at least 90 days before medical devices were introduced into interstate commerce for commercial distribution. Pre-market notifications were required when a device that was already on the market was about to be significantly changed or modified in design or intended use, and the change could significantly affect the safety or effectiveness of the product. 21 C.F.R. § 807.81. A device was deemed to be “misbranded” under 21 U.S.C. § 352(o) if a device manufacturer failed to submit necessary pre-market notification.

10. The FDCA and its implementing regulations provided a mechanism that allowed FDA, and others, to identify and monitor adverse events and malfunctions involving medical devices. Medical device reports (MDRs) were one of the post-market surveillance tools that FDA used to monitor device performance and detect potential device-related safety issues.

11. Medical device manufacturers were required to submit MDRs within 30 calendar days after becoming aware of a device malfunction pursuant to 21 U.S.C. § 360i(a) and 21 CFR Part 803 if the malfunction was likely to cause or contribute to serious injury or death if it recurred. Device malfunctions were defined as a failure of the device to perform as intended or meet its performance specifications, including all claims made in the device labeling under 21 CFR § 803.3.

12. The FDCA and its implementing regulations required device manufacturers to notify FDA about device corrections—which included modifications, adjustments, and

relabeling—within 10 working days of initiating the device correction if the correction was initiated to reduce a risk to health posed by the device. 21 CFR § 806.10.

13. A device was deemed to be “misbranded” under 21 U.S.C. § 352(t)(2) if the manufacturer failed or refused to file any material or information required by or under 21 U.S.C. § 360i, including an MDR or a device correction.

14. The FDCA prohibited the introduction, or causing the introduction, of misbranded medical devices into interstate commerce, pursuant to 21 U.S.C. § 331(a).

LeadCare Ultra Application for FDA Clearance

15. In or around November 2012, MAGELLAN sought clearance from FDA to introduce into the market its newly developed LeadCare Ultra device. MAGELLAN submitted a Traditional 510(k) application to FDA (the “LeadCare Ultra 510(k) application”), which claimed that the LeadCare Ultra was substantially equivalent to the already-cleared LeadCare II device. In its application, MAGELLAN described LeadCare Ultra as “an *in vitro* diagnostic device that relies on electrochemistry . . . and a unique sensor to detect lead in whole blood . . . When a sample of whole blood is mixed with Treatment Reagent (a diluted solution of hydrochloric acid), [lead is separated from the red blood cells] and lead becomes available for detection.”

16. MAGELLAN’s LeadCare Ultra 510(k) application contained performance testing comparing LeadCare Ultra’s performance to a reference method for testing blood lead concentrations using standardized blood samples, donor blood, and human and animal blood spiked to certain lead concentrations. The reference method was called graphite furnace atomic absorption spectrometry (GFAAS). MAGELLAN’s performance testing also included a clinical study in which 394 blood samples were collected. Of the 394 blood samples collected, 148 samples were within range (1.9-65 µg/dL). MAGELLAN represented to FDA that the clinical data “met

the acceptance criteria, defined as average bias within the range of ± 2 $\mu\text{g/dL}$ in the concentration range of 1.9 to 10 $\mu\text{g/dL}$ and $\pm 10\%$ for concentrations above 10 $\mu\text{g/dL}$.”

17. On or about January 14, 2013, FDA issued a Hold Memo for MAGELLAN’s LeadCare Ultra 510(k) application, which noted several deficiencies and requested additional studies and documentation concerning, among other things, the operation of LeadCare Ultra within various temperature and humidity ranges.

Discovery of LeadCare Malfunction

18. While conducting the temperature and humidity studies requested by FDA in the Hold Memo, MAGELLAN discovered a malfunction affecting the LeadCare Ultra device (the “Malfunction”).

19. The Malfunction tended to result in lower blood lead values when the blood sample was tested shortly after it was mixed with treatment reagent (sometimes referred to as “T0” for 0 minutes of incubation) and higher blood lead values if the blood-treatment reagent mixture were allowed to sit, or “incubate,” for several hours or days before testing (sometimes referred to as “T[amount of incubation time],” such as “T4” for four hours of incubation time or “T24” for 24 hours of incubation time). When the Malfunction occurred, the lower blood lead value was often below that of the GFAAS device for the same sample. With incubation, the higher blood lead value was often closer to that of GFAAS but could be higher than GFAAS.

20. The Malfunction was first observed in or around June 27, 2013, when a MAGELLAN employee performed the temperature and humidity studies requested by FDA. This employee forwarded the results of this study to other MAGELLAN employees who expressed concerns over the findings.

21. At least as early as June 28, 2013, MAGELLAN’s senior executive team was aware of the Malfunction affecting LeadCare Ultra.

22. MAGELLAN did not notify FDA about the results of its temperature and humidity studies that showed the Malfunction.

FDA Clearance of LeadCare Ultra

23. FDA—unaware of the Malfunction—cleared the LeadCare Ultra device for marketing and distribution on or about August 20, 2013. In its clearance letter, FDA emphasized, “We remind you, however, that the device labeling must be truthful and not misleading.”

24. The label for the FDA-cleared Ultra device made accuracy claims based on its method comparison study, as shown below:

ACCURACY:

The accuracy of the LeadCare Ultra Blood Lead Testing System was determined by a Method Comparison study at two hospital laboratory sites. Three hundred ninety-four (394) results, from a combination of spiked and unspiked blood samples, were generated. One hundred forty-eight results were within the claimed analytical range of 1.9 – 65.0 µg/dL. The LeadCare Ultra results were plotted versus the results obtained by the Reference Method, GFAAS. The LeadCare Ultra average bias from GFAAS and the scatter plot of LeadCare Ultra vs. GFAAS results, with the linear regression, are provided in Table 2 and Graph 1, respectively.

Table 2: LeadCare Ultra Average Bias from GFAAS

GFAAS (µg/dL)	Predicted LeadCare Ultra (µg/dL)	Avg. Bias (µg/dL)	Bias (%)
1.90	1.95	0.05	2.4%
5.00	5.01	0.01	0.2%
10.00	9.96	-0.04	-0.4%
20.00	19.85	-0.15	-0.7%
30.00	29.74	-0.26	-0.9%
40.00	39.64	-0.36	-0.9%
50.00	49.53	-0.47	-0.9%
60.00	59.42	-0.58	-1.0%
65.00	64.37	-0.63	-1.0%

25. MAGELLAN’s method comparison study, however, did not control for the amount of time that the blood-treatment reagent incubated before testing, which is to say that the laboratories participating in the method comparison study were free to run the tests at any time after mixing the blood sample and treatment reagent as permitted by the LeadCare Ultra label. The

LeadCare Ultra label's instructions for use stated in part: "After mixing the blood with the Treatment Reagent, analyze it in less than 48 hours if stored at room temperature. If stored refrigerated, analyze within 7 days." Thus, if the normal workflow of these laboratories included sufficient incubation time after mixing, the study was unlikely to show the effects of the Malfunction.

26. The label for the FDA-cleared LeadCare Ultra device also stated:

Childhood lead poisoning is a major, preventable problem in the United States. Numerous studies have shown that exposure to lead can result in damage to the nervous, hematopoietic, endocrine, renal, and reproductive systems causing lifelong physical and mental health problems. Children are particularly susceptible to the effects of lead as their nervous systems are still developing.

In 2012, based on the increased body of evidence demonstrating there is no safe level of lead in the blood, experts established a new reference value to identify children who have elevated blood lead levels (BLL). According to the Centers for Disease Control (CDC) website (www.cdc.gov/nceh/lead), this level is based on the U.S. population of children ages 1-5 years who are in the top 2.5% of children when tested for lead in their blood (when compared to children who are exposed to more lead than most children). Currently this reference value is 5 µg/dL.

Confirmation of the Malfunction and Delayed Release of LeadCare Ultra

27. MAGELLAN did not release LeadCare Ultra to the market shortly after FDA clearance because of concerns about the Malfunction. From in or around August 2013 until in or around December 2013, MAGELLAN designed and conducted multiple studies comparing LeadCare Ultra test results measured (a) immediately after blood samples were mixed with treatment reagent and (b) after allowing the blood-treatment reagent to incubate for various time periods ("the 2013 Malfunction Studies"). While the Malfunction did not appear in every experiment, the 2013 Malfunction Studies repeatedly showed that the Malfunction occurred when

testing various types of blood samples, at various lead concentrations, and using various sensors and treatment reagents.

28. MAGELLAN knew that the Malfunction was likely to cause or contribute to serious injury or death if it recurred.

29. MAGELLAN released LeadCare Ultra for sale to customers in or around December 2013. MAGELLAN did not notify customers or FDA in 2013 that the Malfunction could cause false lows and false highs, especially if testing was conducted immediately after mixing blood samples with treatment reagent.

Discovery and Confirmation of the Malfunction in LeadCare II

30. During the 2013 Malfunction Studies, MAGELLAN conducted studies to determine whether the Malfunction affected LeadCare II sensors and treatment reagent as well as LeadCare Ultra. Those studies confirmed that the Malfunction was not an isolated problem with LeadCare Ultra but was “a general phenomenon” that also affected LeadCare II when it was used to test venous samples.

31. Prior to November 2016, MAGELLAN did not inform customers and FDA that the Malfunction was likely to cause inaccurate test results when LeadCare II was tested using venous samples.

LeadCare Ultra Customer Letter

32. Beginning in or around August 2014 and continuing through in or about October 2014, certain LeadCare Ultra customers independently discovered the Malfunction after they observed inaccurate and changing lead test results. These customers reported to MAGELLAN that they had received unexpectedly low test results when samples were tested immediately after being

mixed with treatment reagent, as the label allowed, and had found that the lead test result was higher if the sample was tested an hour after the sample was mixed with treatment reagent.

33. On or about November 24, 2014, MAGELLAN sent LeadCare Ultra customers a letter about the Malfunction (the “LeadCare Ultra Customer Letter”).

34. The LeadCare Ultra Customer Letter advised customers to allow the blood-treatment reagent mixture to sit for a minimum of 24 hours before testing. This advice contradicted the LeadCare Ultra label, which permitted users to analyze the sample immediately after mixing the blood sample and treatment reagent and permitted users to analyze the mixture within 48 hours if the mixture was kept at room temperature or within seven days if the mixture was refrigerated.

Overdue Filing of the LeadCare Ultra MDR

35. Prior to April 2015, MAGELLAN did not notify FDA about (a) MAGELLAN’s discovery of the Malfunction and (b) MAGELLAN’s change to the LeadCare Ultra user instructions, communicated directly to customers via the LeadCare Ultra Customer Letter.

36. On or about April 2, 2015, MAGELLAN submitted an MDR about the Malfunction (the “LeadCare Ultra MDR”). MAGELLAN did not receive a response from FDA following its submission of the LeadCare Ultra MDR.

37. In or around August 2015, MAGELLAN approved an engineering change order (ECO) that changed the LeadCare Ultra label, user guide, and website to incorporate the 24-hour incubation instruction.

38. MAGELLAN did not notify FDA of the change to the device and product insert, nor did FDA clear the significantly changed device.

Overdue Notification to FDA about LeadCare II Malfunction

39. In or around November 2016, MAGELLAN submitted an amendment to the LeadCare Ultra MDR disclosing that the Malfunction also affected LeadCare II (the “LeadCare II MDR”).

40. The LeadCare II MDR was submitted by MAGELLAN on or around November 7, 2016. However, the LeadCare II MDR was not properly filed and was not received by FDA until in or around 2017.

The 2017 Recall

41. In or around 2017, FDA contacted MAGELLAN with questions about the Malfunction and ultimately found that MAGELLAN’s data showed that LeadCare Devices could not accurately test venous samples, regardless of the recommended incubation times.

42. In or around May 2017, FDA recommended a recall of all LeadCare Devices using venous samples.

COUNT ONE

**Introduction of Misbranded Devices into Interstate Commerce
(Failure to Timely File Medical Device Reports)
(21 U.S.C. §§ 331(a), 333(a)(1))**

43. The United States Attorney re-alleges and incorporates by reference paragraphs 1-42 of this Information.

44. From in or around December 2013 through in or around May 2017, within the District of Massachusetts and elsewhere, the defendant,

MAGELLAN DIAGNOSTICS, INC.,

caused to be introduced into interstate commerce misbranded medical devices, to wit, the LeadCare Ultra and LeadCare II products, which were distributed to customers outside Massachusetts even though necessary medical device reports pursuant to 21 U.S.C. § 360i(a) and 21 CFR Part 803 reporting product malfunctions had not been filed.

All in violation of Title 21, United States Code, Sections 331(a) and 333(a)(1).

COUNT TWO

**Introduction of Misbranded Devices into Interstate Commerce
(Failure to Provide Pre-Market Notification and Timely File Reports of Correction)
(21 U.S.C. §§ 331(a), 333(a)(1))**

45. The United States Attorney re-alleges and incorporates by reference paragraphs 1-42 of this Information.

46. From in or around November 2014 through in or around May 2017, within the District of Massachusetts and elsewhere, the defendant,

MAGELLAN DIAGNOSTICS, INC.,

caused to be introduced into interstate commerce misbranded medical devices, to wit, the LeadCare Ultra, which were distributed to customers outside Massachusetts with instructions to incubate the blood-treatment reagent samples for 24 hours, even though (i) the defendant failed to provide the FDA pre-market notification at least 90 days before distributing a significantly changed device pursuant to 21 C.F.R. Part 807, and (ii) the defendant did not file the necessary reports of device correction initiated to reduce a risk to health posed by the device pursuant to 21 U.S.C. § 360i(g) and 21 CFR Part 806.

All in violation of Title 21, United States Code, Sections 331(a) and 333(a)(1).

FORFEITURE ALLEGATION

(18 U.S.C. § 982(a)(7))

The United States Attorney further alleges that:

47. Upon conviction of one or more of the offenses in violation of Title 21, United States Code, Section 331(a), set forth in Counts One and Two of this Information, the defendant, **MAGELLAN DIAGNOSTICS, INC.**, shall forfeit to the United States, pursuant to Title 18, United States Code, Section 982(a)(7), any property, real or personal, that constitutes or is derived, directly or indirectly, from proceeds traceable to the offenses.

48. If any of the property described in Paragraph 47, above, as being forfeitable pursuant to Title 18, United States Code, Section 982(a)(7), as a result of any act or omission of the defendant —

- a. cannot be located upon the exercise of due diligence;
- b. has been transferred or sold to, or deposited with, a third party;
- c. has been placed beyond the jurisdiction of the Court;
- d. has been substantially diminished in value; or
- e. has been commingled with other property which cannot be divided without difficulty;

it is the intention of the United States, pursuant to Title 21, United States Code, Section 853(p), incorporating Title 18, United States Code, Section 982(b)(1), to seek forfeiture of any other property of the defendants up to the value of the property described in Paragraph 47 above.

All pursuant to Title 18, United States Code, Section 982(a)(7).

Respectfully submitted,

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