Roland Tellis (SBN 186269)
rtellis@baronbudd.com
Mark Pifko (SBN 228412)
mpifko@baronbudd.com
Peter Klausner (SBN 271902)
pklausner@baronbudd.com
BARON & BUDD, P.C.
15910 Ventura Boulevard, Suite 1600
Encino, California 91436
Telephone: (818) 839-2333
Facsimile: (818) 986-9698

Timothy G. Blood (149343)
tblood@bholaw.com
Thomas J. O'Reardon II (247952)
toreardon@bholaw.com
BLOOD HURST & O'REARDON, LLP
701 B Street, Suite 1700
San Diego, California 92101
Telephone: (619) 338-1100
Facsimile: (619) 338-1101

Attorneys for Plaintiffs
DINA ANDREN and SIDNEY BLUDMAN, individually, and on behalf of other members of the general public similarly situated

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF CALIFORNIA

DINA ANDREN and SIDNEY BLUDMAN, individually, and on behalf of other members of the general public similarly situated,

Plaintiffs,

vs.

ALERE INC., a Delaware corporation, ALERE HOME MONITORING, INC., a Delaware corporation, ALERE SAN DIEGO, INC., a Delaware corporation,

Defendants.

Case Number: **'16CV1255 GPC NLS**

CLASS ACTION

COMPLAINT FOR:

(1) Violations of California's Unfair Competition Law (Cal. Bus. & Prof. Code §§ 17200, *et seq.*);
(2) Violation of the Consumers Legal Remedies Act (Cal. Civ. Code §§ 1750, *et seq.*);
(3) Fraud; and
(4) Unjust Enrichment

Jury Trial Demanded

For their complaint against Defendants Alere, Inc., Alere Home Monitoring, Inc. and Alere San Diego, Inc., (hereinafter and collectively, "Defendants" or "Alere"), Plaintiffs Dina Andren and Sidney Bludman ("Plaintiffs"), individually, and on behalf of all other members of the general public similarly situated ("the Class"), based on information and belief, allege as follows:

NATURE OF THE ACTION

1. This action is brought on behalf of Plaintiffs and a class of consumers who purchased "INRatio PT/INR Monitors," "INRatio PT/INR Test Strips," "INRatio2 PT/INR Monitors" and "INRatio2 PT/INR Test Strips" (collectively, the "INRatio products"). Plaintiffs' claims concern the unlawful, deceptive and misleading practices conducted by Defendants in connection with the manufacturing, marketing and sales of the INRatio products in violation of California law and the common law.

2. Defendants' INRatio products are electronic testing devices designed (at least, in theory) to help patients who have been prescribed blood-thinners monitor their blood-clotting times, to ensure they are receiving the proper dosage. For patients taking blood-thinners, the ability to monitor and test their blood-clotting times and adjust their dosages accordingly is essential. Failure to take the appropriate dosage of blood-thinners can result in serious bodily injuries and death.

3. Almost immediately after the INRatio products became available to consumers, Defendants learned that the INRatio monitors and testing strips produced erroneous results. Defendants received numerous complaints from users and multiple warning letters from the FDA, notifying them that the results produced by the INRatio products differed from those produced by independent laboratories. Despite this, Defendants continued selling the INRatio products unabated, marketing and advertising them as "accurate," "convenient," "effective," "reliable," "optimal" and "safe."

4. Believing the results are accurate, the erroneous results produced by the INRatio products have misled patients and caused them to improperly adjust their blood-

thinner dosages, increasing the risk and likelihood of serious bodily injury or death.[1]

5. Based on the Defendants' willingness to manufacture, market and sell a defective and life-threatening product to consumers in a deceptive, fraudulent and misleading manner, Plaintiffs bring this action on behalf of themselves and on behalf of the Class.

JURISDICTION AND VENUE

6. Jurisdiction is proper in this Court under 28 U.S.C. § 1332(d)(2). The matter in controversy, exclusive of interest and costs, exceeds the sum or value of $5,000,000 and is a class action in which members of the class of plaintiffs are citizens of states different from Defendants. Further, greater than two-thirds of the members of the Class reside in states other than the states in which Defendants are citizens.

7. In addition, under 28 U.S.C. § 1367, this Court may exercise supplemental jurisdiction over the state law and common law claims because all of the claims are derived from a common nucleus of operative facts and are such that Plaintiffs ordinarily would expect to try them in one judicial proceeding.

8. Venue lies within this judicial district under 28 U.S.C. § 1391(b), (c) and (d), because each of the Defendants transacted business in this District and because a substantial part of the events or omissions giving rise to Plaintiffs' claims in this lawsuit occurred, among other places, in this District.

PARTIES

9. Plaintiff Dina Andren (hereinafter "Plaintiff Andren") is an individual residing in Monroe, New York, and is a citizen of the State of New York.

10. Plaintiff Sidney Bludman ("Plaintiff Bludman") is an individual residing in Chevy Chase, Maryland, and is a citizen of the State of Maryland.

11. Defendant Alere, Inc. is a Delaware corporation authorized to do business in the State of California and nationwide. Alere, Inc., independently and through its

[1] To date, INRatio products have been linked to at least three deaths.

subsidiaries Defendant Alere Home Monitoring, Inc. and Defendant Alere San Diego, Inc., manufactures, markets and sells medical diagnostic testing products (including the INRatio products) for professionals, patients and consumers around the country, including in California. In 2014, Alere, Inc. generated over $1.2 billion in gross profits.

12. Defendant Alere Home Monitoring, Inc. (hereinafter, "AHM") is a Delaware corporation authorized to do business in the State of California and nationwide. It is, and was at all relevant times a wholly owned and controlled subsidiary of Defendant Alere, Inc. AHM assists patients, in California and nationwide, in acquiring the INRatio products, and provides physicians with the necessary tools to allow them to integrate the patient self-testing undertaken with the INRatio products into their practices.

13. Defendant Alere San Diego, Inc. (hereinafter, "ASD") is a Delaware corporation authorized to do business in the State of California and nationwide. It is a wholly owned and controlled subsidiary of Defendant Alere, Inc., with its principal place of business in San Diego, California.

14. The INRatio products were originally manufactured by HemoSense, Inc. (HemoSense), a Delaware corporation based in San Jose, California. HemoSense received FDA approval for the INRatio PT/INR Monitors and INRatio PT/INR Test Strips in 2002 and commercial sales began in 2003. In August of 2007, HemoSense was purchased by Alere, Inc. (then known as Inverness Medical Innovations, Inc.). In 2008, HemoSense transferred its operations to Alere, Inc.'s facility in San Diego, California. In 2013, HemoSense's operations were merged into the Alere San Diego corporate entity.

15. Plaintiffs are informed and believe, and based thereon allege that, at all material times herein, each of the Defendants was the agent, servant, or employee of the other Defendants, and acted within the purpose, scope, and course of said agency, service, or employment, and with the express or implied knowledge, permission, and consent of the other Defendants, and ratified and approved the acts of the other Defendants.

16. Whenever, in this Complaint, reference is made to any act, deed, or conduct of Defendants committed in connection with wrongful acts alleged, the allegation means

that Defendants engaged in the act, deed, or conduct by or through one or more of their officers, directors, agents, employees or representatives, each of whom was actively engaged in the management, direction, control or transaction of the ordinary business and affairs of Defendants.

FACTUAL BACKGROUND

A. The International Normalized Ratio (INR)

17. The International Normalized Ratio ("INR") is a standardized metric used to determine the relative speed at which blood clots in a patient's body. A patient's INR is calculated by comparing a patient's prothrombin time (the speed at which the patient's blood clots) against the normal mean prothrombin time (the average speed for blood-clotting in the general population). The resulting contrast between a patient's prothrombin time and the normal mean prothrombin time is the patient's INR.[2]

18. The INR is a useful measurement for doctors and patients to monitor the blood-clotting speed for patients who have been prescribed anticoagulants ("blood thinners") for certain medical conditions, including but not limited to blood clots, or following the surgical implantation of medical devices, including but not limited to heart valves. Doctors can use the INR measurement to determine whether a patient should increase or decrease his/her dosage of blood thinners.

19. It is essential for doctors and patients to be able to regularly measure a patient's INR and alter the blood-thinner dosage accordingly due to the serious health risks associated with both high and low blood-clotting times. High INRs (indicating a relatively slow blood-clotting time) can lead to excessive bleeding,[3] and generally indicates too high a dosage of blood-thinners. Meanwhile, a low INR (indicating a relatively quick blood-clotting time) can lead to strokes, and generally indicates too *low* a

[2] For example, a patient whose blood-clotting time is double that of the average person's will have an INR of 2.0.

[3] For every increase of just one unit of INR, the estimated risk of bleeding increases between 42% and 44%.

dose of blood-thinners. In both cases, the consequences of having an irregular INR can lead to serious injury and death. For these reasons, many patients who take blood thinners constantly monitor their INRs to ensure they are receiving the proper dosage.

B. INRatio INR Monitoring System

20. In the late 1990s, Defendants developed and manufactured the "INRatio monitor," a point-of-care INR monitor that was designed to help patients who have been prescribed blood-thinners, in particular warfarin, to monitor their INRs at home. Much like those devices used by diabetic patients to monitor their blood-sugar levels, the INRatio monitor worked by having patients insert a blood sample (via an INRatio test strip) into an electronic testing device. The testing device, after analyzing the blood sample, would then reveal the INR via an electronic display (pictured below):

21. The INRatio monitor, paired with the INRatio test strips, was known as the "INRatio testing kit," and Defendants represented that the INRatio testing kit was "accurate," "convenient," "effective," "reliable," "optimal" and "safe" in its marketing, advertising and promotional materials. Defendants make further misrepresentations to consumers by omitting material information from the packaging and marketing materials of the INRatio testing kit, in particular by failing to disclose that the INRatio roducts produce false and misleading results.

22. In October of 2002, the FDA approved the INRatio testing kit for home use and commercial sales began in 2003.

23. Eventually, the INRatio testing kit gave way to the "INRatio2" testing kit. The INRatio2 testing kit operated similarly to its predecessor, pairing an electronic monitor with corresponding test strips.

24. Consistent with its predecessor, Defendants represented that the INRatio2 testing kit was "accurate," "convenient," "effective," "reliable," "optimal" and "safe" in its marketing, advertising and promotional materials. Defendants make further misrepresentations to consumers by omitting material information from the packaging and marketing materials of the INRatio testing kit, in particular by failing to disclose that the INRatio roducts produce false and misleading results, as well as on the packaging of the product itself. In fact, the very reason one would use the INRation2 testing kit is to obtain accurate, reliable and safe results. Indeed, Defendants' tag line is "Knowing now matters."

Alere™ Knowing now matters.™

25. A true and correct copy of some of Defendants' representations concerning the INRatio2 testing kit is as follows:

Alere INRatio® 2

The Alere INRatio®2 PT/INR Monitoring Systems are a handheld blood coagulation system for monitoring patients taking warfarin. Used by healthcare professionals and patients at home, the system consists of a small monitor and disposable test strips. It provides an accurate and convenient measurement of blood clotting time, or PT/INR values. Routine measurements of PT/INR are necessary for the safe and effective management of the patient's warfarin dosing.

Alere INRatio® 2 PT/INR Monitoring Systems

The Alere INRatio® 2 PT/INR Monitor connects reliable results with practical convenience, making it an optimal in-office or home testing solution for anticoagulation management.

Read More ›

Alere INRatio® 2 PT/INR Monitoring System Test Strips

The Alere INRatio® 2 PT/INR Monitor connects reliable results with practical convenience, making it an optimal solution for anticoagulation management. **Read More ›**

C. Defendants' Knowledge of the INRatio's Defective Qualities

26. Almost immediately after the INRatio products became available to the public, Defendants began receiving numerous complaints about the INRatio products' efficacy and accuracy. In particular, some consumers found that the INR results they were getting when using the INRatio products differed from the results they obtained when they sent blood from the same samples to independent labs for testing. The deviations between the INRatio products' test results and those of independent labs were "clinically significant." In most cases, the INRatio products produced INR results that turned out to be incorrectly low, although in numerous other instances, the INRatio produced results that were incorrectly high.

27. In 2007, a team of doctors in London conducted a study that tested five point-of-care INR testing devices, the INRatio products among them, for quality and reliability.[4] The doctors took blood samples from patients and determined the patients' INRs using the five point-of-care testing devices. The doctors then took those same blood samples and sent them to an outside laboratory to obtain secondary INR results. The study determined that among the five point-of-care devices tested, the INRatio products performed the worst, with results that deviated most significantly from the results obtained through the outside laboratory.

D. Defendants' Unlawful Failure to Properly Report and Respond to Complaints

28. Between 2002 and 2014, Defendants received over 18,000 complaints concerning malfunctions with the INRatio products, no less than 3 of which resulted in deaths.

29. In May of 2005, following the receipt of numerous complaints concerning

[4] Moore GW, Henley A, Cotton SS, Tugnait S, Rangarajan S. Clinically significant differences between point-of-care analysers and a standard analyzer for monitoring the International Normalized Ratio in oral anticoagulant therapy: a multi-instrument evaluation in a hospital outpatient setting. Blood Coagul Fibrinolysis 2007, 18(3):287-92.

Defendants' INRatio systems, the FDA conducted an inspection of Defendants' (then) San Jose operations facility.

30. Following the inspection, the FDA sent a warning letter ("2005 warning letter," attached as EXHIBIT A) to Defendants, admonishing them for their failure to file MDR reports.[5] The letter further labeled the INRatio PT/INR Monitors and INRatio PT/INR Test Strips as "misbranded" due to "a serious regulatory problem involving INRatio Test Strips and INRatio Test Meters."[6]

31. The letter stated, "our record indicates your firm had information indicating that INRatio devices were generating clinically significant erroneous values."[7] More importantly, the letter pointed out that, "[i]f the INR is too low, a patient will be prone to blood clots or strokes. If the INR is too high, a patient will be prone to excessive bleeding. Therefore, both high and low test results *have the potential to cause or contribute to a death or serious injury* because they may result in erroneous dosing and thus improper control of [clotting]."[8]

[5] 21 CFR §803.50(a) requires medical device manufacturers to file Medical Device Reporting reports ("MDR reports") to the FDA, within 30 days, after they "receive or become aware of information, from any source, that reasonably suggests that a device [they] market: (1) [m]ay have caused or contributed to a death or serious injury ; or (2) [h]as malfunctioned and this device or a similar device that [they] market would be likely to cause or contribute to a death or serious injury, if the malfunction were to recur." Additionally, 21 U.S.C. § 360i(a)(1) requires device manufacturers to report to the FDA, in compliance with 21 CFR §803, when the manufacturer receives or otherwise becomes aware of information that reasonably suggests its product either caused a death or serious injury, or malfunctioned in a way such that a similar device would be likely to cause death or serious injury were the malfunction to recur. Further, under 21 U.S.C. § 352(t)(2), any failure to comply with 21 CFR § 803.50(a) and 21 U.S.C. § 360i (a)(1) will result in the device being deemed "misbranded."

[6] Exhibit A at 1.

[7] *Id.*

[8] *Id.* at 1-2 (emphasis added).

32. The letter went on to cite specific complaints that had been received by Defendants, wherein the INRatio "provided discrepant results [compared] to lab results" and "[t]his indicates that your device failed to meet its performance specifications or otherwise perform as intended, and therefore malfunctioned."[9] Further, "[a]ll of these erroneous readings were clinically significant and were thus likely to lead to incorrect application of [blood-thinner] therapy, with the likely health consequences already noted."[10]

33. The letter concluded that the Defendants had failed to comply with the Medical Device Reporting regulations because they did not file MDR reports within 30 days of receiving the above mentioned complaints.[11] The letter further concluded that Defendants' internal MDR procedure was inconsistent with all the terms of 21 CFR § 803. In particular, Defendants' internal MDR policy only treated complaints as reportable if an investigation determined that "the device *has* caused or contributed to a death or serious injury."[12] Meanwhile, 21 CFR § 803.50 requires manufacturers to submit MDRs when a device "*may have* caused or contributed to a death." (Emphasis added.) In other words, the FDA concluded Defendants' failure to submit MDRs to the FDA was the result of an unlawful systemic policy.

34. From May 15, 2006 through July 13, 2006, investigators from the FDA conducted another inspection of Defendants' (then) San Jose facility.

35. On November 29, 2006, the FDA sent Defendants another warning letter ("2006 warning letter," attached as EXHIBIT B) wherein Defendants were faulted for numerous failures to comply with statutory regulations.

36. The 2006 warning letter admonished Defendants, *inter alia*, for: 1) failure to

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[9] *Id.* at 2.

[10] *Id.* at 2

[11] *Id.* at 1.

[12] *Id.* at 2, citing Defendants' MDR policy (emphasis added).

investigate complaints involving possible failures of devices to meet any of its specifications; failure to promptly review, evaluate and investigate complaints representing events that are MDR reportable; and 3) failure to file MDRs with the FDA.

37. Despite the above admonishments from the FDA, and despite the thousands of complaints received concerning malfunctions that either caused or were likely to have caused serious injuries or death (including 3 malfunctions which did, in fact, result in deaths), Defendants failed to properly submit MDR reports to the FDA, failed to advise consumers of the FDA's admonishments and the defects plaguing the INRatio products and continued selling the INRatio products unabated until April, 2014, at all times falsely representing to consumers that the device was safe, accurate, reliable and effective.

E. Defendants' Class 1 Recalls of the INRatio and INRatio2 Testing Kits

38. On April 16, 2014, Defendants issued a voluntary recall notice for the INRatio2 test strips, citing the disparity between INR results obtained with the INRatio2 system versus significantly higher INR results when re-testing was performed by an independent laboratory.[13] Defendants' recall notice requested that customers immediately cease using the INRatio2 PT/INR test strips and instead use alternate methods to perform INR testing. Notwithstanding the recall, Defendants did not reimburse consumers for the purchase of these dangerous devices, which were worthless.

39. The FDA classified Defendants' April 16, 2014 recall notice as a "Class 1" recall, as it involved the use of products which would cause serious adverse health consequences or death.

40. On December 5, 2014, Defendants issued a voluntary recall letter for the INRatio PT/INR Monitor and INRatio2 PT/INR Monitor, as well as the INRatio PT/INR Test Strips. [14] The letter stated, "[i]n certain cases an INRatio® PT/INR Testing kit may provide an INR result that is significantly lower than a result obtained using a laboratory

[13] Alere April 16, 2014 Recall Letter, attached as EXHIBIT C.

[14] Alere December 5, 2014 Recall Letter, attached as EXHIBIT D.

INR system."[15] The letter also instructed customers, *inter alia,* to discuss the contents of the letter with their doctors and "arrange with your doctor to have your INR measured using a laboratory method." [16]

41. The FDA classified Defendants' December, 5 2014 recall notice as a "Class 1" recall, as it involved the use of products which would cause serious adverse health consequences or death.

F. The ROCKET AF Trial

42. The damage caused by the INRatio products' failures, Defendants' unlawful refusal to acknowledge or address those failures, and Defendants' continued manufacturing, marketing and selling of a dangerously defective product to unsuspecting consumers, extends beyond the harm suffered by individual users.

43. In September of 2011, a study was published in the New England Journal of Medicine, later known as the "ROCKET AF trial."[17] The purpose of the ROCKET AF trial was to compare the most commonly prescribed blood-thinner, warfarin, to a newer drug called rivaroxaban (hereinafter by its trade name, "Xarelto") to determine which drug was more effective in preventing strokes and embolisms.

44. As part of the methodology, some of the patient-participants were prescribed Xarelto at a fixed dose (the "Xarelto group"), while others were prescribed warfarin at a non-fixed dose (the "warfarin group"). The warfarin group would adjust their dosage based on their INRs, which they were instructed to keep between 2.0 and 3.0. In other words, the warfarin group would constantly monitor their INRs and take whatever dosage of warfarin was necessary to keep their INRs within the appropriate range.

45. The study determined Xarelto to be "noninferior" to warfarin and the

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[15] *Id.*

[16] *Id.* at 2-3.

[17] ROCKET AF being an acronym for "**R**ivaroxaban **O**nce Daily Oral Direct Factor Xa Inhibition **C**ompared with Vitamin **K** Antagonism for Prevention of Stroke and **E**mbolism **T**rial in **A**trial **F**ibrillation."

findings ultimately led to Xarelto's FDA approval.

46. Following the April 16, 2014 and December 5, 2014 recalls of the INRatio products, it was revealed that the warfarin group in the ROCKET AF study had used the INRatio products to monitor their INRs and adjust their dosages accordingly.

47. The revelation that the results of the ROCKET AF study were premised, in part, on data collected from individuals using the INRatio products has called the entire study into question. A comparison of blood samples from over 5,000 of the ROCKET AF participants revealed that the INR data collected using the INRatio products differed from the test results obtained from a third-party laboratory. Johnson & Johnson, makers of Xarelto, turned over the data from the ROCKET AF study to Alere.

48. According to Sidney Wolfe, M.D., founder of the Public Citizen Health Research Group, and F.R. Rosendaal, M.D., Ph.D., chair of the Department of Clinical Epidemiology at Lieden University Medical Center, Lieden University, in writing about the ROCKET AF study and the subsequent revelations relating to the INRatio test results, "[n]othing could more adversely impact the validity of monitoring warfarin's blood-thinning effectiveness . . . than false readings -- whether too high or too low -- generated by the testing device used to monitor the degree of blood thinning (the INR)."[18]

TOLLING OF THE STATUE OF LIMITATIONS

49. Any applicable statutes of limitations have been tolled by Defendants' knowing and active concealment, and misleading actions, as alleged herein. Plaintiffs and members of the Class, as defined below, were kept ignorant of critical information required for the prosecution of their claims, without any fault or lack of diligence on their part. Plaintiffs and members of the Class could not reasonably have discovered the true

[18] Letter from Sidney Wolfe, M.D., founder of the Public Citizen Health Research Group, and F.R. Rosendaal, M.D., Ph.D., chair of the Department of Clinical Epidemiology at Lieden University Medical Center, Liden University, to Stephen Ostroff, M.D., acting commissioner of the FDA, on behalf of Public Citizen Health Research Group, dated December 10, 2015, attached as EXHIBIT E.

nature of the Defendants' defective and fraudulently promoted INRatio products.

50. Defendants knowingly, affirmatively, and actively concealed the true character, quality, and nature of their INRatio products. In particular, Defendants deliberately flaunted the Title 21 regulations requiring them to report the litany of serious and life-threatening malfunctions to the FDA. Plaintiffs and members of the Class reasonably relied upon Defendants' knowing, affirmative, and active concealment. Based on the foregoing, Defendants are estopped from relying on any statutes of limitation as a defense in this action.

51. The causes of action alleged herein did or will only accrue upon discovery of the true nature of the INRatio products, as a result of Defendants' fraudulent concealment of material facts. Plaintiffs and members of the Class did not discover, and could not have discovered, through the exercise of reasonable diligence, the true nature of the unlawful conduct alleged herein.

PLAINTIFFS' CLAIMS AGAINST DEFENDANTS

PLAINTIFF DINA ANDREN

Background

52. Plaintiff Dina Andren was born in New York City, New York, and is currently mother to three children.

53. Plaintiff Andren suffers from a medical condition that requires her to regularly take warfarin (under the trade-name "Coumadin"). As a result, Plaintiff Andren closely monitors her INR.

Plaintiff Andren's INRatio2 Testing Kit

54. Plaintiff Andren purchased an INRatio2 PT/INR testing kit from a pharmacy on April 30, 2015, for $375, and began using the INRatio2 testing kit to monitor her INR.

55. Plaintiff Andren was required to purchase numerous boxes of replacement INRatio test strips in order to continue with her periodic INR testing. The boxes, which contained 48 replacement test strips, ranged in price from $240-$285.

56. When purchasing her INRatio products, Plaintiff Andren relied on Alere's

representations that the products were accurate, convenient, effective, reliable, optimal and safe. Were it not for these representations, Plaintiff Andren would not have purchased or used the INRatio Products. Further, had Plaintiff Andren known that Alere was omitting material information, in particular that Alere knew its INRatio products produced erroneous INR results, Plaintiff Andren would not have purchased or used the INRatio products.

Plaintiff Andren's Medical Complications

57. On the morning of May 24, 2015, Plaintiff Andren tested her INR using her INRatio2 testing kit. The test results indicated an INR of 2.7. Relying on her INRatio2 testing kit and believing her INR was above 2.5, Plaintiff Andren did not take Lovenox.

58. Later that day, Plaintiff Andren was rushed to the hospital where doctors determined she had suffered a stroke.

59. Following her stroke, Plaintiff Andren continued using her INRatio2 and accompanying test strips to closely monitor her INR and adjust her warfarin dosage accordingly.

60. In July of 2015, after having carefully monitored and regulated her INR for over a month following her stroke (as indicated by her INRatio2), Plaintiff Andren suffered a Transient Ischemic Attack ("TIA"), otherwise known as a "mini-stroke."

61. Following her hospitalization for the TIA, Plaintiff Andren returned home where she continued to use her INRatio2 testing kit to monitor her INR.

62. In March of 2016, Plaintiff suffered an additional TIA.

63. While at the hospital, Plaintiff Andren was informed that her INRatio2 testing kit had been the subject of a Class 1 recall. Prior to this, Plaintiff Andren had been unaware of the recall, or any known problems associated with the INRatio products.

PLAINTIFF SIDNEY BLUDMAN

Background

64. Plaintiff Sidney Bludman was born in New York City, New York.

65. For 28 years, Plaintiff Bludman has suffered from a medical condition that

requires him to regularly take warfarin (under the trade-name "Coumadin").

66. For approximately 26 years, Plaintiff Bludman would have his INR tested once a month in a laboratory. For all 26 years, his INR remained fairly consistent, requiring very infrequent minor adjustments of his warfarin dosage.

Plaintiff Bludman's INRatio2 Testing kit

67. Plaintiff Bludman began using an INRatio2 PT/INR testing kit to regularly monitor his INR at home in 2013.

68. Plaintiff Bludman was required to purchase boxes of replacement INRatio2 test strips in order to continue with his periodic INR testing. The boxes contained 24 replacement test strips and cost approximately $120.

69. In using the INRatio products, Plaintiff Bludman relied on Alere's representations that the products were accurate, convenient, effective, reliable, optimal and safe. Were it not for these representations, Plaintiff Bludman would not have purchased or used the INRatio Products. Further, had Plaintiff Bludman known that Alere was omitting material information, in particular that Alere knew its INRatio products produced erroneous INR results, Plaintiff Bludman would not have purchased or used the INRatio products.

Plaintiff Bludman's Medical Complications

70. In February of 2016, his INR (as indicated by his INRatio testing kit) became exceedingly high. As a result of the high INR, Plaintiff Bludman reduced his warfarin dosage.

71. On February 10, 2016, while riding the subway, and after he had lowered his warfarin dosage to offset his supposedly high INR, Plaintiff Bludman suffered a TIA.

72. Upon returning home from the hospital, Plaintiff Bludman began monitoring his INR with his INRatio2 testing kit and comparing those results with the results of blood tests conducted by a laboratory at his hospital. He found that his INR, as indicated by his INRatio2 testing kit, was consistently .4-.6 higher than his INR, as indicated by the results of the lab tests.

73. As a result of his TIA, Plaintiff Bludman is now at a higher risk for future ischemic attacks.

CLASS ACTION ALLEGATIONS

74. Plaintiffs brings this action, on behalf of themselves, and all others similarly situated, as a class action under Rule 23 of the Federal Rules of Civil Procedure.

75. Plaintiffs seek to represent the following classes defined as (and collectively referred to as "Class"):

Nationwide Class

All residents of the United States of America who, during the period January 1, 2009 through the present, purchased, rented or otherwise paid for the use of the INRatio products manufactured, marketed, sold or distributed by Defendants.

California Sub-Class

All residents of the State of California who, during the period January 1, 2009 through the present, purchased, rented or otherwise paid for the use of the INRatio products manufactured, marketed, sold or distributed by Defendants.

Maryland Sub-Class

All residents of the State of Maryland who, during the period January 1, 2009 through the present, purchased, rented or otherwise paid for the use of the INRatio products manufactured, marketed, sold or distributed by Defendants.

New York Sub-Class

All residents of the State of New York who, during the period January 1, 2009 through the present, purchased, rented or otherwise paid for the use of the INRatio products manufactured, marketed, sold or distributed by Defendants.

76. Plaintiffs reserve the right to amend the Class definitions if discovery and further investigation reveals that the Class should be expanded or otherwise modified.

77. Plaintiffs reserve the right to establish sub-classes as appropriate.

78. This action is brought and properly may be maintained as a class action under the provisions of Federal Rules of Civil Procedure 23(a)(1)-(4) and 23(b)(1), (b)(2) or (b)(3), and satisfies the requirements thereof. As used herein, the term "Class Members" shall mean and refer to the members of the Class.

79. Numerosity: While the exact number of members of the Class is unknown to Plaintiffs at this time and can only be determined by appropriate discovery, membership in the Class is ascertainable based upon the records maintained by Defendants. At this time, Plaintiffs are informed and believe that the Class includes hundreds of thousands of members. Therefore, the Class is sufficiently numerous that joinder of all members of the Class in a single action is impracticable under Federal Rule of Civil Procedure Rule 23(a)(1), and the resolution of their claims through the procedure of a class action will be of benefit to the parties and the Court.

80. Ascertainability: Some names and addresses of members of the Class are available from Defendants' records, and others can be ascertained through appropriate notice. Notice can be provided to the members of the Class through direct mailing, publication, or otherwise using techniques and a form of notice similar to those customarily used in consumer class actions arising under California state law and federal law.

81. Typicality: Plaintiffs' claims are typical of the claims of the other members of the Class which they seek to represent under Federal Rule of Civil Procedure 23(a)(3) because Plaintiffs and each member of the Class has been subjected to the same deceptive and improper practices and has been damaged in the same manner thereby.

82. Adequacy: Plaintiffs will fairly and adequately represent and protect the interests of the Class as required by Federal Rule of Civil Procedure Rule 23(a)(4). Plaintiffs are adequate representatives of the Class, because they have no interests which are adverse to the interests of the members of the Class. Plaintiffs are committed to the vigorous prosecution of this action and, to that end, Plaintiffs have retained counsel who are competent and experienced in handling class action litigation on behalf of consumers.

83. Superiority: A class action is superior to all other available methods of the fair and efficient adjudication of the claims asserted in this action under Federal Rule of Civil Procedure 23(b)(3) because:

(a) The expense and burden of individual litigation make it economically unfeasible for members of the Class to seek to redress their claims other than through the procedure of a class action.

(b) If separate actions were brought by individual members of the Class, the resulting duplicity of lawsuits would cause members to seek to redress their claims other than through the procedure of a class action; and

(c) Absent a class action, Defendants likely would retain the benefits of their wrongdoing, and there would be a failure of justice.

84. Common questions of law and fact exist as to the members of the Class, as required by Federal Rule of Civil Procedure 23(a)(2), and predominate over any questions which affect individual members of the Class within the meaning of Federal Rule of Civil Procedure 23(b)(3).

85. The common questions of fact include, but are not limited to, the following:

(a) Whether Defendants engaged in unlawful, unfair, misleading, or deceptive business acts or practices in violation of California Business & Professions Code sections 17200, *et seq*.;

(b) Whether Defendants engaged in any unfair or deceptive acts or practices in violation of the Consumers Legal Remedies Act sections 1750, *et seq.;*

(c) Whether Defendants engaged in any common law fraud;

(d) Whether Defendants were unjustly enriched by the above-described acts or practices;

(e) Whether Plaintiff and members of the class sustained damages, and if so, the appropriate measure of damages; and

(f) Whether Plaintiff and members of the Class are entitled to an award of reasonable attorneys' fees, pre-judgment interest, and costs of this suit.

86. In the alternative, this action is certifiable under the provisions of Federal Rule of Civil Procedure 23(b)(1) and/or 23(b)(2) because:

(a) The prosecution of separate actions by individual members of the Class would create a risk of inconsistent or varying adjudications with respect to individual members of the Class which would establish incompatible standards of conduct for Defendants;

(b) The prosecution of separate actions by individual members of the Class would create a risk of adjudications as to them which would, as a practical matter, be dispositive of the interests of the other members of the Class not parties to the adjudications, or substantially impair or impede their ability to protect their interests; and

(c) Defendants have acted or refused to act on grounds generally applicable to the Class, thereby making appropriate final injunctive relief or corresponding declaratory relief with respect to the Class as a

whole and necessitating that any such relief be extended to members of the Class on a mandatory, class-wide basis.

87. Plaintiffs are not aware of any difficulty which will be encountered in the management of this litigation which should preclude its maintenance as a class action.

FIRST CAUSE OF ACTION
Violation of the California Consumers Legal Remedies Act
(Cal. Civil Code §§ 1750, *et seq.)*

88. Plaintiffs incorporate by reference in this claim for relief each and every allegation of the preceding paragraphs, with the same force and effect as though fully set forth herein.

89. Plaintiffs bring this cause of action on behalf of themselves and the members of the Class.

90. This cause of action is brought under the California Consumers Legal Remedies Act, California Civil Code sections 1750, *et seq.* (hereinafter, "CLRA"). Plaintiffs and members of the Class are consumers as defined by California Civil Code section 1761(d). The INRatio products are goods within the meaning of California Civil Code section 1761(a).

91. Defendants violated and continue to violate the CLRA by engaging in the following practices proscribed by California Civil Code section 1770(a) in transactions with Plaintiff and members of the Class, which were intended to result in, and did result in, the sale of the INRatio products:

> (5) Representing that [the INRatio products] have . . . characteristics . . . [and] benefits . . . which they do not have . . .
>
> (7) Representing that [the INRatio products] are of a particular . . . quality . . . if they are of another.
>
> (9) Advertising goods . . . with intent not to sell them as advertised.

92. Defendants violated the CLRA by representing, in advertisements and promotional materials, that the INRatio products were "accurate," "convenient," "effective," "reliable," "optimal" and "safe," when they were not.

93. Defendants had direct knowledge that their INRatio products were producing false and erroneous results and giving consumers false and erroneous information concerning their INRs.

94. Defendants also knew that false and erroneous INRs would likely lead to consumers improperly adjusting their blood-thinner dosages, significantly increasing the risk and likelihood of serious bodily injury or death.

95. Defendants also had direct knowledge that the false and erroneous INRs being produced by their INRatio products had caused, or likely caused, serious injuries and deaths.

96. Despite the direct knowledge described in paragraphs 111-114, Defendants continued to falsely represent, in advertisements and promotional materials, that the INRatio products were "accurate," "convenient," "effective," "reliable," "optimal" and "safe" and continued selling the INRatio products to unknowing consumers.

97. At this time, Plaintiffs do not seek damages under this cause of action. Under Section 1782 of the CLRA, on May 25, 2016, Plaintiffs notified Defendants in writing of the particular violations of Section 1770 of the CLRA and demanded that Defendants rectify the problems associated with the behavior detailed above, which acts and practices are in violation of California Civil Code section 1770.

98. If Defendants fail to respond adequately to Plaintiffs' above-described demand within 30 days of Plaintiffs' notice, under California Civil Code section 1782(b), Plaintiffs will amend the Complaint to request damages and any other relief permitted by California Civil Code section 1780.

99. Defendants' conduct is malicious, fraudulent, and wanton, and Defendants

intentionally mislead and conceal material information from consumers in order to increase the sales of the INRatio products.

100. Defendants' misrepresentations and omissions were material to Plaintiffs and members of the Class. Plaintiffs and members of the Class would not have purchased, rented, paid for or used the INRatio products had it not been for Defendants' misrepresentations and concealment of material facts. Plaintiffs and members of the Class were damaged as a result of Defendants' material misrepresentations and concealment of material facts.

SECOND CAUSE OF ACTION
Violation of Unfair Competition Law
(California Business & Professions Code §§ 17200, *et seq.)*

101. Plaintiffs incorporate by reference in this claim for relief each and every allegation of the preceding paragraphs, with the same force and effect as though fully set forth herein.

102. Plaintiffs bring this cause of action on behalf of themselves and the members of the Class.

103. California Business and Professions Code section 17200 prohibits "any unlawful, unfair or fraudulent business act or practice." For the reasons described above, Defendants have engaged in unfair, or fraudulent business acts or practices in violation of California Business and Professions Code sections 17200, *et seq*.

104. Defendants misrepresentations and omissions of material facts, as set forth herein, constitute and unlawful practice because they violate California Civil Code Sections 1572, 1573, 1709, 1710, 1711 and 1770.

105. Defendants' conduct as described herein violates not only the "unlawful" prong of California Business and Professions Code sections 17200, *et seq.*, but also constitutes a violation of the "unfair" prong. Defendants' conduct offends public policy and is immoral, unethical, oppressive, unscrupulous and substantially injurious to consumers. Any justification for Defendants' practices is outweighed by the

consequences and harm to Plaintiffs and the Class.

106. There were reasonable alternatives available to Defendants to further Defendants' legitimate business interests, other than the conduct described herein.

107. Defendants' conduct was also "fraudulent, misleading, or likely to deceive the public" within the meaning of California Business and Professions Code section 17200.

108. Defendants' misrepresentations and concealment of material facts were made with the knowledge of their effect, and were done to induce Plaintiff and members of the class to purchase the INRatio products. Plaintiffs and members of the Class saw and justifiably relied on Defendants' misrepresentations and concealment of material facts on the marketing and promotional materials, as well as the packaging, when purchasing and using the INRatio products.

109. Defendants' conduct caused and continue to cause financial injury to Plaintiffs and members of the Class in the amounts they paid for the INRatio products. Defendants' misrepresentations and omissions were material to Plaintiffs and members of the Class. Plaintiffs and members of the Class would not have purchased and used the INRatio products had it not been for Defendants' misrepresentations and concealment of material facts. Nor would Plaintiffs and members of the Class have improperly adjusted their blood-thinner dosages based on the results obtained from the INRatio products, and in doing so, increased the risk and likelihood of serious injury and death, had it not been for Defendants' misrepresentations and concealment of material facts. Plaintiffs and members of the Class have suffered injury in fact, and have lost money as a result of Defendants' fraudulent conduct.

110. Defendants' misrepresentations and omissions alleged herein are objectively material to the reasonable consumer, and they were material to Plaintiffs and members of the Class. Reliance upon the misrepresentations and omissions discussed herein may therefore be presumed as a matter of law. The materiality of such representations and omissions also establishes causation between Defendants' conduct and Plaintiffs' and

members of the Class' injuries.

111. Defendants have thus engaged in unlawful, unfair, and fraudulent business acts entitling Plaintiffs and members of the Class to judgment and equitable relief against Defendants, as set forth in the Prayer for Relief, including restitution to reimburse them for the amounts they paid for the INRatio products.

112. Additionally, under Business and Professions Code section 17203, Plaintiffs and members of the Class seek an order requiring Defendants to immediately cease such acts of unlawful, unfair, and fraudulent business practices, and requiring Defendants to correct their actions.

THIRD CLAIM FOR RELIEF
Fraud

113. Plaintiffs incorporate by reference in this claim for relief each and every allegation of the preceding paragraphs, with the same force and effect as though fully set forth herein.

114. Plaintiffs bring this cause of action on behalf of themselves and the members of the Class.

115. Defendants knowingly and deliberately falsely marketed the INRatio products as "accurate," "convenient," "effective," "reliable," "optimal" and "safe" when they knew the INRatio products were anything but. Meanwhile, Defendants concealed and suppressed material facts, namely, that the INRatio products produced false and erroneous data concerning blood-clotting times, causing consumers to improperly adjust their blood-thinner dosages and increase the risk and likelihood of serious bodily injury and death.

116. Plaintiffs and members of the Class justifiably relied on the reasonable expectation that Defendants would act in compliance with the law, which included disclosing material facts concerning the false and erroneous data produced by the INRatio products as well as marketing and promoting the INRatio products honestly and ethically.

117. Had the true nature of the Defendants' INRatio products been disclosed to

Plaintiffs and members of the Class, they would not have purchased the INRatio products, nor would they have relied on them for blood monitoring.

118. Defendants knew their concealment and suppression of materials facts was false, misleading, they were fully aware that their promotional and marketing materials contained false and misleading statements, and they were fully aware that the promotional and marketing materials would be relied upon by consumers when deciding to purchase and use the INRatio products.

119. As a result of Defendants' fraudulent omissions and misrepresentations, Plaintiffs and members of the Class have been injured in fact, suffered a loss of money and increased their likelihood of succumbing to serious bodily injury and death. Plaintiffs and members of the Class would not have purchased the INRatio products, nor would they have relied on them for blood monitoring, had it not been for Defendants' concealment of material facts and false and misleading statements contained in their promotional materials, marketing materials and packaging.

120. Plaintiffs and members of the Class justifiably relied upon Defendants' knowing, affirmative, and active concealment. By concealing material information, Defendants intended to induce Plaintiffs and members of the Class into purchasing and using the INRatio products .

121. As a direct and proximate result of Defendants' misleading statements, omissions and active concealment of material facts, Plaintiffs and each member of the Class has been damaged in an amount according to proof at trial.

FOURTH CLAIM FOR RELIEF

Unjust Enrichment

122. Plaintiffs incorporate by reference in this claim for relief each and every allegation of the preceding paragraphs, with the same force and effect as though fully set forth herein.

123. Plaintiffs bring this cause of action on behalf of themselves and the members of the Class.

124. By their wrongful acts, Defendants were unjustly enriched at the expense of Plaintiffs and members of the Class.

125. Defendants knowingly, fraudulently, systematically, and uniformly marketed, promoted and sold their defective and dangerous INRatio products using false and misleading statements while omitting and concealing material facts.

126. Plaintiffs and members of the Class relied on Defendants' fraudulent, false and misleading statements, in addition to Defendants' omissions and concealment of material fact in order to purchase the INRatio products.

127. Thus, Plaintiffs and members of the Class were unjustly deprived.

128. It would be inequitable and unconscionable for Defendants to retain the profit, benefit and other compensation they obtained from their fraudulent, deceptive, and misleading conduct alleged herein.

129. Plaintiffs and members of the Class seek restitution from Defendants, and seek an order of this Court disgorging all profits, benefits, and other compensation obtained by Defendants from their wrongful conduct.

PRAYER FOR RELIEF

Plaintiffs, on behalf of themselves and all others similarly situated, request the Court to enter judgment against Defendants, as follows:

1. Certifying the Class, as requested herein, certifying Plaintiffs as the representatives of the Class, and appointing Plaintiffs' counsel as counsel for the Class;

2. Ordering that Defendants are financially responsible for notifying all members of the Class of the alleged conduct discussed herein;

3. Awarding Plaintiffs and the members of the Class compensatory damages in an amount according to proof at trial;

4. Awarding restitution and disgorgement of Defendants' revenues and/or profits to Plaintiffs and members of the Class;

5. Awarding declaratory and injunctive relief as permitted by law or equity, including: enjoining Defendants from continuing the unlawful practices as set forth

herein, and directing Defendants to identify, with Court supervision, victims of its conduct and pay them restitution and disgorgement of all monies acquired by Defendants by means of any act or practice declared by this Court to be wrongful;

6. Awarding interest on the monies wrongfully obtained from the date of collection through the date of entry of judgment in this action;

7. Awarding attorneys' fees, expenses, and recoverable costs reasonably incurred in connection with the commencement and prosecution of this action; and

8. For such other and further relief as the Court deems just and proper.

Dated: May 26, 2016

BARON & BUDD, P.C.

/s/ Mark Pifko
By: Mark Pifko

Roland Tellis (SBN 186269)
Mark Pifko (SBN 228412)
Peter Klausner (SBN 271902)
BARON & BUDD, P.C.
15910 Ventura Boulevard, Suite 1600
Encino, California 91436
Telephone: (818) 839-2333
Facsimile: (818) 986-9698

Timothy G. Blood (149343)
Thomas J. O'Reardon II (247952)
BLOOD HURST & O'REARDON, LLP
701 B Street, Suite 1700
San Diego, California 92101
Telephone: (619) 338-1100
Facsimile: (619) 338-1101

Attorneys for Plaintiffs DINA ANDREN and SIDNEY BLUDMAN, individually, and on behalf of other members of the public similarly situated

DEMAND FOR JURY TRIAL

Plaintiffs hereby demand a trial of their claims by jury to the extent authorized by law.

Dated: May 26, 2016

BARON & BUDD, P.C.

/s/ Mark Pifko
By: Mark Pifko

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Peter Klausner (SBN 271902)
BARON & BUDD, P.C.
15910 Ventura Boulevard, Suite 1600
Encino, California 91436
Telephone: (818) 839-2333
Facsimile: (818) 986-9698

Timothy G. Blood (149343)
Thomas J. O'Reardon II (247952)
BLOOD HURST & O'REARDON, LLP
701 B Street, Suite 1700
San Diego, California 92101
Telephone: (619) 338-1100
Facsimile: (619) 338-1101

Attorneys for Plaintiffs
DINA ANDREN and SIDNEY BLUDMAN, individually, and on behalf of other members of the public similarly situated

EXHIBIT A

Inspections, Compliance, Enforcement, and Criminal Investigations

HemoSense Corporation 04-Oct-05

Department of Health and Human Services

Public Health Service
Food and Drug Administration
San Francisco District
1431 Harbor Bay Parkway
Alamada, CA 94502-7070
Telephone: 510-337-8700

Via Federal Express

October 4, 2005

James D. Merselis
President and CEO
HemoSense Corporation
651 River Oaks Parkway
San Jose, CA 95134

WARNING LETTER

Dear Mr. Merselis:

Your firm manufactures the INRatio Test Strips and the INRatio Test Meters, which are intended to determine International Normalization Ratio (INR) value, a measure used to monitor blood coagulation and adjust anticoagulant medications. The INRatio Test Strips and INRatio Test Meters are devices as defined in Section 201 (h) of the Federal, Food, Drug, and Cosmetic Act (the Act). From May 16- June 1, 2005, the Food and Drug Administration (FDA) inspected your firm's establishment in San Jose, California Our review of your operations yielded information that revealed a serious regulatory problem involving INRatio Test Strips and INRatio Test Meters.

Our inspection disclosed that these devices are misbranded within the meaning of Section 502(t)(2) [21 U.S.C. 352(t)(2)] of the Federal Food, Drug and Cosmetic Act (the Act), in that your firm failed to furnish material or information required by or under section 519 [21 U.S.C. 360(i)] of the Act and the Medical Device Reporting (MDR) regulation set forth in 21 CFR Part 803. The MDR regulation requires device manufacturers to report within 30 days of receiving or otherwise becoming aware of information that reasonably suggests that a device that they marketed (1) may have caused or contributed to a death or serious injury; or (2) has malfunctioned and that device or a similar device marketed by the manufacture would be likely to cause or contribute to a death or serious injury if the malfunction were to recur [21 CFI 803.50(a)].

Our review indicates that your firm had information indicating that INRatio devices were generating clinically significant erroneous values. INR values are used to adjust anticoagulant medication dosages an must be accurate in order to permit appropriate use of those drugs. If the INR is too low, a patient will be prone to form blood clots or strokes. If the INR is too high, a patient will be prone to excessive bleeding. Therefore, both high and low test results have the potential to cause or contribute to a death or serious

injury, because: they may result in erroneous dosing and thus improper control of coagulation.

Based on our review, we find that your firm failed to submit an MDR to FDA, as required by 21 CFR 803.50(a)(1), after receiving information which reasonably suggested that your INRatio devices may have caused or contributed to a serious injury. The information contained in complaint #00111 indicates that after a high INRatio test result of 6.1, the patient went to the hospital, was tested by the hospital lab, which found a significantly lower INR value, and an adjustment was made to the patient's dose of anticoagulant medication. This event satisfies the definition of a serious injury since it required medical intervention to preclude permanent impairment of a body function or permanent damage to a body structure [21 CFR 803.3].

In addition, your firm failed to submit MDR reports to FDA, as required by 21 CFR 803.50(a)(2), after receiving information which reasonably suggested that your INRatio devices malfunctioned and these devices or a similar device marketed by your firm would be likely to cause or contribute to a death or serious injury if the malfunction were to recur. Your firm failed to submit an MDR malfunction report as required in the following instances:

The information contained in complaints # 00071, #00134, #00166, #00176 and #00347 reasonably suggests that your devices malfunctioned and would be likely to cause or contribute to a serious injury to the patient. Those complaints indicate that your devices provided discrepant results compoundared to lab results (i.e for complaint # 00134; **[redacted]** compared to **[redacted]** for #00166, **[redacted]** compared to **[redacted]** for #00176, **[redacted]** compare toift and for #00347 **[redacted]** compared to **[redacted]** respectively). This indicates that your device failed to meet its performance specifications or otherwise perform as intended, and therefore malfunctioned as that term is defined in 21 CFR 803.3. As already explained, erroneous INR readings have strong potential to cause or contribute to serious injury o death because they may result in erroneous control of coagulation. All of these erroneous readings were clinically significant and were thus likely to lead to incorrect application of anticoagulant therapy, with the likely health consequences already noted. In fact, the latter four of these complaints were received after your company had information regarding the similar malfunction reported in complaint #00111, which as already explained in fact appears to have contributed to a reportable serious injury.

We acknowledge that your firm has submitted to this office a response dated June 14, 2005 concerning ou investigator's observations noted on form FDA-483. We have reviewed your response and have concluded that it is inadequate in that your response does not provide sufficient detail and documentation for us to evaluate whether preventive actions are adequate to prevent the recurrence of the observations. Specifically, your revised MDR procedure is not consistent with all of the terms of 21 CFR 803 and may nc lead to proper determination of when an event requires reporting to FDA under part 803 as an MDR. Thus, that procedure itself does not appear to comply with 21 CFR 803.17. For example, page#3 of 8, item 7.5 states that, "The complaint is a reportable event if the investigation determines that the device has cause or contributed to a death, serious injury, or if the malfunction were to recur, that the device would likely cause or contribute to a death or serious injury," (emphasis added) Similarly, Page # 5 of 8, Appendix A-MDR Decision Tree for Death/Serious Injury, item #1 states, "Does the information reasonably suggest that the device caused or contributed to a death?". Under 21 CFR 803.50, manufacturers must report if they have information that reasonably suggests that a device they market "may have caused or contributed to a death" (emphasis added). HemoSense's revised MDR procedures appear to narrow the conditions under which an event must be reported . This may result in the lack of adequate MDR reporting by HemoSense.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure that all requirements of the Act are being met. You are responsible for investigating and determining the causes of the violations identified by FDA.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. You should take prompt action to correct these deviations . Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions ihclude, but are not limited to, seizure, injunction, and/or civil money penalties.

Please notify this office in writing within (15) working days of receipt of this letter, of the specific steps you have taken to correct these violations and preclude their recurrence. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time frame within which corrections will be completed. Your response should address each deficiency brought to your attention during the inspection and in this letter, and should include copies of any documentation demonstrating tha corrections have been made.

Please direct your reply and any questions to Lawton W. Lum, Compliance Officer, United States Food and Drug Administration, 1431 Harbor Bay Parkway, Alameda, CA 94502.

Sincerely,
/s/

Barbara J. Lassens

San Francisco District
District Director

Page Last Updated: 07/08/2009
Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.

U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Ph. 1-888-INFO-FDA (1-888-463-6332)
Contact FDA

EXHIBIT B

Inspections, Compliance, Enforcement, and Criminal Investigations

HemoSense, Inc. 29-Nov-06

Department of Health and Human Services

Public Health Service
Food and Drug
Administration

San Francisco District
1431 Harbor Bay Parkway
Alameda, CA 94502-7070
Telephone: 510/337-6700

WARNING LETTER

VIA FEDERAL EXPRESS

November 29, 2006

James D. Merselis
President and CEO
HemoSense, Inc.
651 River Oak Parkway
San Jose, CA 951341907

Dear Mr. Merselis:

During an inspection of your firm located in San Jose, California on May 15, 2006 through July 13, 2006, investigators from the United States Food and Drug Administration (FDA)determined that your firm manufactures the INRatio INR System, an in vitro diagnostic system that provides a quantitative prothrombin time value with the use of fresh capillary whole blood. 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.

This inspection revealed that these devices are adulterated within the meaning of section 501(h) of the Ac (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 (C.F.R.), Part 820. We received your response dated July 27, 2006, and an August 30, 2006, from Mr. Doug Rundle, Vice President, Quality Assurance and Regulatory Affairs, concerning our investigator's observations noted on the form FDA 483, List or inspectional Observations that was issued to you. We address your response below, in relation to each or the noted violations. These violations include, but are not limited to, the following:

1. Failure of management with executive responsibility of ensuring that quality system requirements are effectively established and effectively maintained as required in 21 C.F.R. 820.20(b)(3)(1).

For example:

- Quality audits failed to identify deviations in complaint handling.
- Devices not meeting performance specifications are not being investigated
- Products labeled and distributed with the wrong strip code were not investigated

We have reviewed. your responses and have concluded that they are inadequate because your corrective and preventive actions to address the specific observation have not been completed. Please provide the District Office with a copy of your root cause analysis and your corrective action(s) in the prevention of this quality deviation.

2. Failure to investigate complaints involving the possible failure of a device, labeling, or packaging to meet any of its specifications as required in 21 C.F.R. 820.198(c).

For example:

- Complaint **[redacted]** The date of the event and the date your firm received the complaint was February 7, 2006. The complaint involved discrepant results between the INRatio INR device MR and the Lab INR (**[redacted]**). No investigation was performed because the packaged identified an expiration date of January 31, 2006; however, the strips were validated to meet specifications up to a 15 months shelf life from the manufactured date. The package represents a 12 month shelf life and although you are aware of your 15 month validation data, you failed to perform an investigation.
- Complaint **[redacted]**: The date of the event and the date your firm received the complaint was April 28, 2006. A "Professional" user reported an InRatio INR device reading of **[redacted]**, which is "Way off'. No investigation was performed because the package, identified an expiration date of March 31, 2006. However, your validation study demonstrates a shelf life of 15 months, and you failed to perform an investigation.
- Complaint **[redacted]** The date of the event and the date your firm received the complaint was March 1, 2006. The complaint involved discrepant results in two patients as follows:

1. Patient #**[redacted]**: InRatio INR of **[redacted]** Retest identified **[redacted]**; and another Retest identified **[redacted]**

2. Patient #**[redacted]**: In Ration INR of **[redacted]**; Retest identified #**[redacted]**

The complaint was not reviewed until May 14, 2006, and your firm determined that an investigation was not required as the packaged identified an expiration date of April 30, 2006.

We have reviewed your responses and have concluded that they are inadequate because your corrective and preventative action is not completed. The effectiveness of your actions will be evaluated during our follow-up investigation.

3. Failure to promptly review, evaluate, and investigate complaints representing events that' are MDR reportable under 21 CFR Part 803, as required in 21 C.F.R. 820.198(d).

For example:

- Complaint #**[redacted]** was received on December 21, 2005. On December 18, 2005, patient's INRatio = **[redacted]**, however, **[redacted]** sample contained **[redacted]** and patient was **[redacted]** from various sites. The physician ordered lab test and Lab INR = **[redacted]**. On February 14, 2006, your firm determined that an investigation was needed; as of our inspection date of May 15, 2006, an investigation had not been performed.
- Complaint # **[redacted]** was received on September 9, 2005. On September 7, 2005, patient's INRatio = **[redacted]**. The patient experienced **[redacted]** and **[redacted]** and was admitted to the hospital with an INRatio = **[redacted]**. On January 19, 2006, your firm determined that an investigation was needed; however, an investigation was not performed until March 28, 2006, 200 days from the receipt of the compliant.
- Complaint # **[redacted]** received on March 1, 2006. On February 14, 2006, patient's INRatio = **[redacted]**. The patient started **[redacted]** from the **[redacted]** and **[redacted]**. The subject was admitted to the hospital with an INRatio = **[redacted]** and the patient **[redacted]**. On April 7, 2006, your firm determined that an investigation was required, but did not perform one because the "strips" lot number was not provided.

We have reviewed your responses and have concluded that it is inadequate because your corrective and preventive action is not completed and FDA has not evaluated the effectiveness of your actions. We acknowledge your firm's commitment to complete the investigations for complaint numbers **[redacted]** and **[redacted]**.

4. Failure to investigate the cause of nonconformities relating to product, processes, and the quality system as required in 21 C.F.R. 820.100(a)(2).

For example: Over **[redacted]** INRation Test Strips were labeled with the wrong strip code. The purpose of the strip code is to set the meters variable in its calculation of the INR. You opened a NCMR (Non-conforming Material Report) number **[redacted]** on February 27, 2006 to investigate the cause. On March 24, 2006 the NCMR was closed; however, no investigation into the cause of the nonconformity was performed.

We have reviewed your responses and have concluded that they are inadequate because it is unclear whether a failure investigation was performed to determine the root cause of this quality deviation. In addition, your responses do not indicate whether a corrective and preventive action was initiated to prevent the recurrence of releasing strips with the wrong code.

5. Failure to ensure that all personnel are trained to adequately perform their assigned responsibilities as required in 21 C.F.R. 820.25(b).

For example:

- The following were not investigated per SOP **[redacted]**. Complaint numbers **[redacted]**
- The following complaints were not filed within 30-days as required by SOP **[redacted]** Complaint numbers **[redacted]**

We have reviewed your responses and have concluded that it is inadequate. Your responses states that you have conducted additional training with appropriate personnel. It is unknown if a root cause analysis was performed to identify the cause of the non conformity. Retraining your employees may not correct and/or prevent the recurrence of this observation because you might not know the root cause. It is your responsibility to determine the cause of this quality failure and develop a corrective and preventive action plan to prevent its recurrence. The effectiveness of your corrective action(s) will be evaluated during our follow-up investigation.

Based on our review of your responses, we find that retraining your employees was required in five of the eight observations noted on the Form FDA-483. It is your responsibility to establish procedures for identifying training needs and to ensure that all personnel are trained to adequately perform their assigned responsibilities as required in 21 C.F.R. 820.25(b).

Our inspection also revealed that your INRatio INR devices are misbranded under section 502(t)(2) of the Act, 21 U.S.C. 352(tx2), 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, U.S.C. 360i, and 21 C.F.R. Part 803 - Medical Device Reporting (MDR) regulation. Significant deviations include, but are not limited to, the following:

Failure to report, within 30 days of receiving or otherwise becoming aware of information, from any source, that reasonably suggests that a device marketed by the manufacturer: (1) may have caused or contributed to a death or serious injury; or (2) has malfunctioned and such device or a similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury, if the malfunction were to recur as required in 21 CFR 803.50(a).

For example:

- Complaint **[redacted]** received on December 21, 2005, On December 18, 2005, the patient's INRatio = **[redacted]** for which patient's **[redacted]** sample contained **[redacted]** and the patient was **[redacted]** from more than one site. Patient was admitted to hospital and the Lab INR = **[redacted]**. The MDR reportable event was submitted to the FDA on February 3, 2006, over 40 days after the receipt of the complaint.
- Complaint **[redacted]** received on December 19, 2005. On that day, the patient's INRatio = **[redacted]** with a retest of **[redacted]**. The complaint was identified as a discrepant result, meeting your MDR reporting requirement to file a "product malfunction" report. An MDR event report was submitted to the FDA on April 17, 2006, over 115 days after the receipt of the complaint.

- Complaint **[redacted]** received on March 2, 2006. Patient's INRatio = **[redacted]** and the Lab INR = **[redacted]**. This value exceeded the 95% confidence limit of **[redacted]**. This event represents a device malfunction similar to that in Complaint **[redacted]** (received March 1, 2006) that also exceeded the 95% confidence limit. That malfunction event resulted in a death and a MDR reportable event was filed within 30-days. However, this similar event was not filed until April 11, 2006, over 38 days after the receipt of the complaint.

We have reviewed your responses and have concluded that they are inadequate because sufficient details and documentation of your root cause analysis were not provided for us to evaluate whether your preventive actions are adequate to prevent the recurrence of the observation.

You should take prompt action to correct the violation(s) addressed in this letter. Failure to promptly correct these violation(s) may result in regulatory' action being initiated by die Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil money penalties. Also, federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, premarket approval applications for Class II devices to which the Quality System regulation deviations are reasonably related will not be approved until the violations have been corrected. Requests for Certificates to Foreign Governments will not be granted until the violations related to the subject devices have been corrected.

Please notify this office in writing within fifteen (15) working days from the date you receive this letter of the specific steps you have taken to correct the noted violations, including an explanation of how you plan to prevent these violation(s), or similar violation(s), from occurring again. Include documentation of the corrective action you have taken. If your planned corrections will occur over time, please include a timetable for implementation of those corrections . If corrective action cannot be completed within S working days, state the reason for the delay and the time within which the corrections will be completed.

Your response should be sent to: Lawton W. Lum, Compliance Officer, 1431 Harbor Bay Parkway, Alameda, California 94502. If you have any questions about the content of this letter please contact him a 510-337-6792.

Finally, you should know that this letter is not intended to be an all-inclusive list of the violation(s) at you facility. It is your responsibility to ensure compliance with applicable laws and regulations administered b FDA. The specific violation(s) noted in this letter and in the Inspectional Observations, Form FDA 483, (FDA 483), issued at the closeout of the inspection may be symptomatic of serious problems in your firm' manufacturing and quality assurance systems. You should investigate and determine the causes of the violation(s), and take prompt actions to correct the violation(s) and to bring your products into compliance.

Sincerely yours,

Sincerely yours,

/S/

Barbara J. Cassens
District Director

EXHIBIT C

URGENT: MEDICAL DEVICE RECALL

Alere INRatio®2 PT/INR Professional Test Strips (PN 99008G2)

April 16, 2014

Dear Healthcare Professional,

Alere San Diego is initiating a voluntary recall for the Alere INRatio®2 PT/INR Professional Test Strips. This action is being initiated as a result of several complaints of patients who had a therapeutic or near-therapeutic INR with the Alere INRatio®2 PT/INR Professional Test Strip but a significantly higher INR (outside of therapeutic range) when performed by a central laboratory.

We have received nine serious adverse event reports, three of which described bleeding associated with patient deaths. The reason for the adverse event reports was significantly different test results between the Alere INRatio®2 Professional Test Strip and local laboratory plasma INR. The Alere INRatio®2 PT/INR Professional Test Strip INR results were reported as lower than the laboratory results by a range of 3.1 – 12.2 INR units, when the tests were performed within 1 hour to 1 day of one another. The root cause for this issue has not yet been determined; therefore we cannot determine the patient conditions or circumstances that may contribute to the discrepancy. Given these reports, we are concerned that the INRatio®2 PT/INR Professional Test Strips may report an inaccurately low INR result.

The Alere INRatio®2 PT/INR Professional Monitoring System, consisting of the Alere INRatio®2 PT/INR Monitor and the Alere INRatio®2 PT/INR Professional Test Strip, is intended for use in the quantitative determination of International Normalized Ratio (INR) in fresh capillary whole blood to monitor the effect of warfarin on clotting time by health care professionals. The Alere INRatio®2 PT/INR Professional Monitoring System is intended for use outside of the body (*in vitro* diagnostic use). The Alere INRatio®2 PT/INR Professional Monitoring System is not intended to be used for screening purposes.

Limitations: The Alere INRatio®2 PT/INR Professional Monitoring System is not intended for use in patients who are transitioning from heparin treatment to warfarin therapy.

Our customers should immediately STOP using the Alere INRatio®2 PT/INR Professional Test Strip (PN 99008G2) and use an alternative method to perform PT/INR testing, such as a plasma-based laboratory INR test, an alternative Alere product, or an alternative point of care monitoring system from a different manufacturer. All unused Alere INRatio®2 PT/INR Professional Test Strips should be returned to Alere San Diego.

As part of this recall, your Alere representative will contact you to discuss a timeline for transition from your current INRatio®2 PT/INR Professional Test Strip to the INRatio PT/INR Test Strip (PN 100139).

Alere's INRatio®2 PT/INR Professional Test Strips (PN 99008G2) are not being manufactured and distributed in the United States by Alere at this time.

Alere sincerely apologizes for the difficulty that this may cause to you and your facility. We greatly value our relationship with you.

URGENT: MEDICAL DEVICE RECALL

Our records indicate that you have received the Alere INRatio®2 PT/INR Professional Test Strips manufactured by Alere San Diego.

CUSTOMER REQUIRED ACTION

- Immediately stop using the Alere INRatio®2 PT/INR Professional Test Strip (PN 99008G2) and use an alternative method to perform PT/INR testing. If you are able to transition to the Alere INRatio PT/INR Test Strip (PN 100139), ensure you are following the current instructions for using the device.
- You can identify the affected product by using the attached visual reference guide. The side of the box will indicate REF 99008G2. The individually packaged test strips will indicate INRatio®2 PT/INR Test Strip in the upper left corner of the foil package.
- It is mandatory that any unused product be returned to Alere. To enable this process, Alere will provide you a label to return your product free of charge. This label will include a Return Goods Authorization number (RGA#). It is important that you use this label when returning product to Alere. Your account will be credited once Alere receives the product back with the RGA#.
    - Indicate the amount of unused product that will be returned for credit on the attached Reply Form.
    - Indicate on the Reply Form the method by which Alere should send you the Return Goods Authorization number (RGA#). You can choose to receive an RGA# from Alere by e-mail, FAX, or mail. You may contact Alere Customer Service at 877-866-5309 for any questions regarding the product return process.
- If you have forwarded product to another customer, please provide a copy of this letter to them.
- Please complete and FAX or e-mail the enclosed Reply Form within 10 days to confirm your receipt of this notice. If you have questions regarding this notification, please contact Alere Technical Service by phone at 844-292-5373 or by E-mail at INRatio.Notification@alere.com.
- Please return unused product to Alere using the RGA# provided by Alere.

Please FAX or e-mail the completed Reply Form to:
Alere San Diego, Inc.
Fax: 1-858-805-8457
Email: Responses.ts@alere.com

We apologize for any inconvenience that this may cause you and your patients. We appreciate your attention and cooperation in this matter.

Sincerely,

Keith McLain
VP, Quality & Compliance, Alere San Diego

URGENT: MEDICAL DEVICE RECALL

Please complete this form even if you do not have any involved product and Fax Back to Technical Service at Fax Number 1-858 805 8457 or email to Responses.ts@alere.com.

URGENT MEDICAL DEVICE RECALL: REPLY FORM

I have been notified by Alere San Diego of the recall of the INRatio®2 PT/INR Professional Test Strips (PN 99008G2).

Please check the appropriate boxes:

☐ I have no record of receipt of this product and therefore will take no further actions.

☐ I have read the letter and have discontinued use of the product. I will return the following quantity of strips or kits for credit once I have received an RGA# from Alere (if you no longer have affected inventory, please indicate zero (0) in the "Quantity to Return" field below):

Product	Part Number	Quantity to Return	Units	Send RGA# by:*
INRatio®2 PT/INR Professional Test Strips	**PN 99008G2**		☐ Kits ☐ Strips	☐ Email ☐ Mail ☐ Fax

*Please provide email address, mailing address or FAX number below.

☐ I have forwarded this notification to our customers/consignees to which we have distributed product.

Please complete the following information:

DATE: _____

AUTHORIZED SIGNATURE: _____

PRINT NAME: _____

TITLE: _____ DEPARTMENT: _____

INSTITUTION: _____

ADDRESS: _____

CITY: _____ STATE: _____ PHONE: _____

POSTAL CODE: _____ COUNTRY: _____

EMAIL: _____

FAX: _____

PO Ref: *ASD414INR* What is the name of your distributor company? _____

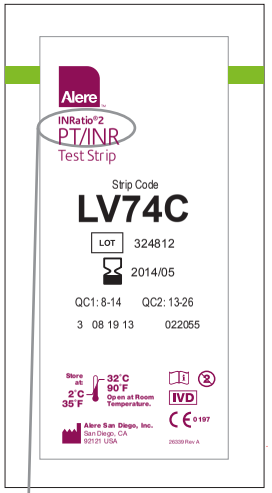
Please FAX the completed form to 1-858-805-8457 or email a PDF to Responses.ts@alere.com.
To satisfy global requirements for regulatory reporting, please complete and return this form within 10 business days of receipt.

INRatio®/INRatio®2 Test Strip
Visual Reference Guide for Identification of Recalled Product

Recalled Test Strip

Alere INRatio®2 PT/INR
Professional Test Strip

Strip Pouch



INRatio®2 Test Strip

Side of Product Box

99008G2

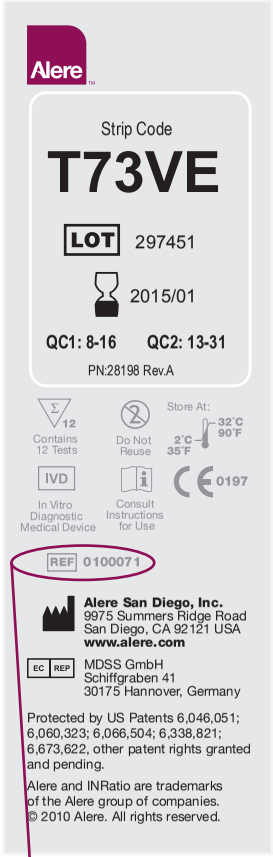
Available Test Strip

Alere INRatio® PT/INR
Test Strip*

Strip Pouch

INRatio® Test Strip

Side of Product Box



100071

Side of Product Box

100139

*Compatible with all INRatio®/ INRatio®2 Monitors.

EXHIBIT D

URGENT: MEDICAL DEVICE CORRECTION

Alere™ INRatio® PT/INR Monitor System

December 5, 2014

Dear Valued Customer,

This letter contains important information concerning the Alere™ INRatio® PT/INR Monitor system (INRatio® Monitor or INRatio® 2 Monitor and INRatio® Test Strips) that has been prescribed to you for monitoring your blood clotting time (PT/INR) while you are on warfarin therapy. A complete list of the affected INRatio® products is attached to this notice (Appendix A). You should discuss this information with your doctor.

In certain cases an INRatio® PT/INR Monitor system may provide an INR result that is significantly lower than a result obtained using a laboratory INR system. The plasma-based laboratory INR method is considered the most accurate and reliable INR method.

This issue can arise if you have certain medical conditions. The INRatio® PT/INR Monitor system should NOT be used if you have any of the medical conditions listed below. **You should contact your doctor to determine if any of these medical conditions apply to you:**

- Anemia (low hemoglobin or low red blood cell count). Your hematocrit should be between 30 – 55%
- Any conditions associated with elevated fibrinogen levels (Note: fibrinogen is the protein from which a clot is formed)
    - acute inflammatory conditions (for example viral or bacterial infections such as pneumonia or flu)
    - chronic inflammatory conditions (for example rheumatoid arthritis, Crohn's disease, ulcerative colitis, infectious liver diseases such as hepatitis, or inflammatory kidney diseases such as diabetic nephropathy and glomerulonephritis)
    - severe infection (for example sepsis)
    - advanced stage cancer or end stage renal disease requiring hemodialysis
- any bleeding or unusual bruising

If you have any of these conditions your doctor should immediately switch you to a laboratory INR method for monitoring your INR and warfarin therapy. If you are unsure whether you have one of these conditions, you should consult your doctor.

Incorrect results can also occur if you do not carefully follow the instructions for performing the test. Please ensure you take the following precautions to reduce the risk of this issue occurring:

- If your INRatio® INR result falls within the therapeutic range, but you have symptoms of delayed clotting such as bleeding or bruising, you should consult your doctor immediately and arrange for testing by an alternate method.
- Only use the Alere INRatio® PT/INR Monitor system if your hematocrit is within a range of 30% to 55%. **You should contact your doctor to arrange for a hematocrit measurement (a red blood cell anemia test), if such a test has not been recently performed** or there are any signs or symptoms of blood loss.

- Apply **ONLY** one large drop of blood immediately to the test strip. Never add more blood to a test strip after the test has begun. Applying additional sample may result in a discrepant result. **If in doubt, repeat the test with a fresh drop of blood from a new fingerstick site using a new lancet on a fresh test strip**.
- The monitor should be on a stable surface during the test. Do not move the monitor during the test.

In addition to the precautions described above, Alere recommends that you **arrange with your doctor to have your INR measured using a laboratory INR method.** The plasma-based laboratory INR method is considered the most accurate and reliable INR method. Your doctor will adjust your warfarin therapy if necessary at this time according to the degree of the difference between the Alere device and laboratory method. Also, your doctor has received a notification to investigate whether you have any of the conditions that can lead to these falsely low INR results. Testing is recommended to ensure you do not have conditions that could result in the INRatio® PT/INR Monitor system giving a result that is much lower than the laboratory INR method. If a much lower result is observed, your doctor should immediately switch you to an alternative method for monitoring your INR and warfarin therapy.

As part of its commitment to ensuring the safety of patients, Alere has reported these device concerns to the U.S. Food and Drug Administration and is conducting a thorough investigation into these events.

Customers with questions regarding this issue can contact Alere INRatio Recall Hotline at 1-877-929-2579. For additional information customers should go to www.inr-care.com.

Adverse events or quality problems experienced with the use of this product may be reported to the FDA's MedWatch Adverse Event Reporting program either online, by regular mail or by fax.

- Complete and submit the report **Online:** www.fda.gov/medwatch/report.htm
- **Regular Mail or Fax** Download form www.fda.gov/MedWatch/getforms.htm or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178.

URGENT: MEDICAL DEVICE CORRECTION

CUSTOMER REQUIRED ACTION

- **Ensure you have discussed this letter with your doctor**.
- Ensure you have read and understand the precautions described in the current product labeling (Alere INRatio® PT/INR Test Strip Package Insert; Alere INRatio®2 PT/INR Home Monitoring System User Guide; INRatio® Self Test User Guide) and the additional precautions in this notice describing medical conditions that may increase the risk of obtaining a lower than expected INR result. Note: if you need an additional copy of the product labeling, please contact1-877-866-5313.
- Do not use the INRatio® PT/INR Monitor system (INRatio® Monitor or INRatio® 2 Monitor and INRatio® Test Strips) if you have any of the medical conditions described in this notice.
- **Speak to your doctor about performing a hematocrit measurement (red blood cell anemia test) and periodic comparisons with a laboratory INR method.**
- Please complete the enclosed Reply Form (Appendix B – the last page of this notice) and **return it within 10 days** to confirm receipt of this notice, using one of the following methods:
  - Return the response via US Postal Service in the enclosed postage paid envelope

    OR
  - FAX the response to **1-877-929-2580**

    OR
  - E-mail the response to Alere4319@stericycle.com
- If you have questions regarding this notification, please contact Alere INRatio Recall Hotline by phone at 1-877-929-2579. Additionally we have established a website providing information and frequently asked questions. www.inr-care.com.

We apologize for any inconvenience that this may cause you. We appreciate your attention and cooperation in this important matter.

Sincerely,

Keith McLain, VP Quality Alere San Diego

URGENT: MEDICAL DEVICE CORRECTION

Appendix A: Product List

Product	Ref Number	Product Description
INRatio® Test Strips	0100071	Alere INRatio® PT/INR Test Strips, Box of 12
	0100139	Alere INRatio® PT/INR Test Strips, Box of 48
INRatio® Monitors	0100004	Alere INRatio® PT/INR System Professional
	0100007	INRatio® Prothrombin Time (PT) Monitoring System
INRatio®2 Monitors	0200431	Alere INRatio®2 PT/INR Professional Testing System
	0200432	Alere INRatio®2 PT/INR Home Monitoring System
	55128A	Alere INRatio®2 PT/INR Professional Monitoring System
	55130	Alere INRatio®2 PT/INR Monitor

If you would like to receive an additional copy of the labeling for your product, please contact Alere at 1-877-866-5313.

URGENT: MEDICAL DEVICE CORRECTION

Appendix B: Reply Form

This is a sample Urgent Medical Device Correction. Please use the barcoded Reply Form included with the Urgent Medical Device Correction you receive in the mail. You may also call 1-877-929-2579 or send an email to Alere4319Web@stericycle.com if you have additional questions regarding this notice.

EXHIBIT E

PUBLICCITIZEN

1600 20th Street, NW • Washington, D.C. 20009 • 202/588-1000 • www.citizen.org

December 10, 2015

Stephen Ostroff, M.D.
Acting Commissioner
Food and Drug Administration
Department of Health and Human Services
WO 2200
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Dear Dr. Ostroff:

Public Citizen, a consumer advocacy organization with 400,000 members and supporters, writes to urge the Food and Drug Administration (FDA) to further investigate the potentially dangerous situation involving a drug approval and the role of FDA Commissioner nominee Dr. Robert Califf, then Co-Chairman of the industry Steering Committee advising Johnson and Johnson on the study, especially his role in choosing the poorly-performing measuring device that was central to interpreting the study.

Serious concerns have been raised about the possible impact of inaccurate measurements, by a device called INRatio, on subjects' anticoagulation while on warfarin during the ROCKET AF trial, which sought to compare the most commonly prescribed standard anticoagulant (blood thinner) drug warfarin with the newer drug rivaroxaban (Xarelto). Public Citizen's Health Research Group has now analyzed data from the FDA's Manufacturer and User Facility Device Experience (MAUDE) database, which tracks adverse reports on medical devices, and found that between INRatio's approval in 2002 and November of this year, **there have been 9,469 malfunction reports and 1,445 injury reports to the FDA with the INRatio devices from people not in the study. This same device was also used for the study**. Many of these reports were publicly available before the ROCKET AF study began.

Background

This important study, ROCKET AF, compared the safety and effectiveness of the blood thinner rivaroxaban in preventing strokes and heart attacks with that of the older, standard blood thinner, warfarin, in patients with a heart arrhythmia called atrial fibrillation. The FDA has always taken the position, for this and other studies, that patients in the warfarin group must be carefully monitored to ensure that their warfarin dose keeps their international normalized ratio (INR; a

measure of blood thinning status) in the effective therapeutic range (2 to 3) so there is a proper basis for comparison with the experimental drug, in this case rivaroxaban, for which INRs are not a useful measure the drug's blood thinning status.[1] Time in therapeutic range (TTR) measures this control. It reflects how well the physicians have used the results from the INR-measuring devices to adjust patients' doses to stay in the desired therapeutic range. At a September 8, 2011, meeting of the Cardiovascular and Renal Drugs Advisory Committee, the FDA criticized the relatively inadequate control in the warfarin-treated subjects in the ROCKET AF study,[2] but ROCKET AF Johnson & Johnson Steering Committee Co-Chairman Robert Califf vigorously defended this criticism at the meeting, including the statement that "we gave warfarin not only in an acceptable way, we gave it in a commendable way during this trial."[3] He also stated that "there's increasing evidence that TTR has no effect on the benefit for novel anticoagulants versus warfarin."[4]

Nothing could more adversely impact the validity of monitoring warfarin's blood-thinning effectiveness in keeping patients in the desired therapeutic range than false readings — whether too high or too low — generated by the testing device used to monitor the degree of blood thinning (the INR). It first became clear 10 years ago that there were dangerous measuring inaccuracies in a widely used home INR-measuring device, known as INRatio (now manufactured by Alere), the same device used for all warfarin-treated subjects in the ROCKET AF study.

In 2005, more than a year before ROCKET AF began, FDA had warned the company that then manufactured the device, HemoSense Corporation, about this problem, stating, **"Our review indicates that your firm had information indicating that INRatio devices were generating clinically significant erroneous values. … If the INR is too low, a patient will be prone to form blood clots or strokes. If the INR is too high, a patient will be prone to excessive bleeding. Therefore, both [erroneously] high and low test results have the potential to cause or contribute to a death or serious injury, because: they may result in erroneous [warfarin] dosing and thus improper control of coagulation"** [emphasis added].[5]

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[1] Food and Drug Administration. FDA draft briefing document for Cardiovascular and Renal Drugs Advisory Committee. September 8, 2011. http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/CardiovascularandRenalDrugsAdvisoryCommittee/UCM270796.pdf. Accessed December 10, 2015. PDF page 147.

[2] *Ibid.* PDF pages 13-15.

[3] Food and Drug Administration. Transcript of the September 8, 2011, Cardiovascular and Renal Drugs Advisory Committee meeting. http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/CardiovascularandRenalDrugsAdvisoryCommittee/UCM277588.pdf. Accessed December 10, 2015. PDF page 88.

[4] *Ibid.* PDF pages 89.

[5] Food and Drug Administration. Inspections, compliance, enforcement, and criminal investigations: HemoSense Corporation. October 4, 2005. http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2005/ucm075594.htm. Accessed December 10, 2015.

On December 5, 2014, Alere issued an urgent medical device correction acknowledging INRatio errors in measuring INR in patients with certain conditions. The FDA classified this as a Class I recall, defined as a recall that "involve[s] situations when it is likely that use of these devices will cause serious health problems or death."[6]

Despite the FDA's criticism of the inadequacy of controlling the INR range of patients on warfarin in ROCKET AF, relative to comparable studies with other newer blood-thinning drugs, Dr. Califf's defense at the advisory committee meeting against this criticism failed to include any mention ofa serious underlying problem with the INR readings, namely the inaccuracy of many INRatio readings of patients on warfarin, incorrectly lower or higher than their actual INRs. This could certainly contribute to the difficulty of physicians being able to achieve adequate anticoagulation. The FDA also failed to discuss this problem either in its briefing materials or during its presentation at the September 8, 2011, meeting.

In addition, warfarin-treated subjects in the study with *erroneously low* INRatio INR readings who actually had high INRs would be at risk of serious bleeding because of the higher INR. Warfarin-treated subjects in the study whose INRs were incorrectly read as low could have been subjected to further risk of bleeding if they were given more warfarin to raise their INR. Beyond presenting serious harm to these subjects, extra bleeding in the warfarin-treated subjects also could have made the bleeding comparison with rivaroxaban more favorable to this newer drug in the ROCKET AF study. *Erroneously high* readings could, conversely, have led to reducing the warfarin dose or temporarily stopping the drug because of the mistaken belief that the INR exceeded the desired therapeutic range when, in fact, with a truly normal or low INR, warfarin needed to be continued or even increased. This also had attendant risks, such as an increased risk of embolic strokes.

Because of recent publicity about the problems with the INRatio devices, the European Medicines Agency (EMA), the European equivalent of the FDA, has very recently stated that it "is currently investigating whether the data generated from the INRatio device could have had any impact on the Rocket trial results and the extent of this impact, if applicable."[7] EMA spokeswoman Rebecca Harding told *Regulatory Focus* that the manufacturer of Xarelto, Bayer, recently informed the agency that the defect in the INR device could have an impact on the study results. "Due to the defect, it is now thought that the INR device has impacted the clotting results measured for the warfarin arm, which might affect the overall results for Xarelto as compared

[6] Food and Drug Administration. Medical device recalls: Alere San Diego Inc., Alere INRatio and INRatio2 PT/INR Monitor System (Professional and Prescription Home Use) - falsely low INR test results. Updated April 8, 2015. http://www.fda.gov/MedicalDevices/Safety/ListofRecalls/ucm429496.htm. Accessed December 10, 2015.

[7] Project on Government Oversight. Drug problems: European regulator investigating trial led by FDA nominee. November 30, 2015. http://www.pogo.org/blog/2015/11/regulator-investigating-clinical-trial-led-by-fda-nominee.html. Accessed December 10, 2015.

with warfarin," Harding said in an email.[8] It should be noted that only months after ROCKET AF began, a paper was published raising concerns about the accuracy of the INRatio device. This study, published in 2007, meticulously assessed the INR results of five point-of-care devices and showed clearly that INRatio performed worst among those tested when compared with the gold-standard laboratory test for measuring the INR.[9] In 10 percent of patients, the discrepancy was more than 1 INR unit, a difference which would almost always lead to different therapeutic actions and, possibly, to harm to patients. The study referred to earlier analyses also showing clinically significant discrepancies with gold-standard laboratory tests. A publication in 1996 by one of us (Dr. Frits Rosendaal) found that for every increase of just one unit of INR, the bleeding risk increases between 42 percent and 44 percent, emphasizing the importance of accurate INR measurement to avoid needless bleeding episodes.[10]

Newly Analyzed FDA Data on Serious Injuries From Faulty INRatio Devices

Public Citizen's Health Research Group has now analyzed data from the FDA's MAUDE data base, which tracks reports of adverse events associated with medical devices submitted to the FDA and found that between INRatio's approval in 2002 and November of this year, **there have been 9,469 malfunction reports and 1,445 injury reports to the FDA with the INRatio devices**.

Injury reports include decisions to increase anticoagulation (warfarin) because of inaccurately low INR readings on the INRatio device, or, much less commonly, to decrease warfarin because of inaccurately high readings. Although many of these cases were not accompanied by bleeding due to previous over-anticoagulation, they were still listed as injury because they put patients needlessly at risk, often necessitating treatment with vitamin K (a warfarin antagonist) to prevent bleeding or plasma or blood transfusions, and often involving hospitalization. The injury cases chosen here and presented below are a sample of those in which bleeding occurred, limited to cases reported up to July 31, 2009.

Malfunction reports usually contain evidence that the INRatio INR reading turned out to be incorrectly low when compared with a standard laboratory INR reading. Just as often, the reverse was true, and the INRatio reading was confirmed to be actually higher than a standard laboratory

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[8] Brennan Z. EMA investigating validity of clinical trial led by FDA commissioner nominee. *Regulatory Focus.* December 3, 2015. http://www.raps.org/Regulatory-Focus/News/2015/12/03/23713/EMA-Investigating-Validity-of-Clinical-Trial-Led-by-FDA-Commissioner-Nominee/. Accessed December 10, 2015.

[9] Moore GW, Henley A, Cotton SS, et al. Clinically significant differences between point-of-care analysers and a standard analyser for monitoring the INR in oral anticoagulant therapy.*Blood Coagul Fibrinolysis.* 2007:18(3):287-292.

[10] van der Meer FJ1, Rosendaal FR, Vandenbroucke JP, Briët E. Assessment of a bleeding risk index in two cohorts of patients treated with oral anticoagulants. *Thromb Haemost*. 1996;76(1):12-6.

INR. The difference between malfunction and injury reports is that at least at the time the malfunction report was filed, bleeding had not occurred nor had patients been treated with any of the measures described in the injury section above. The INRatio malfunction reports described below are consistent with the FDA's definition of "malfunction": "**A malfunction is reportable when it is likely to cause or contribute to a death or serious injury if it were to recur. The regulation assumes that a malfunction will recur**" [emphasis added].[11]

Injury Reports

The injury reports are divided into two groups. The first group consists of cases reported to the FDA before the initiation of the ROCKET AF study on December 21, 2006. There were a total of 63 such cases during this interval. The second group are those cases that occurred in the general population while the study was ongoing, until July 31, 2009, but not including any subjects in the study or patients with bleeding injuries after July 31, 2009. There were a total of 173 injury cases reported during this latter interval.

Summarized in the table below are FDA MAUDE injury reports from the first group for patients who experienced serious bleeding injuries.

FDA Cases of Serious Injuries with Faulty INRatio Devices (pre-ROCKET)

Event Date	INRatio INR	Lab INR	Treatment	Injury
03/04/05	1.8	8.0 (after Hosp'n*)	Increased warfarin (after 1.8 INR)	Hospitalized* 2 days later; 3 days after this, in hospital with spinal bleed and lower body paralysis 1
10/12/05 Three pts	1.7 1.9 1.5	2.6 4.8 3.3		Rectal bleeding and bruising Lab INRs measured < 1hour after INRatio
2/24/06	1.9	9.0 (next day)		Bruises and a swollen arm
3/1/06	1.3	6.0 in hospital	Hospitalized	Coughing blood and nosebleed
3/27/06	2.6	6.3		Lost vision in one eye for 5 minutes
4/4/06	1.6	8.0	Hospitalized	
5/18/06	2.4	>7.8		Vaginal and gum bleeding
7/6/06	1.2	20.9	Hospitalized	Nose and ear bleeding
4/29/05	2.8 2.8	4 days after 2nd 2.8, 15.0	Warfarin after low readings, then hosp'n	**Death** after high reading in hosp. Dr. does not trust device but is incredulous as to what occurred

[11] Food and Drug Administration. Medical Device Reporting: An Overview. April 1996. http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm106752.pdf. Accessed December 10, 2015.

The above cases, publicly available before ROCKET AF began, illustrate the clinical importance of large differences between the INRatio results and the actual INRs as determined in a standard clinical laboratory assay.

For the three patients in the October 12, 2005, entry, all of the laboratory determinations were made within an hour of the INRatio readings. The INRatio readings averaged 1.7, below the therapeutic range for most patients, but the laboratory readings averaged over 3.5, more than twice as high and above the theraputic range for many patients. Their clinical picture "rectal bleeding and bruising" also reflected overcoagulation, not undercoagulation as implied by the low INRatio results.

The first and last patients on the above chart were both treated with warfarin because of lower (1.8 and 2.8, respectively) INRatio readings. Their hospital readings, after this mistaken additional warfarin treatment, were 8.0 and 15.0. The first patient subsequently had a "spinal bleed" and suffered lower-body paralysis, and the second patient died.

Summarized in the table below are FDA MAUDE injury reports from the second group for patients who experienced serious bleeding injuries.

FDA Cases of Serious Injuries and Faulty INRatio Devices:same time as ROCKET)

Event Date	INRatio INR	Lab INR	Treatment	Injury
1/26/07	5.8	17 next day, hosp	Vitamin K, plasma, 7 units of blood	Coughing up blood, massive internal bleeding
4/17/07	1.8	5.2	To emergency room	Rectal bleeding
7/2/07	2.5	13	To emergency room	Blood in urine
7/25/07	1.6	6.0	Hosp'n; blood Transfsd; Vit K	Rectal bleeding
1/17/08	1.6	10.5 (next day)	More warfarin after 1.6 value	Bleeding, with surgery to remove hematoma (blood collection)
7/03/08	3.5	17		Actively bleeding
10/9/08	2.0 2.9	6.5 6.5	Hospitalized All tests same day	Bloody urine

FDA Cases of Serious Injuries and Faulty INRatio Devices (parallel to ROCKET) (continued)

Event date	INRatio INR	Lab INR	Treatment	Injury
11/6/08*	2.24	10		*same patient on two consecutive days: 11/6/and 11/7/08)
11/6/08*	2.4	10	Emerg Room	Bleeding
12/17/08	2.8	14	Hospitalized	Coughing blood
11/5/07	2.2	8.6 in e.r.	Warfarin 12 mg daily after Low 2.2 value	**Death**: Cerebral hemorrhage the Day after e.r. visit with 8.6 INR

In the table below are the URLs for all of the cases presented in the tables above for the first and second groups for patients who experienced serious bleeding injuries.

Date of event	**URL of FDA record of 20 selected bleeding events up through July 31, 2009**
3/4/05	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=590040
10/12/05	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=645722
2/24/06	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=691866
3/1/06	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=697378
3/27/06	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=705997
4/4/06	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=700389
5/18/06	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=721891
7/6/06	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=732853
4/29/05	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdr

	foi__id=598141
1/26/07	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=812418
4/17/07	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=841186
7/2/07	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=886234
7/25/07	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=896633
1/17/08	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=991946
7/3/08	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=1081222
10/9/08	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=1211112
11/6/08 11/7/08	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=1253401
12/17/08	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=1276766
11/5/07	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=952621

Malfunction Reports

There were 652 MAUDE malfunction reports for INRatio devices posted before ROCKET AF began, all, according to the FDA definition on page 4 (above), "**likely to cause or contribute to a death or serious injury if it were to recur.**"

For the majority of these reports, most of which had both INRatio and comparable laboratory results for the same patient, the difference between the INRatio and the laboratory result was at least 1 INR unit. Discrepancies of this magnitude can lead to inappropriate adjustments in

anticoagulation therapy if one value is in the therapeutic range and the other is not. In many cases the INRatio reading was higher than the gold-standard laboratory reading, suggesting that the patient might be overcoagulated. In many other malfunction cases, as was the case in all of the bleeding cases above, the INRatio reading was significantly lower than the gold-standard laboratory reading, leading to falsely derived concerns that the patient might not be getting enough warfarin.

Conclusion

The findings from these 1,445 FDA INRatio injury reports and almost 10,000 malfunction reports in patients not in the study raise serious questions about both the validity of the findings from ROCKET AF in the face of the inaccuracies of the INRatio INR measurements in the study and whether this device should be allowed to stay on the market in view of the ongoing harm to patients using it.

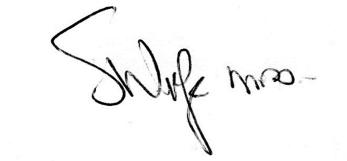
Because INRatio was determined to be substantially equivalent to similar earlier FDA-cleared devices under the 510(k) provision of the device law, there was no requirement to prove that its results were equivalent to those obtained in standard laboratory INR assays before allowing it to be sold. The injury data in this report show that INRatio is dangerously different in too many instances from this gold-standard laboratory test for INR measurement, but this fact was only discovered after the FDA allowed the device on the market in 2002.The MAUDE report information included here is not from patients in the ROCKET AF study but in patients being monitored with the same INRatio device both before the study began and while it was ongoing.

The information in this letter also is being sent to Dr. Guido Rasi, Executive Director of the European Medicines Agency. The former has opened an investigation into the possible implications of this faulty medical device on its interpretation of the ROCKET AF results, and the FDA has recently acknowledged some kind of review of the matter.[12] We urge the FDA to initiate a thorough investigation to answer the question posed by the EMA. For obvious reasons of conflict of interest, Dr. Califf, the current nominee for Commissioner of the FDA, should recuse himself from any FDA review of this matter. He should, however, be prepared to answer relevant questions and provide evidence about the basis of the decision of the ROCKET AF Steering Committee, which he co-chaired, to use the INRatio device in the ROCKET AF study

[12] Silverman E. J&J blood thinner under review for trial overseen by FDA nominee Califf. *Pharmalot.* December 7, 2015. http://www.statnews.com/pharmalot/2015/12/07/fda-xarelto-robert-califf-drug/.

despite multiple injury and malfunction cases that had been reported to the FDA prior to the initiation of ROCKET AF.

Sincerely,



Sidney M. Wolfe, M.D.
Founder and Senior Adviser
Public Citizen Health Research Group

F.R. Rosendaal, M.D., Ph.D.
Professor and Chair, Department of Clinical Epidemiology
Leiden University Medical Center, Leiden University
Leiden, The Netherlands